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David Barrière, Arsène Ella, Hans Adriaensen, Charles Roselli, Philippe Chemineau, et al.. In vivo magnetic resonance imaging reveals the effect of gonadal hormones on morphological and functional brain sexual dimorphisms in adult sheep. Order of Authors. Psychoneuroendocrinology, 2019, 10.1016/j.psyneuen.2019.104387 . hal-02380175

**HAL Id: hal-02380175**

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## Manuscript Details

**Manuscript number** PNEC\_2019\_79\_R3

**Title** In vivo magnetic resonance imaging reveals the effect of gonadal hormones on morphological and functional brain sexual dimorphisms in adult sheep.

**Article type** Research Paper

### Abstract

Sex differences in brain and behavior are produced by the perinatal action of testosterone, which is converted into oestradiol by the enzyme aromatase in the brain. Although magnetic resonance imaging (MRI) has been widely used in humans to study these differences, the use of animal models where hormonal status can be properly manipulated are necessary to explore the mechanisms involved. We used sheep, a recognized model in the field of neuroendocrinology, to assess brain morphological and functional sex differences and their regulation by adult gonadal hormones. To this end, we performed a voxel-based morphometry and a resting state functional MRI approach to assess sex differences in gonadally intact animals. We demonstrated significant sex differences in grey matter concentration (GMC) at the level of the gonadotropic axis; i.e. not only within the hypothalamus and pituitary, but also within the hippocampus and the amygdala of intact animals. We then performed the same analysis one month after gonadectomy and found that some of these differences were reduced following gonadectomy, especially in the hypothalamus and amygdala. By contrast, we found few differences in the organization of the functional connectome between males and females either before or after gonadectomy. As a whole, our study identifies brain regions that are sexually dimorphic in sheep brain at the resolution of MRI and highlights the role of gonadal hormones in the maintenance of these differences.

**Keywords** sex differences; sheep; voxel-based morphometry; resting state fMRI; gonadectomy.

**Manuscript category** Preclinical studies

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**Suggested reviewers** Tracy Melzer, Kevin Whittingstall, Gerard Thompson, Lance Kriegsfeld

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**Highlights :**

- Brain sex differences can be observed by using MRI in sheep, a well-recognized model in neuroendocrinology.
- Adult male and female brains show important sexual dimorphisms.
- Gonadectomy reduces these differences, showing their dependence on adult circulating hormone levels.

**In vivo magnetic resonance imaging reveals the effect of  
gonadal hormones on morphological and functional brain  
sexual dimorphisms in adult sheep.**

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## **Abstract**

Sex differences in the brain and behavior are produced by the perinatal action of testosterone, which is converted into estradiol by the enzyme aromatase in the brain. Although magnetic resonance imaging (MRI) has been widely used in humans to study these differences, the use of animal models, where hormonal status can be properly manipulated, is necessary to explore the mechanisms involved. We used sheep, a recognized model in the field of neuroendocrinology, to assess brain morphological and functional sex differences and their regulation by adult gonadal hormones. To this end, we performed voxel-based morphometry and a resting-state functional MRI approach to assess sex differences in gonadally intact animals. We demonstrated significant sex differences in gray matter concentration (GMC) at the level of the gonadotropic axis, *i.e.*, not only within the hypothalamus and pituitary but also within the hippocampus and the amygdala of intact animals. We then performed the same analysis one month after gonadectomy and found that some of these differences were reduced, especially in the hypothalamus and amygdala. By contrast, we found few differences in the organization of the functional connectome between males and females either before or after gonadectomy. As a whole, our study identifies brain regions that are sexually dimorphic in the sheep brain at the resolution of the MRI and highlights the role of gonadal hormones in the maintenance of these differences.

**Key words:** sex differences, sheep, voxel-based morphometry, resting state fMRI, gonadectomy.

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- 40    - Brain sex differences can be observed by using MRI in sheep, a well-recognized model in
- 41    neuroendocrinology.
- 42    - Adult male and female brains show important sexual dimorphisms.
- 43    - Gonadectomy reduces these differences, showing their dependence on adult circulating
- 44    hormone levels.



## **Introduction**

Males and females show various sexually dimorphic traits in adulthood at the behavioral level that relate to the structure and function of the brain (McCarthy et al., 2015). Characterizing these sexual differences is of importance not only to gain a global understanding of the normal brain but also to gain insights into various brain disorders that are of differential prevalence and progression between males and females (Miller et al., 2017). Sex differences related to reproductive function are one of the most prominent types of sexual dimorphism, as both the neuroanatomical and functional organization of the gonadotropic axis differ widely between males and females.

In mammalian species, the classic view of sexual differentiation holds that these sex differences develop under the perinatal influence of testosterone and/or estradiol derived from the neural aromatization of testosterone (Alexander et al., 2011; Bakker and Baum, 2008). The brain develops as male in the presence of these hormones, and testicular testosterone in male embryos is necessary for the expression of male-typical hormonal and associated behavioral responses later in life, a process known as masculinization. Testosterone exposure not only masculinizes the brain but also actively defeminizes it so that males are unable to exhibit female-typical behavioral or physiological responses. By contrast, the absence of hormonal exposure predisposes animals to display female-typical adult sexual behaviors and hormone responses, a process known as feminization. While the early actions of sex steroids are necessary for the maturation and/or organization of several brain structures and neural circuits (Arnold, 2009), the differentiated neural circuits in adults are then responsible for sex-typical responses when sex steroids are synthesized by the mature gonad. Thus, the permanent developmental effects of sex steroids are usually referred to as “organizational”, while the transient or reversible effects observed during adulthood are referred to as “activational”.

While these effects have been studied mostly in rodents, similar mechanisms exist in many other mammalian species. The sheep is an animal model that offers a unique opportunity to study brain mechanisms underlying sexual differentiation for several reasons, including the ability to perform long-term blood or cerebrospinal fluid sampling (Clarke and Cummins, 1982), the ability to manipulate the hormonal milieu in the fetus or adult (Clarke and Cummins, 1982; Perkins and Roselli, 2007) and the abundance of information that exists characterizing reproductive physiology and behavior in this species (for review Roselli and Stormshak, 2010, 2009). Sexual differentiation of the sheep brain is dependent on testosterone and androgen receptor signalling during gestation (Cheng et al., 2010; Foster et al., 2002; Robinson et al., 1999; Roselli and Stormshak, 2010). While these studies, performed at the cellular or molecular levels, are very informative, they only examined a limited number of hypothalamic nuclei. Thus, information about other possible sexually dimorphic brain regions is lacking.

Magnetic resonance imaging (MRI) allows investigation at the level of the whole brain and has been widely used in humans to study sex differences in the function and organization of the brain (Burke et al., 2016, 2012). MRI is now a routine approach in neuroscience due to several advantages, including its noninvasive nature and the ability to perform longitudinal studies that allow changes within the same individuals to be tracked over time. However, due to ethical considerations, it is not possible to experimentally manipulate the hormonal milieu in humans, thus highlighting and reinforcing the usefulness of animal models such as sheep.

Some evidence suggests that gray and white matter content in sheep brain are sexually dimorphic, but because of the suboptimal resolution of the images and the lack of the appropriate neuroinformatic tools (namely, a brain template and atlas), the data could not be analyzed properly (Nuruddin et al., 2013). We recently established the tools necessary for conducting MRI experiments in sheep (Ella et al., 2017; Ella and Keller, 2015). In this study, we employed these tools to map and compare sexually dimorphic brain structures and

94 connectivity in rams and ewes. This comparison was performed by using voxel-based  
95 morphometry (VBM) to assess neuroanatomical differences in gray matter concentrations  
96 (GMC) according to sex. We also validated resting-state functional MRI to assess basal  
97 dynamic activity differences between sexes. Finally, we tested which sex differences are  
98 programmed during sexual differentiation (organizational effect) or due to adult gonadal  
99 hormones (activational effect) by analyzing the effect of gonadectomy.

## **Materials and Methods**

**Animals.** Experiments were performed at the National Institute for Agronomic Research (Institut national pour la recherche agronomique, INRA) in Nouzilly, France (latitude 47°, 32N and longitude 0°, 46E) on adult Ile-de-France sheep (*Ovis aries*). A total of 24 animals (4 years old) were used: 12 ewes ( $50.33 \pm 0.71$  kg) and 12 rams ( $70.91 \pm 0.92$  kg). Animals were maintained indoors during the experiment and were fed daily with barley straw, Lucerne hay and commercial concentrate and had access to water and mineral blocks *ad libitum*. All procedures were performed in accordance with the European directive 2010/63/EU for animal protection and welfare used for scientific purposes and approved by the local ethical committee for animal experimentation (CEEA VdL, Tours, France, authorization N° 10465).

**Experimental protocol.** Animals were scanned twice in October and November 2017 at the CIRE platform (INRA Nouzilly, France, <http://www.val-de-loire.inra.fr/cire>). One week before the first scan, progesterone vaginal sponges (flugestone acetate, Chronogest CR 20 mg, MSD, Beaucouze, France) were placed in ewes to induce and maintain a luteal-like phase until the first day of the scan. On the day of the scan, sheep were weighed, and a blood sample was collected by jugular venipuncture to check the hormonal status of the animal. After the first scan, vaginal sponges were retrieved from the ewes, and both ewes and rams were gonadectomized following established procedures. To this end, the sheep were fasted 24 h before surgery. Following premedication with an i.v. injection of thiopental (14 mg/kg body weight, BW; Nesdonal, Merial, Villeurbanne, France), the sheep were intubated and maintained under anesthesia with a closed circuit of 3 to 4 % isoflurane (Vetflurane, Virbac, Carros, France) and 100 % oxygen. Castration and ovariectomy were conducted under sterile surgical conditions. Local anesthesia with lidocaine (4 %, Lurocaïne, Vétquinol, Luré, France) was given prior to scrotal incision in males and laparotomy in females. Testicles or ovaries were

surgically extracted, and the tissues were sutured. The entire procedure was performed within 20 minutes. Postoperative ventilation with oxygen was maintained until the first signs of awakening appeared. The sheep were then housed individually for 6 hours in a padded stall before being put back with congeners. They received an anti-inflammatory drug for 2 days (2 mg/kg BW flunixin meglumine, Finadyne®, Intervet, Beaucouzé, France), an antiedema medication: (1 mg/kg BW of furosemide, Dimazon®, Intervet, Beaucouzé, France) at the end of surgery and 3 mg/kg BW hydrochlorothiazide with 0.03 mg/kg BW dexamethasone (Diurizone®, Vétoquinol, Luré, France) for 2 days. One month after the surgery, a second scan session was performed; the sheep were again weighed, and blood samples were collected as described above to assess the efficiency of the surgery (**Figure 1A and Figure S1**).

**Testosterone and progesterone assays.** Plasma was obtained from heparinized blood after 30 min of centrifugation at 3500 g. The concentration of testosterone was determined in duplicate samples using a radioimmunoassay as previously described (Hochereau-de Reviers et al., 1990). The sensitivity of this assay was 0.1 ng.mL<sup>-1</sup>. The concentration of plasma progesterone was determined in duplicate samples using an immunoenzymatic assay as previously described (Chasles et al., 2016). The sensitivity of the progesterone assay was 0.25 ng.mL<sup>-1</sup> (**Figure 1A**).

**Anesthesia protocol.** Before scanning, the sheep were first anesthetized by an intrajugular administration of a ketamine/xylazine mix (1 mg.mL<sup>-1</sup> ketamine/0.1 mg.mL<sup>-1</sup> xylazine, volume of injection 6.5 mL). After induction, the animal was intubated (8.5 mm probe, SON612, Centravet, France) and ventilated manually. The jugular vein was catheterized for a continuous infusion of 0.1 mg.mL<sup>-1</sup> ketamine/xylazine mix (1.5 mL.min<sup>-1</sup>), which permits preservation of both pupillary and palpebral reflexes and of the regular spontaneous respiratory rate.

Since MRI investigation in animals requires that animals be sedated, we developed a specific protocol of anesthesia for both functional and morphometric acquisition. Indeed, functional connectivity is highly sensitive to the pharmacological class of anesthetics used, and numerous studies have demonstrated that the widely used isoflurane gas obscures the naturally occurring functional connectivity by inducing synchronous cortico-striatal fluctuations and silencing subcortical activity (Kalthoff et al., 2013; Liu et al., 2013; Paasonen et al., 2018). For this reason, we chose to use a low dose of ketamine/xylazine mix (Imalgene 500 mg/Rompun 2 %, Centravet, France) for functional acquisitions and progressively replaced this with a standard isoflurane anesthesia for morphological acquisitions to reduce motion artifacts during long scanning.

**Scanning procedure.** Sheep were placed on the MRI-compatible mechanical bed of a 3 Tesla VERIO Siemens system (Erlangen, Germany). They were gently restrained with a belt on the mechanical bed while their head was placed within a circular rigid coil ( $^1\text{H}$ , 24 channels, phased array, receiver only, 20/28 cm, P-H24LE-030, Siemens, Germany). During the functional resting state scanning procedure, sheep were ventilated continuously using an anesthesia system with an integrated ventilator (Aestiva MRI-compatible, GE Healthcare, Germany) delivering a 1:1 oxygen/air mix with a current volume of 500 mL for ewes and 650 mL for rams and the frequency rate set at 16 bpm. Heart rate and  $\text{O}_2$  saturation were monitored continuously using an oximeter probe placed on the right hind paw (oxytip+ probe MRI-compatible, GE Healthcare, Germany) and maintained at  $87.21 \pm 1.002$  bpm and  $89.83 \pm 8.84$  % for ewes and  $78.19 \pm 9.28$  bpm and  $87.63 \pm 6.18$  % for rams, respectively (for details see **Figure S1**). After the functional resting state scanning procedure, the intravenous ketamine anesthesia regimen was progressively replaced by gas anesthesia using isoflurane added to the air mix at a

concentration of  $2.8 \pm 0.14$  % in ewes and  $3.07 \pm 0.01$  % in rams using the same ventilatory parameters (**Figure S1**).

#### **MRI data acquisition.**

Left-right orientation within the images was ensured by placing an  $\alpha$ -tocopherol acetate capsule (Toco 500 mg,  $\alpha$ -tocopherol acetate, Alkopharm, France) on the right side of the sheep's head. After positioning, a first localizer sequence was performed to align the brain on the anterior commissure-posterior commissure (AC-PC) axis within the field of view (FOV). Then, two successive gradient echoes (GRE) field maps were acquired using the same acquisition parameters: repetition time (TR) = 500 ms, echo time (TE) = 4.92 ms and 7.38 ms, number of excitations (NEX) = 1, flip angle (FA) = 55 degree, field of view =  $166 \times 166 \times 166$  mm<sup>3</sup> within a  $64 \times 64 \times 64$  matrix for a final voxel size =  $2.6 \times 2.6 \times 2.6$  mm<sup>3</sup>. Both GRE field maps were acquired within the axial acquisition plane, but a left-right encoding direction was used on the first acquisition (LR-GRE); then, a right-left encoding direction was used on the second acquisition (RL-GRE). Both LR- and RL-GRE images were acquired to calculate inhomogeneity correction maps that were used within the functional analysis processing. Then, a spin-echo echo-planar imaging (SE-EPI) sequence of 8.5 min was acquired in the axial plane using the following parameters: TR=3260 ms, TE = 24 ms, NEX = 1, FOV =  $170 \times 170 \times 45$  mm<sup>3</sup> within a  $110 \times 110 \times 90$  matrix for a final voxel size =  $1.5 \times 1.5 \times 2$  mm<sup>3</sup>. This sequence generated 150 volumes that were used for resting-state fMRI analysis. Finally, a T1-weighted 3D magnetization-prepared rapid acquisition of gradient echo (MPRAGE) sequence was acquired using the following parameters: TR = 2500 ms, TE = 3.18 ms, FA = 12 degrees, NEX = 2, FOV =  $190 \times 190 \times 190$  mm within a  $384 \times 384 \times 384$  matrix for a final voxel size  $0.5 \times 0.5 \times 0.5$  mm<sup>3</sup>. T1-weighted images were used for voxel-based morphometry analysis. Four rams were excluded from the analysis because of excessive motion during imaging acquisition, ( $n_{\text{(final)}} = 8$  males

and 12 females). The final translations were less than 0.4 mm, and rotations did not exceed 0.006 radians (0.3 degrees) in our acquisitions (**Figure S2**).

**Functional MRI (fMRI) data preprocessing.** Resting-state fMRI data were preprocessed in MATLAB (R2017b, MathWorks) with SPM8 (<http://www.fil.ion.ucl.ac.uk/spm>) using the SPMMouse Toolbox (Sawiak et al., 2014, 2009) and FSL5.1 (<https://fsl.fmrib.ox.ac.uk>). In the first step of preprocessing, the EPI images were time corrected, realigned and resliced to the first volume, corrected for inhomogeneity using the GRE field maps and coregistered with their corresponding T1 anatomical images using SPM8. Thereafter, T1 anatomical images were segmented using our previously published tissue priors (Ella et al., 2017), first to create specific brain masks for each T1 image (gray matter (GM)+white matter (WM)+cerebrospinal fluid (CSF) = Brain Mask) and second to normalize both T1 and EPI images onto our brain template (Ella et al., 2017) using the affine matrix calculated by SPM8 during the segmentation step. Finally, normalized images were masked to remove soft tissue using the brain masks generated previously and spatially smoothed with a Gaussian kernel of 8 mm full-width at half-maximum (FWHM). In the second step of preprocessing, EPI images were processed using FSL. The effect of the six previously calculated motion parameters, including translations and rotations and out brain signals, was removed from the data through linear regression using the FEAT toolbox (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FEAT>). Then, acquisition artifacts (ghosting) were identified using the *melodic* function. Briefly, *melodic* decomposes the signal of the 4D smoothed images into independent spatial components. These components were thresholded ( $p < 0.01$ ) and visually inspected for artifacts, which were removed using the *regfilt* function of FSL (Kelly et al., 2010). Finally, a bandpass filtering (0.1 Hz-0.005 Hz) was applied to the time series (**Figure 1B**).



**Construction of resting-state functional networks.** Pre- and post-gonadectomy, processed functional images of each animal (40 data sets) were segmented into 86 anatomical regions of interest (ROIs) (43 regions in each hemisphere) using the GM areas of our sheep atlas (Ella et al., 2017) and the REX function of the CONN toolbox (<https://www.nitrc.org/projects/conn>; **Figure 1B**). For each sheep, functional correlation coefficients ( $r$  values) were computed between the time courses of each pair of ROIs and then transformed to z-scores using Fisher's z transformation, resulting in an 86x86 matrix of normalized correlation coefficients for each animal. Networks of altered connectivity were computed, extracted and plotted using Network-Based Statistics (NBS, <http://brain-connectivity-toolbox.net/comparison/nbs>; Zalesky et al., 2010), the Brain Connectivity Toolbox (<http://brain-connectivity-toolbox.net>; Rubinov and Sporns, 2010), the BrainNet Viewer toolbox (<https://www.nitrc.org/projects/bnv/>; Xia et al., 2013) and in-house developed MATLAB scripts. **As the sample size was unbalanced between both sexes (8 males *versus* 12 females), we estimated the type 2 error ( $\beta$  value = 0.898) to assess the number of permutations necessary to reach a  $\beta$  value = 0.95 ( $n = 1500$ ).** Statistical comparisons between groups were made at the global network level (*i.e.*, conjunction of all ROIs). The NBS methodology works in two steps: first, the statistical hypothesis is tested at each connection, and its statistical significance is determined; second, the connections are thresholded by a user-defined significance ( $p < 0.05$ ,  $< 0.01$  and  $< 0.001$ ); the subnetwork components (groups of nodes and edges such that a path can be found between any pair of network members) were found; and their size (number of surviving connections) was determined. The component significance was determined through permutation testing ( **$n = 5000$** ), where the test subjects are randomly permuted between groups and the chance of randomly finding networks of similar size determined, outputting a family-wise error rate-corrected significance ( $\alpha_{\text{FWE}}$ , 0.05). Differences between gonad-intact males and females and the effect of gonadectomy on males and females were determined using analysis of variance

(ANOVA) with group or time as a factor. A  $p$  value  $< 0.05$  after correction was considered statistically significant. Considering the individual variability and as a control to test our statistical power, we compared two random groups balanced for sex (4 males and 6 females in each group; **Figure S3**). At the baseline, male and female  $z$  scores described a Gaussian distribution ( $K2_{(Males)} = 11.96$ ;  $p = 0.0025$  and  $K2_{(Females)} = 13.93$ ;  $p = 0.0009$ ; D'Agostino & Pearson normality test) that was significantly different ( $p < 0.0001$ ;  $t = 4.995$ ;  $df = 354$ , paired  $t$ -test) with a shift of female values to the right. After gonadectomy,  $z$  scores also followed Gaussian distributions ( $K2_{(Males)} = 20.41$ ;  $p < 0.0001$  and  $K2_{(Females)} = 22.93$ ;  $p < 0.0001$ ) and were significantly different between the sexes ( $p < 0.0001$ ;  $t = 9.848$ ;  $df = 354$ ), again with a shift of the female values to the right. When baseline  $z$  scores for males and females were mixed, the Gaussian distributions were conserved ( $K2_{(Males)} = 14.77$ ;  $p = 0.0006$  and  $K2_{(Females)} = 18.58$ ;  $p < 0.0001$ ), but the curves were superimposed and not significantly different ( $p = 0.4382$ ;  $t = 0.7758$ ;  $df = 708$ ). The same effect was observed after gonadectomy ( $K2_{(Males)} = 20.53$ ;  $p < 0.0001$  and  $K2_{(Females)} = 21.5$ ;  $p < 0.0001$ ;  $z$  score comparison:  $p = 0.8802$ ,  $t = 0.1507$ ;  $df = 708$ ).

**Voxel-Based Morphometry (VBM) data preprocessing.** VBM data were preprocessed with SPM8 and SPMouse 1.1 Toolbox. First, each T1 anatomical image was aligned to the stereotaxic space by registering each image to our anatomical template image (Ella et al., 2017) using SPMouse. Then, each image was bias corrected and segmented into probability maps of GM, WM, and CSF using the default settings in the SPM8 toolbox and our GM, WM, CSF probability maps (Ella et al., 2017). The transformation matrices obtained were used to normalize and resample ( $0.5 \times 0.5 \times 0.5 \text{ mm}^3$ ) the GM, WM and CSF probability maps. To produce a more accurate registration within each sheep as well as across all sheep, the

Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) algorithm, which is an automated, unbiased, and nonlinear template building program (Ashburner, 2007), was applied using the strategy described by (Asami et al., 2012). First, a subject-specific template was created by the DARTEL algorithm using the previous tissue class images (GM, WM, and CSF maps) obtained from each sheep at both time points (before and after gonadectomy). The DARTEL procedure releases individual-specific flow field maps, permitting the application of diffeomorphic normalization on each tissue class of images to spatially normalize each time point on a subject-specific template space. Each normalized tissue class of images was modulated by the determinant of the Jacobian to account for the expansion and/or contraction of brain regions over time. Then, a population-specific template was created by the DARTEL algorithm using all of the subject-specific templates of the tissue class of images. Here, the DARTEL procedure releases population-specific flow field maps, permitting the application of diffeomorphic normalization from each animal onto each tissue class of images. Finally, each tissue class image was modulated by the determinant of the Jacobian, and the final modulated GM images were spatially smoothed by convolving with a 4 mm full-width at half-maximum (FWHM) isotropic Gaussian kernel to create GMC maps (**Figure 1B**) (Sumiyoshi et al., 2017).

**Voxel-Based Morphometry, statistics and analysis.** Statistical Parametric Mapping (SPM8) was used to reveal the temporal and regional changes in gray matter occurring in GMC maps. Second level analysis from SPM, a flexible factorial model that is equivalent to a 2×2 mixed-model ANOVA, was used first to compare male *versus* female and then pregonadectomy *versus* postgonadectomy groups. Brain volume was used as a covariate (**Figure S4A**) with between-subject factor group and within-subject factor condition. The factors included in the analysis were subjects, group (male, female), and time (pregonadectomy, postgonadectomy). A brain

mask was used to constrain the analysis. For each cluster, the significance of the peak voxel was set as  $p < 0.005$  ( $\beta$  value = 0.990,  $t_{(35)} = 2.7238$ ), and the minimum cluster extent was set to 300 voxels. The results are presented on an axial brain slice series generated by the xjView plugin (<http://www.alivelearn.net/xjview/>) of SPM, and the corresponding surfacing results were assembled with a BrainNet viewer, which allows the generation of both brain mesh and brain plots for visualizing data. To assess the effect of individual variability and as a control test for statistical power, we compared two random groups balanced for sex (4 males and 6 females in each group (**Figure S4**)). At baseline, the comparison shows only a small significant unilateral cluster on slices 14 and 12 corresponding to the left lateral *gyrus*, which was not observed previously ( $p = 0.005$ ,  $\beta$  value = 0.990,  $t_{(35)} = 2.7238$ , voxel threshold = 300), while the comparison performed after the gonadectomy reveals no significant differences between the groups.

**Postprocessing statistical analysis.** VBM cluster peaks revealed by flexible factorial analysis data were identified using our atlas and a personal procedure developed in MATLAB. For each comparison, ROI masks from Ella's atlas were used to extract GMC values of corresponding regions within the GMC map using REX plugging. Endocrine, physiological, functional connectivity and GMC data were compiled and analyzed using Prism 6.02 software (GraphPad Software, San Diego, CA) and were compared using two-way ANOVA with repeated measures followed by the two-stage setup method of Benjamini, Krieger and Yekutieli as recommended by the software. Statistical significance was defined as  $p < 0.05$  for these analyses.

## **Results**

### **Morphological and functional sexual dimorphism in the adult sheep brain.**

#### VBM analysis

Using a voxel-based morphometry (VBM) approach, we found 37 brain regions that were sexually dimorphic in intact sheep (see **Table S1 and S2** for detailed statistics). Specifically, our VBM analysis found that the gray matter concentration (GMC) within the left and right *gyrus ectolateralis*, left and right hippocampus, pituitary gland and right amygdala were significantly higher in intact females than in intact males (red clusters, **Figure 2A**). In contrast, GMC values in the hypothalamus and both posterior gyri sigmoideus were significantly higher in intact males *versus* luteal phase females (blue clusters, **Figure 2A**). Comparison between the same animals before and after gonadectomy reveals that only 22 brain regions were still dimorphic. Among them, four bilateral cortical regions of the gyri ectolateralis, both entolateral and lateral gyri, and the occipital lobe, still exhibited higher GMC values in gonadectomized females than in gonadectomized males (red clusters, **Figure 2B**). GMC values in the posterior gyri sigmoideus were still higher in gonadectomized males than in gonadectomized females (blue, clusters, **Figure 2B**). The volumes of several dimorphic subcortical structures, such as the right amygdala and the hypothalamus, decreased after gonadectomy and were no longer different between males and females. Moreover, we observed a large regression of the volume of the hippocampal cluster (120 mm<sup>3</sup> within the intact male/intact female comparison *versus* 15 mm<sup>3</sup> within the gonadectomized male/gonadectomized female comparison) and a large increase (10 times) of the volume of the pituitary cluster (28 mm<sup>3</sup> within the intact male/intact female comparison *versus* 280 mm<sup>3</sup> within the gonadectomized male/gonadectomized female comparison).

Using our anatomical atlas (Ella et al., 2017), we collected GMC values within the bilateral hippocampus, hypothalamus, pituitary gland and gyri ectolateralis to evaluate the effect of

gonadectomy on these structures. Within the hippocampus (**Figure 3A**), we observed a left-right asymmetry in both males and females as previously reported (Sadeghi et al., 2017; Samara et al., 2011), which was preserved after gonadectomy. In addition, we observed bilateral sexual dimorphism in the hippocampus with higher GMC values in luteal phase females than in intact males. This hippocampal sexual dimorphism was lost after gonadectomy. Within the hypothalamus (**Figure 3B**), no left-right asymmetry was observed, but significantly higher GMC values were found in intact males compared to luteal phase females. The sexual dimorphism in the hypothalamus was also eliminated after gonadectomy. No side asymmetry was observed within the pituitary gland (**Figure 3C**), but significantly higher GMC values were observed in luteal phase females compared to intact males. GMC concentration in the pituitary increased significantly in both sexes after gonadectomy, but sexual dimorphism was preserved. Finally, analysis of GMC within the gyri ectolateralis (**Figure 3D**) revealed no left-right asymmetry, but GMC values were significantly higher in luteal phase females when compared to gonad-intact males.

#### Resting-state fMRI analysis

The analysis of the functional connectome between intact males and females revealed a sexually dimorphic brain network composed of 332 functional connections shared between 77 functional nodes (**Figure 4A**, all statistics are available in **Table S3**). Intact luteal phase females displayed higher functional connectivity than intact males (**Figure 4B**). Three internal subnetworks involving the frontal region (red nodes), the occipitoparietal region (orange nodes) and the diencephalic region (yellow nodes) compose this dimorphic network. When we focused on the sexually dimorphic brain regions highlighted by our previous VBM analysis, we observed that both the left and right hippocampus, hypothalamus pineal gland and gyrus ectolateralis display higher functional connectivity in luteal phase females when compared to

369 intact males (**Table S3**). Notably, the hippocampus displayed stronger bilateral connections in  
 370 luteal phase females than in intact males within the geniculate nucleus, the parahippocampal  
 371 cortex, the periaqueductal gray substance (PAG), the suprasylvian *gyrus*, the cingulate cortex,  
 372 the pineal gland, the temporal lobe and the thalamus. The hypothalamus displayed stronger  
 373 bilateral connections in luteal phase females than in intact males within the lateral septal  
 374 nucleus, the preoptic hypothalamic area, the subfornical organ and the substantia nigra.  
 375 Importantly, the connectivity between the hypothalamus and the pituitary gland was also  
 376 significantly higher in luteal phase females than in intact males. Finally, the gyrus ectolateralis  
 377 displayed stronger bilateral connections in luteal phase females than in intact males within the  
 378 gyri entolateralis and the lateral gyri.

379 Surprisingly, the analysis of the functional connectome between gonadectomized males and  
 380 females revealed a similar brain network also composed of 332 functional connections shared  
 381 between 80 functional nodes (**Figure 4C**, all statistics are available in **Table S4**). This  
 382 functional network is characterized by higher functional connectivity in gonadectomized  
 383 females when compared to gonadectomized males (**Figure 4D**) and displayed the same internal  
 384 frontal, occipitoparietal and diencephalic subnetworks. Although it was statistically marginal,  
 385 some changes in resting-state functional connectivity were also detected within the  
 386 hippocampus, hypothalamus, and gyrus ectolateralis. Similar temporal correlations were  
 387 observed within the previously described structures. Additional bilateral connections were  
 388 observed within the gyrus ectolateralis, midbrain, left lateral *gyrus* and right nucleus of the  
 389 horizontal limb of the diagonal band (NHLDB) of gonadectomized females compared to  
 390 gonadectomized males. Within the hypothalamus, similar functional connectivity was observed  
 391 to that described in intact animals. Additional functional connectivity was observed with the  
 392 lateral septal nucleus bilaterally in gonadectomized females when compared to gonadectomized  
 393 males and with the right bed nucleus of the stria terminalis (BNST), the left globus pallidum

and the left NHLDB. Finally, the gyrus ectolateralis also displayed similar higher functional connections with previously described structures and additional bilateral functional connectivity with the cingulate cortex, the occipital lobe, the suprasylvian gyrus and the hippocampus. Functional connections were also observed with the right parahippocampal cortex, the right posterior sylvian gyrus and the right temporal lobe in gonadectomized females when compared to gonadectomized males.

## **Effect of gonadal secretion on brain morphology and functional connectivity in both male and female adult sheep brains.**

### VBM analysis

To evaluate the sex-specific effects of gonadectomy, we evaluated both brain morphology and functional connectome modifications before and after gonadectomy in males and females. In males, VBM analysis revealed 29 regions with significant GMC modifications induced by gonadectomy (see **Table S5** for detailed statistics). We found significantly higher GMC values within the bilateral amygdala and the pituitary gland after gonadectomy (red clusters, **Figure 5A**). On the other hand, the GMC values were significantly decreased after gonadectomy within the medial mamillary nucleus, the periaqueductal gray substance (PAG), the pons and the medial preoptic hypothalamic area (blue clusters, **Figure 5A**). In females, VBM analysis revealed 22 regions with significant GMC modifications induced by gonadectomy (see **Table S6** for detailed statistics). We found significantly higher GMC values only within the pituitary gland (red clusters, **Figure 5B**). By contrast, GMC values were significantly decreased within the medial mamillary nucleus, *medulla oblongata* (MO), pons and preoptic hypothalamic area (blue clusters, **Figure 5B**). Interestingly, after gonadectomy, GMC values were also reduced within both gyri ectolateralis but only within the right hemisphere (**Figure 5B**).



Using our anatomical atlas, we collected GMC values within the bilateral amygdala and PAG in males and within the subfornical organ and NHLDB in females, which display sex-specific modifications after gonadectomy. In males, GMC was significantly increased after gonadectomy within the amygdala (**Figure 6A left panel**). On the other hand, the GMC values within the PAG were significantly decreased after gonadectomy (**Figure 6A, right panel**). In females, GMC values were significantly decreased after gonadectomy within the subfornical organ (**Figure 6B left panel**). GMC values within the NHLDB were also significantly decreased after gonadectomy (**Figure 6B, right panel**).

#### Resting-state fMRI analysis

The analysis of the functional connectome between intact and gonadectomized males revealed a brain network sensitive to gonadal hormones composed of 66 functional connections shared between 52 functional nodes (**Figure 7A**, all statistics are available in **Table S7**). This functional network was significantly higher in gonadectomized males (**Figure 7A, Right panel**) and was characterized by modifications of rostrocaudal functional connectivity and by intense modifications of functional connectivity within the diencephalon. Importantly, the pituitary gland, which is a critical structure in reproductive function and shows significant variations of GMC after gonadectomy, displayed increased functional connectivity together with the preoptic hypothalamic area, the BNST and the subfornical organ. By contrast, the analysis of the functional connectome between intact and gonadectomized females revealed a brain network sensitive to gonadal hormones composed of 94 functional connections shared between 65 functional nodes (**Figure 7B**, all statistics are available in **Table S8**). This functional network was also significantly higher in gonadectomized females (**Figure 7B, Right panel**) and was characterized by an interhemispheric modification of functional connectivity and, as previously described in males, by intense modifications of functional connectivity

444 within the diencephalon. As observed in males, the pituitary gland also displayed an increase  
445 in GMC after gonadectomy in females along with an increase in the functional connectivity  
446 within the medial septal nucleus, the BNST, the septum, the NHLBD, the preoptic  
447 hypothalamic area and the subfornical organ.

## **Discussion**

Our study is the first to report a detailed VBM analysis in sheep and to establish resting-state fMRI in this species. Thanks to these methodological developments, we were able to highlight brain sexually dimorphic territories and networks of functional connectivity differing between males and females, mainly in the hypothalamus and pituitary. We also showed that these differences are partly due to adult circulating levels of gonadal hormones, as some of these differences vanished following gonadectomy, suggesting that the differences observed are due to the activational effects of circulating gonadal hormones. These data add a high degree of neuroanatomical precision compared to the previous MRI report of differences between the sexes in sheep (Nuruddin et al., 2013) and were made possible through the construction of an adapted brain template and atlas of the ovine brain (Ella et al., 2017; Ella and Keller, 2015).

### **Sex differences in intact animals.**

#### **VBM analysis**

First, our VBM analysis revealed clear differences in GMC between intact males and females in five main areas: the hippocampus, the hypothalamus—especially the arcuate region—the pituitary, the amygdala and the gyrus ectolateralis. For all these regions, with the exception of the hypothalamus, GMC was higher in males than in females. On the whole, the differences measured in the hypothalamus and pituitary, which are key components of the gonadotropic axis, are not very surprising because the axis is known to be highly sexually dimorphic. Indeed, sexual differences have been previously reported in other species or by other approaches in these areas. For example, similar to our results, MRI studies in humans have reported that the volume of the hypothalamus is larger in men than women (Goldstein et al., 2001; Makris et al., 2013). The hypothalamic cluster differing significantly between males and females appears to

473 include the region of the arcuate nucleus, a structure where the numbers of neurons expressing  
474 kisspeptin, neurokinin B and dynorphin (KNDy neurons) as well as progesterone receptors are  
475 higher in female than in male sheep (Cheng et al., 2010). This difference is linked to the fact  
476 that KNDy neurons mediate the negative feedback of progesterone on GnRH secretion in  
477 females. In the hypothalamic cluster, other regions, such as the ventromedial nucleus, are also  
478 known to be sexually dimorphic, being larger in males than females (Flanagan-Cato, 2011).  
479 Finally, it is important to note that a limitation of our study is the level of resolution that is  
480 achievable using our MRI conditions (500  $\mu$ m isovoxel resolution). This level of resolution  
481 prevents visualization of very small neuron clusters, such as the sexually dimorphic nucleus of  
482 the medial preoptic area, which has been consistently shown to be larger in males than females,  
483 including in sheep (Roselli and Stormshak, 2010). In the pituitary, we found that females have  
484 a higher concentration of gray matter than males. A recent human MRI study demonstrated that  
485 the pituitary fossa, which grossly reflects the volume of the pituitary, is larger in women than  
486 men (Pecina et al., 2017), thus corroborating our observations.

487 In the amygdala, we confirmed the sexual dimorphism previously reported in sheep (Nuruddin  
488 et al., 2013) and recently in humans (Lotze et al., 2019). At the cellular level, it has been shown  
489 that the size of neurons in the amygdala, as well as the content in estradiol receptors, is higher  
490 in male than female sheep (Alexander et al., 2001; Perkins et al., 1995). In other animal models,  
491 for example, in the rat, the volume of the medial amygdala is also higher in males than females  
492 (Cooke et al., 1999). The hippocampus is another brain region that appears to be sexually  
493 dimorphic in our study. As the hippocampus is a primary site for the regulation of cognitive  
494 processes such as stress responses or spatial memory, which are also influenced by gonadal  
495 hormones, such a difference is not surprising (Juraska, 1991; McCarthy and Konkle, 2005). In  
496 addition, our results showing that part of the anterior hippocampus is larger in females than  
497 males is congruent with a recent MRI study in mice (Meyer et al., 2017). Finally, the difference

measured in the gyrus ectolateralis is more surprising because it is not known as a traditional region related to sex differences. Given the lack of anatomical and functional data regarding this region in sheep, it is difficult to interpret this result. It has been shown that the gyrus ectolateralis is part of the visual cortex (Clarke and Whitteridge, 1976), but further studies will be needed to assess the nature and role of this dimorphism.

We performed the same VBM comparison one month following gonadectomy to assess whether the differences observed are due to adult circulating levels of gonadal hormones. It is striking to note that most of the observed differences diminished significantly after gonadectomy, particularly in the hypothalamus and amygdala. Interestingly, adult castration of male rats induces a reduction of the volume of the medial amygdala to a level comparable to that observed in females, demonstrating that adult hormone manipulation can completely reverse the sexual dimorphism observed in intact animals. Interestingly, this region is also rich in aromatase and steroid receptors in adult sheep (Lehman et al., 1993; Roselli et al., 1998).

#### Resting-state fMRI

In addition to VBM analysis, our study is the first to report that the resting state connectome differs between male and female sheep. This analysis revealed a sexually dimorphic brain network composed of 332 functional connections shared between 77 functional nodes that displays increased functional connectivity in intact luteal phase females when compared to intact males. Three internal subnetworks involving the frontal region, the occipitoparietal region and the diencephalic region compose this dimorphic network, with the diencephalic region being by far the most sexually dimorphic. Interestingly, the functional connectivity within the diencephalic region and especially in the hypothalamic regions showed the highest degree of sexual dimorphism. Finally, these sexual differences were not significantly influenced

by adult circulating gonadal hormones, as the network differing between the sexes was not influenced by gonadectomy.

#### **Sex differences in gonadectomized animals.**

##### **VBM analysis**

When considering the effect of gonadectomy within each sex in the VBM analysis, it is striking to observe that gonadectomy induced very similar changes in GMC at the level of the hypothalamus and pituitary in both males and females. The fact that gonadectomy abolishes negative feedback (of testosterone for the males and progesterone for the females) is in line with a similar response of the hypothalamic-pituitary axis in both sexes. However, it is notable that in terms of GMC variations, the responses of the hypothalamus and pituitary were opposite. While an increase of GMC was observed in the pituitary following gonadectomy, a clear reduction was measured in the whole hypothalamus. The increase in GMC observed in the pituitary is in line with previous data showing that ovariectomy induces a strong increase in the number and size (2- to 3-fold hypertrophy) of the LH cell population in ewes (Polkowska et al., 1980).

By contrast, the medial preoptic area of the hypothalamus is long known to be highly sexually dimorphic in many species, including humans (Swaab et al., 1992). The size of the ovine sexually dimorphic nucleus, measured either by Nissl staining or the expression of aromatase, is significantly larger in adult rams than in ewes and is not affected by gonadectomy (Roselli et al., 2004, 2000). In contrast, gonadectomy induced a significant reduction in GMC in the hypothalamus in both sexes. This pattern of response remains to be explained in terms of cellular mechanisms.

##### **Resting-state fMRI**

When analyzing the effect of gonadectomy within each sex for resting-state fMRI, it is striking to first notice that within each sex, gonadectomy induced an increase in functional connectivity. The pituitary gland, which displayed an increase in GMC after gonadectomy, also expressed an increase in functional connectivity within the preoptic hypothalamic area and the BNST. However, intense modifications of functional connectivity within the diencephalon diverged according to sex. Indeed, while changes in males were characterized by rostrocaudal modifications of functional connectivity, changes were mostly interhemispheric in females. The meaning of such differences remains to be explored in the future.

### **General considerations**

As already mentioned, differences between sexes or between intact and gonadectomized animals are mainly located at the level of the hypothalamus and pituitary, reflecting differences in the regulation of the gonadotropic axis. To fully validate the role of adult circulating sex steroids, especially testosterone and progesterone, in the maintenance of these sexual differences and determine which of these hormones is involved, it will be necessary in a future study to supplement gonadectomized animals with adult levels of circulating steroids and see whether we are able to restore the initial pattern of differences observed in intact animals. Finally, it is important to consider several limitations that arise from the segmentation of our brain atlas and the use of anesthetics in preclinical fMRI investigation. First, the current level of anatomical/functional mapping of sheep brain neuroanatomy is far less precise than those in other species such as rodents. Even if more than 80 brain structures have been segmented so far, it should be remembered that MRI segmentation is dependent upon the contrasts on MRI images that can differ from histological observations. Consequently, each label includes many brain structures, and thus labeling would differ from the expectation of the reader. Second, in our analysis, we failed to find any functional connectivity that was higher in males than in

females. Indeed, sex differences in ketamine sensitivity have been reported to affect the depth, duration and efficacy of anesthesia (Molina et al., 2016). Thus, even though measures of heart rate and O<sub>2</sub> saturation during functional acquisitions are similar between sexes (Figure S1), a differential effect of ketamine on the resting-state network cannot be excluded. Moreover, the greater sensitivity to ketamine displayed by males could obscure differences physiologically present in males rather than in females, explaining the lack of higher functional connectivity in males compared to females. Finally, our analysis was performed using Ella's Sheep brain template and its associated probabilistic tissue maps, which were created from 18 ewes. Recent studies have proposed using a more specific template to improve the segmentation step (Fillmore et al., 2015; Huang et al., 2010). Hence, the development of a mixed brain template (including males and females) with a higher number of animals (n = 100, sex ratio 1:1) will be mandatory to improve the segmentation step and further develop future MRI studies using sheep.

In conclusion, we demonstrated that MRI is a suitable method to study neuroendocrine mechanisms that sustain sexual differences in the sheep brain and by inference in other large animal models. In this context, sheep offer a unique mammalian model in which to study neuroendocrine sexual differentiation and same-sex sexual partner preferences. Indeed, males showing spontaneous preference for other rams (male-oriented) represent as many as 8 % of the ram population (Roselli et al., 2011; Charles E. Roselli and Stormshak, 2009; Roselli and Stormshak, 2010). The understanding of the biological determinants and underlying neural networks mediating sexual attraction and mate selection are still quite incomplete in these animals. Thus far, evidence supports the idea of an organization of neural substrates by testosterone during prenatal development (C. E. Roselli and Stormshak, 2009). While much attention has been given to the sexually dimorphic nucleus of the hypothalamus, a structure that



595 cannot be observed in MRI due to the limits of resolution, MRI could provide new insights on  
596 whether the anatomy of other brain structures differ in male-oriented sheep.

## **Acknowledgment**

We thank Didier Chesneau and Chantal Porte for their valuable help at different stages of this project. We thank all the shepherds, especially Damien Capo, Olivier Lasserre and Didier Dubreuil, from the experimental unit (UEPAO) for the care provided to the animals. We are also grateful to Anne-Lyse Lainé, Corinne Lacie and Dominique Gennetay from the laboratoire de Phénotypage-Endocrinologie for hormonal assays. We thank all the staff from the CIRE platform for their help during surgeries and imaging sessions, especially Gilles Gomot, Christian Moussu and Frédéric Elleboudt. Finally, we thank Julie Bakker, Charlotte Cornil and Jacques Balthazart for helpful feedback on this manuscript. This project was funded by grants from the French Agence Nationale de la Recherche (ANR) and the regional council Centre-Val-de-Loire (Pherobouc project).

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755

## **Figures**

**Fig 1.** Overview of the experiment. **A.** Experimental design and concentrations of testosterone and progesterone before and after gonadectomy in both males and females. **B.** Processing workflow for functional connectivity and voxel-based morphometry (VBM) analysis. Both functional and anatomical images are coregistrated onto the Ella' sheep brain template and then processed using a dedicated processing developed from SPM and FSL toolbox. **C.** 3D rendering of the Ella' sheep brain template and atlas. Sheep brain atlas is composed by a mosaic of 86 anatomical region of interest (ROI) which were used to create the functional connectivity matrix and functional networks analysis to identify brain territories revealed by the VBM analysis (for further information, see Material & Method section). Data are compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons test and expressed as mean  $\pm$  SEM; \*\*\*  $p < 0.001$ .

768 **Fig 2.** Morphological brain sexual dimorphisms in intact and gonadectomized animals. Male  
 769 *versus* female VBM comparison before and after the gonadectomy procedure. **A. left panel:**  
 770 brain plots representing the surface map of regional grey matter concentration (GMC)  
 771 differences between gonad-intact male *versus* luteal phase female sheep. **A. right panel:** brain  
 772 slices showing GMC differences between intact male *versus* intact female sheep. **B. left panel:**  
 773 brain plots representing the surface map of GMC differences between gonadectomized male  
 774 *versus* gonadectomized female sheep. **B. right panel:** brain slices showing GMC differences  
 775 between gonadectomized male *versus* gonadectomized female sheep.  
 776 Ecto = ectolateralis gyrus ; Hippo = hippocampus ; Pit = pituitary gland ; Hypo = hypothalamus.  
 777 Data are the results of interaction analysis (**A**) males versus females at the baseline (**B**) males  
 778 *versus* females after gonadectomy using a  $p$  value  $< 0.005$  ( $\beta$  value = 0.990) corresponding to  
 779  $t_{(35)} = 2.7238$  and a cluster threshold set at 300 voxels. N = 20 animals (8 males and 12 females).

780 **Fig 3.** Effect of gonadectomy on sexually dimorphic structures. The mean values of Grey Matter  
781 Concentration (GMC) were evaluated bilaterally in **A.** hippocampus, **B.** hypothalamus, **C.**  
782 pituitary gland and **D.** ectolateralis gyrus for both male and female sheep before and after  
783 gonadectomy.  
784 Data were compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons  
785 test and expressed as mean  $\pm$  SEM; \* $p < 0.05$ ; \*\*  $p < 0.01$  and \*\*\*  $p < 0.001$ . N = 20 animals  
786 (8 males and 12 females).



787 **Fig 4.** Functional brain sexual dimorphisms in intact and gonadectomized sheep. **A.** Sagittal  
788 and dorsal view of the sexually dimorphic brain functional network between entire males *versus*  
789 entire females. **B.** Mean connectivity values within the previous network between entire males  
790 and entire females. **C.** sagittal and dorsal view of the sexually dimorphic brain functional  
791 network between gonadectomized males *versus* gonadectomized females. **D.** Mean  
792 connectivity values within the previous network between gonadectomized males and  
793 gonadectomized females.

794 The sexually dimorphic functional network are the results of interaction analysis between (A)  
795 males *versus* females at the baseline and between (C) males *versus* females after gonadectomy  
796 using network-based statistics (NBS; connection-level threshold  $p$ -uncorrected < 0.001,  
797 networks were significant at  $p < 0.05$  family-wise error (FWE) corrected), nodes and edges  
798 colour coded according to statistical strength ( $t$ -value). Both comparison of the mean values of  
799 the networks were evaluated using a two-tailed Student t-test and expressed as mean  $\pm$  SEM;  
800  $*p < 0.05$ . N = 20 animals (8 males and 12 females).

801 **Fig 5.** Effect of the gonadectomy procedure in both males and females on brain morphology.  
802 **A. left panel:** brain plots representing the surface map of regional grey matter concentration  
803 (GMC) differences between entire male *versus* gonadectomized male. **A. right panel:** brain  
804 slices showing GMC differences between entire male *versus* gonadectomized male. **B. left**  
805 **panel:** brain plots representing the surface map of GMC differences between entire female  
806 *versus* gonadectomized female. **B. right panel:** brain slices showing GMC differences between  
807 entire female *versus* gonadectomized female.

808 PAG : periaqueductal grey ; Amyg = amygdala ; Pit = pituitary gland ; Hypo = hypothalamus ;  
809 MPOA = medial preoptic area. Data are the results of interaction analysis between (A) baseline  
810 *versus* gonadectomy in males and between (B) baseline *versus* gonadectomy in female using  
811 a  $p$  value  $< 0.005$  ( $\beta$  value = 0.990) corresponding to  $t_{(35)} = 2.7238$  and a cluster threshold set at  
812 300 voxels.  $N = 8$  in male group and  $n = 12$  in female group.

813 **Fig 6.** Effect of the gonadectomy procedure on non-sexually dimorphic structures in both male  
814 and female sheep. In males, the mean grey matter concentration (GMC) values were evaluated  
815 bilaterally within **A.** the amygdala (Left), and the periaqueductal grey substance (PAG, Right).  
816 In females, the mean GMC values were evaluated bilaterally within **B.** the subfornical organ  
817 (Left), and the nucleus of the horizontal limb of the diagonal band (NHLDB, Right).  
818 Data were compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons  
819 test and expressed as mean  $\pm$  SEM; \* $p < 0.05$  and \*\*\*  $p < 0.001$ . N = 8 in male group and n =  
820 12 in female group.

821 **Fig 7.** Effect of the gonadectomy procedure on brain functional connectivity in male and female  
822 sheep. **A.** Sagittal and dorsal view of the altered functional network induced by gonadectomy  
823 in males. **B.** Mean connectivity values within the previous network between entire *versus*  
824 gonadectomized males. **C.** Sagittal and dorsal view of the altered functional network induced  
825 by gonadectomy in females **D.** right panel: Mean connectivity values within the previous  
826 network between gonad-intact or luteal phase females versus gonadectomized females.

827 The sexually dimorphic functional network are the results of interaction analysis between (**A**)  
828 baseline *versus* gonadectomy in male group and between (**B**) Baseline versus gonadectomy in  
829 female group using network-based statistics (NBS; connection-level threshold  $p$ -uncorrected  $<$   
830 0.05, networks were significant at  $p < 0.05$  family-wise error (FWE) corrected), nodes and  
831 edges colour coded according to statistical strength ( $t$ -value). Both comparison of the mean  
832 values of the networks were evaluated using a two-tailed Student t-test and expressed as mean  
833  $\pm$  SEM; \* $p < 0.05$  and \*\*  $p < 0.01$ . N = 8 in male group and n = 12 in female group.

## **Supplementary Figures**

**Fig S1.** Physiological parameters recorded during the acquisition of functional scanning in males and females, before and after the gonadectomy procedure. (A) animal weight, (B) Heart rate, (C) O<sub>2</sub> saturation, (D) isoflurane concentration.

Data are compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons test and expressed as mean  $\pm$  SEM; \*\*\*  $p < 0.001$ .

**Fig S2.** Motions parameters recorded during the acquisitions. (A) Translations, (B) rotations, (C) estimation of the breath during the acquisition, (D) a significant correlation is observed between the Y-translation motion (Up-down motions) and breathing.

Data are expressed as mean  $\pm$  SD; Correlation was estimated using a two-tailed parametric Pearson test \*\*  $p < 0.001$ .

**Fig S3.** Control testing of individual variability in functional data. Here, we compared two group of sheep after randomly grouped (4 males and 6 females in each group) to insure our statistical power. (A) Distribution of Z score in intact males (shaded blue) and intact females (shaded red) is associated with a significant network in females. (B) Distribution of Z score in mix 1 (shaded blue) and mix 2 (shaded red) is not associated with a significant network in intact animals. (C) Distribution of Z score in gonadectomized males (shaded blue) and gonadectomized females (shaded red) is associated with a significant network in females. (B) Distribution of Z score in mix 1 (shaded blue) and mix 2 (shaded red) is not associated with a significant network in gonadectomized animals. The sexually dimorphic functional network are the results of interaction analysis entire male x luteal females at the baseline (A) and male x females after gonadectomy using network-based statistics (NBS; connection-level threshold p-

858 uncorrected  $< 0.001$ , networks were significant at  $p < 0.005$  family-wise error (FWE)  
 859 corrected), nodes and edges colour coded according to statistical strength (t-value).  
 860  
 861 **Fig S4.** Control testing of individual variability in morphological data. Here, we compared two  
 862 group of sheep after randomly grouped (4 males and 6 females in each group) to insure our  
 863 statistical power. (A) Statistical analytical design showing the flexible factorial design used in  
 864 the study. The last column correspond to the brains volumes which are used as covariate. (B)  
 865 Comparisons of GMC between the mix 1 and the mix 2 at the baseline. A significant cluster  
 866 within the left lateral *gyrus* is observable. (C) Comparisons of GMC between the mix 1 and the  
 867 mix 2 after gonadectomy. No significant cluster observable.  
 868 Data are the results of interaction analysis Mix 1 x Mix 2 at baseline (B) and Mix 1 x Mix 2 at  
 869 gonadectomy (C) using a  $p$  value = 0.005 ( $\beta$  value = 0.990) corresponding to  $t_{(35)} = 2.7238$  and  
 870 a cluster threshold set at 5 voxels.

## **Supplementary Tables**

**Table S1.** Sexually dimorphic brain regions sensitive to the gonadectomy procedure. Data are compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons test and expressed as mean  $\pm$  SEM; \* $p < 0.05$ ; \*\*  $p < 0.01$  and \*\*\*  $p < 0.001$ .

**Table S2.** Sexually dimorphism brain region insensitive to the gonadectomy procedure. Data are compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons test and expressed as mean  $\pm$  SEM; \* $p < 0.05$ ; \*\*  $p < 0.01$  and \*\*\*  $p < 0.001$ .

**Table S3.** Sexually dimorphic brain functional connections. The sexually dimorphic functional network between entire males *versus* entire females has been calculated in network-based statistics (NBS; connection-level threshold  $p$ -uncorrected  $< 0.001$ , networks were significant at  $p < 0.05$  family-wise error (FWE) corrected), nodes and edges colour coded according to statistical strength ( $t$ -value).

**Table S4.** Sexually dimorphic brain functional connections. The sexually dimorphic functional network between gonadectomized males *versus* gonadectomized females has been calculated in network-based statistics (NBS; connection-level threshold  $p$ -uncorrected  $< 0.001$ , networks were significant at  $p < 0.05$  family-wise error (FWE) corrected), nodes and edges colour coded according to statistical strength ( $t$ -value).

**Table S5.** Effect of the gonadectomy procedure on brain morphology in males. Data are compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons test and expressed as mean  $\pm$  SEM; \* $p < 0.05$ ; \*\*  $p < 0.01$  and \*\*\*  $p < 0.001$ .

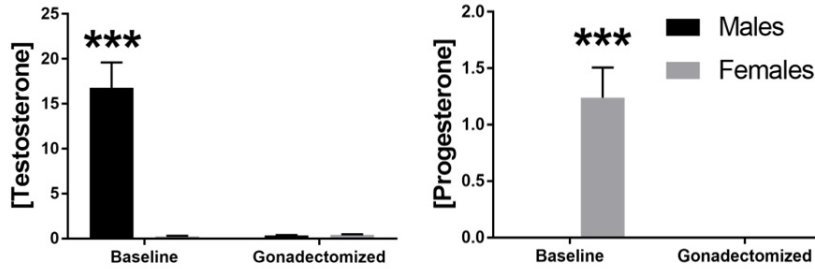
**Table S6.** Effect of the gonadectomy procedure on brain morphology in females. Data are compared using a two-way ANOVA followed by Holm-Sidak multiple comparisons test and expressed as mean  $\pm$  SEM; \* $p < 0.05$ ; \*\* $p < 0.01$  and \*\*\* $p < 0.001$ .

**Table S7.** Effect of the gonadectomy procedure on resting state functional connectivity in males. The network has been calculated in network-based statistics (NBS; connection-level threshold  $p$ -uncorrected  $< 0.05$ , networks were significant at  $p < 0.05$  family-wise error (FWE) corrected), nodes and edges colour coded according to statistical strength ( $t$ -value).

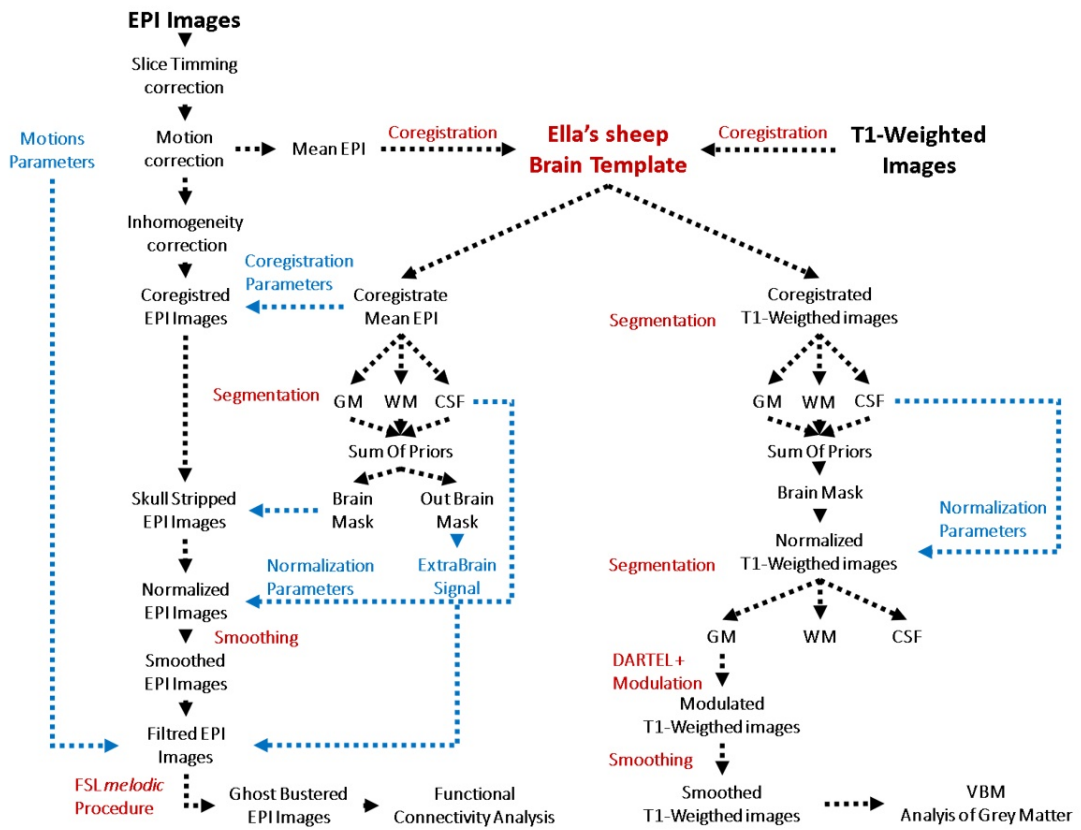
**Table S8.** Effect of the gonadectomy procedure on resting state functional connectivity in females. The network has been calculated in network-based statistics (NBS; connection-level threshold  $p$ -uncorrected  $< 0.05$ , networks were significant at  $p < 0.05$  family-wise error (FWE) corrected), nodes and edges colour coded according to statistical strength ( $t$ -value).



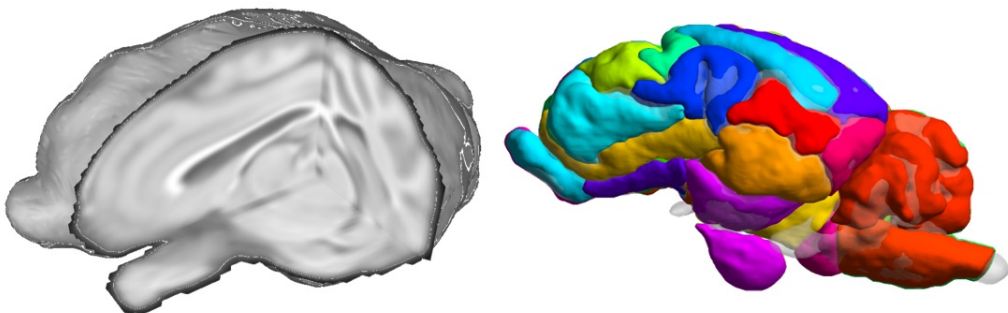
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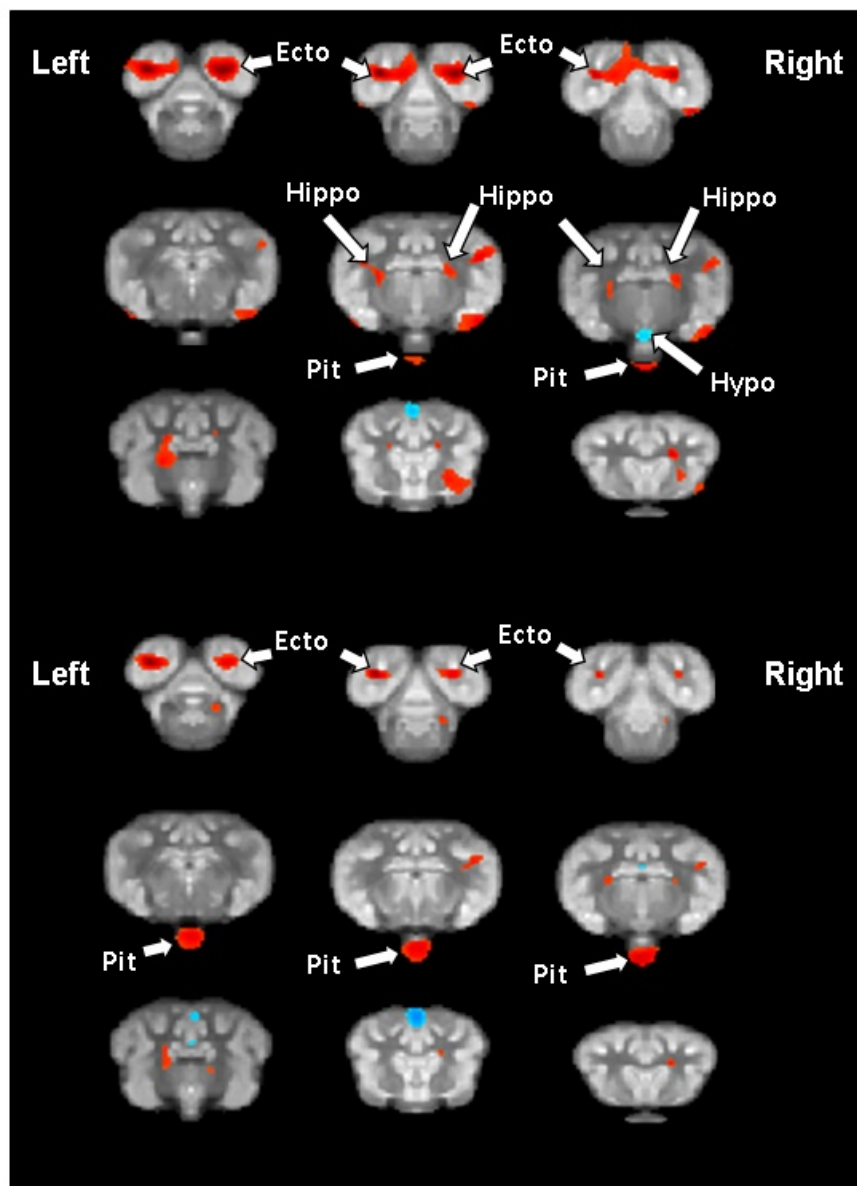
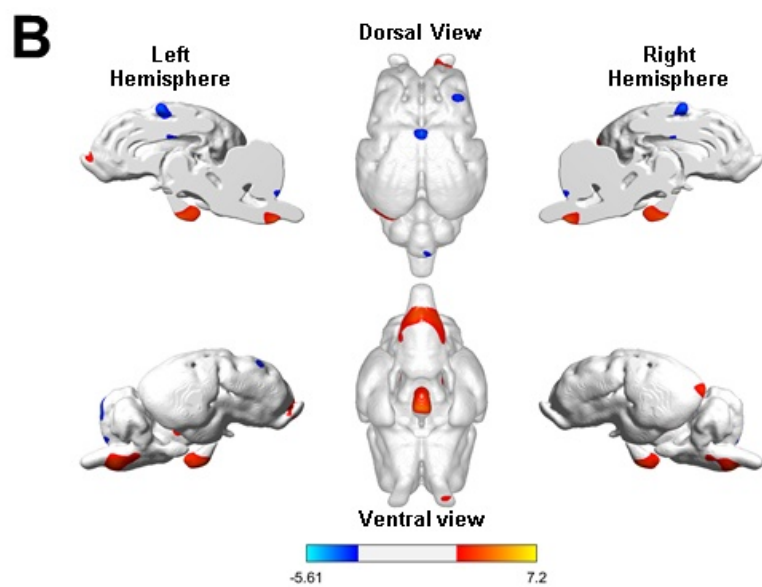
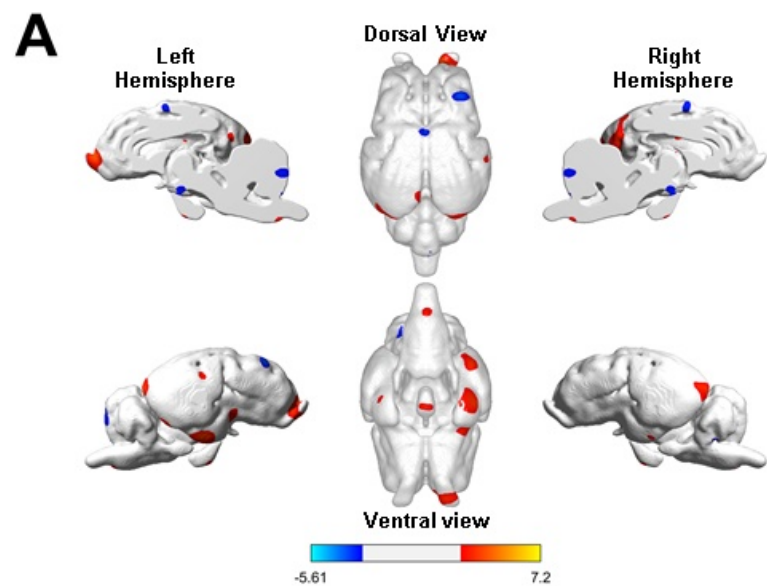


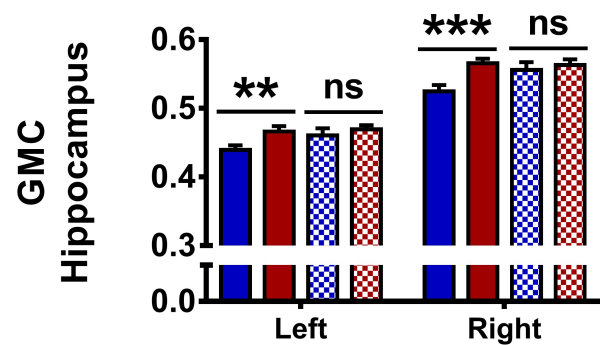
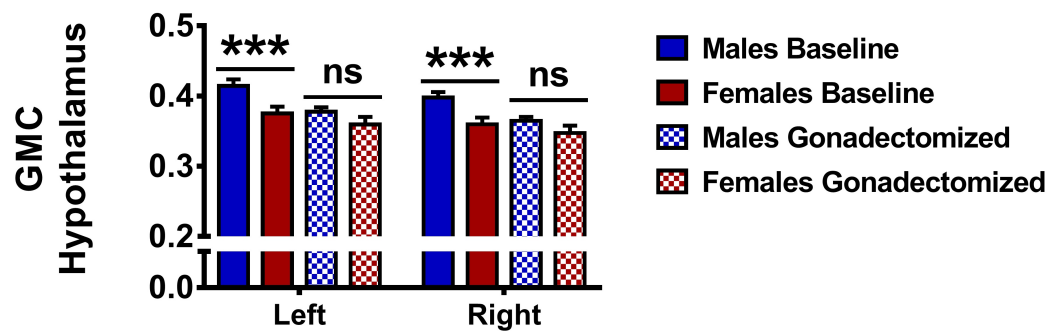
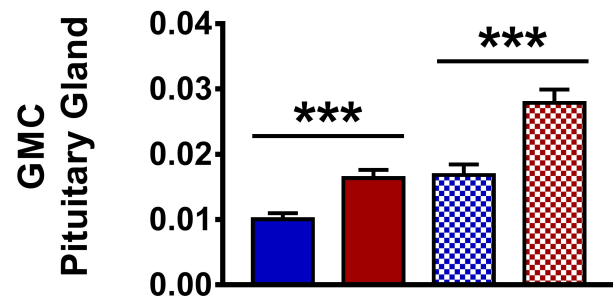
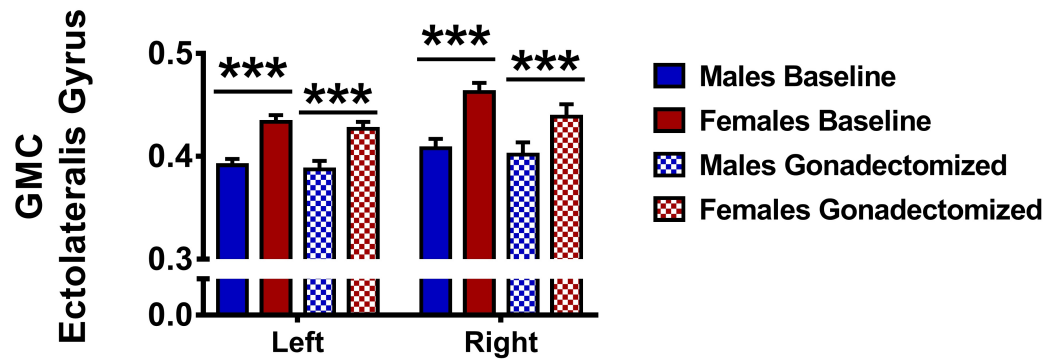
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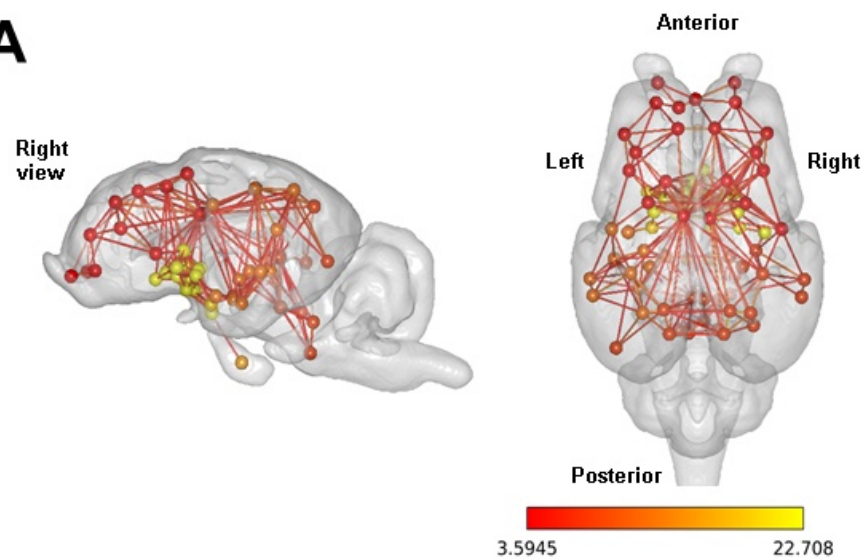
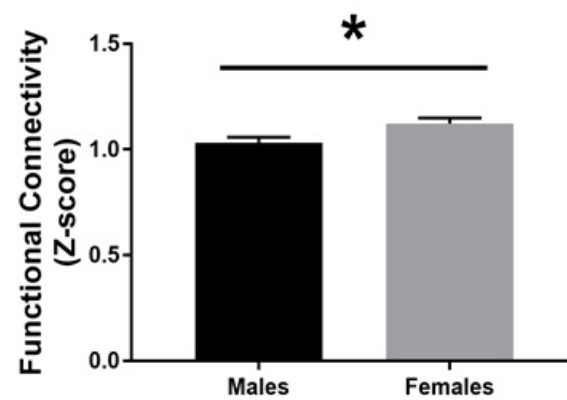
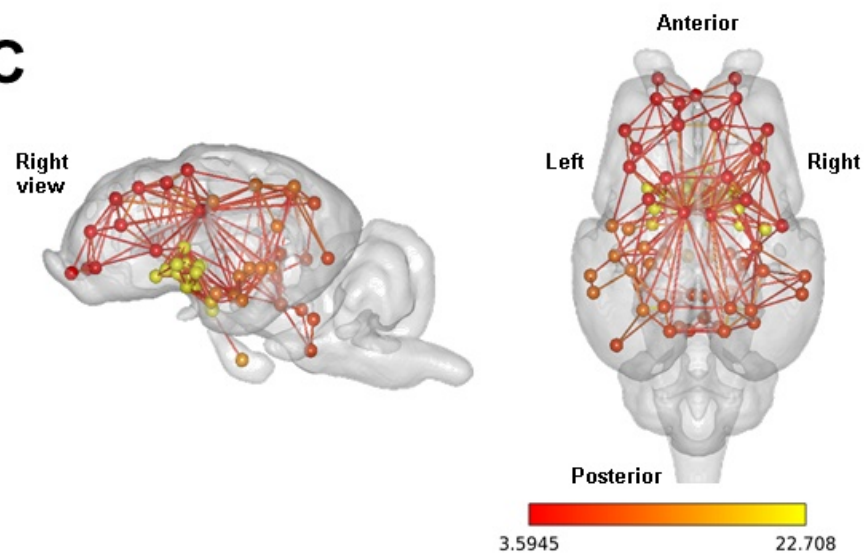
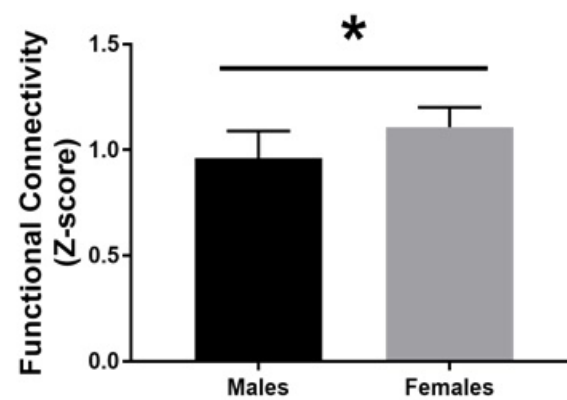


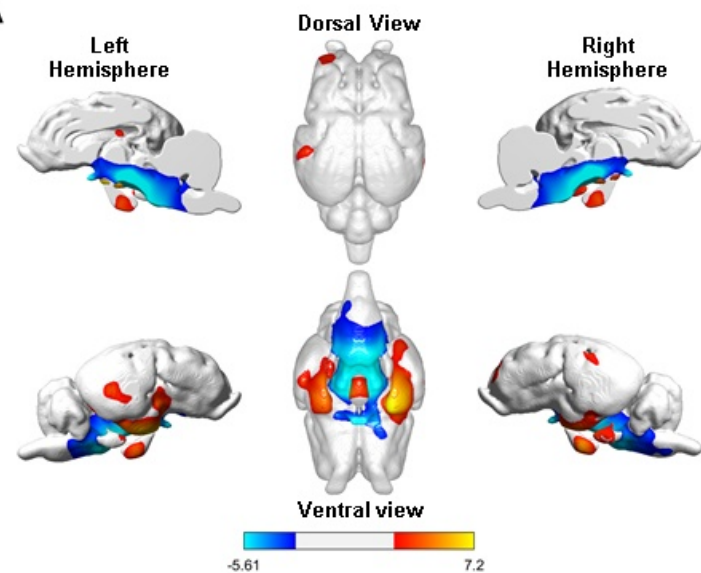
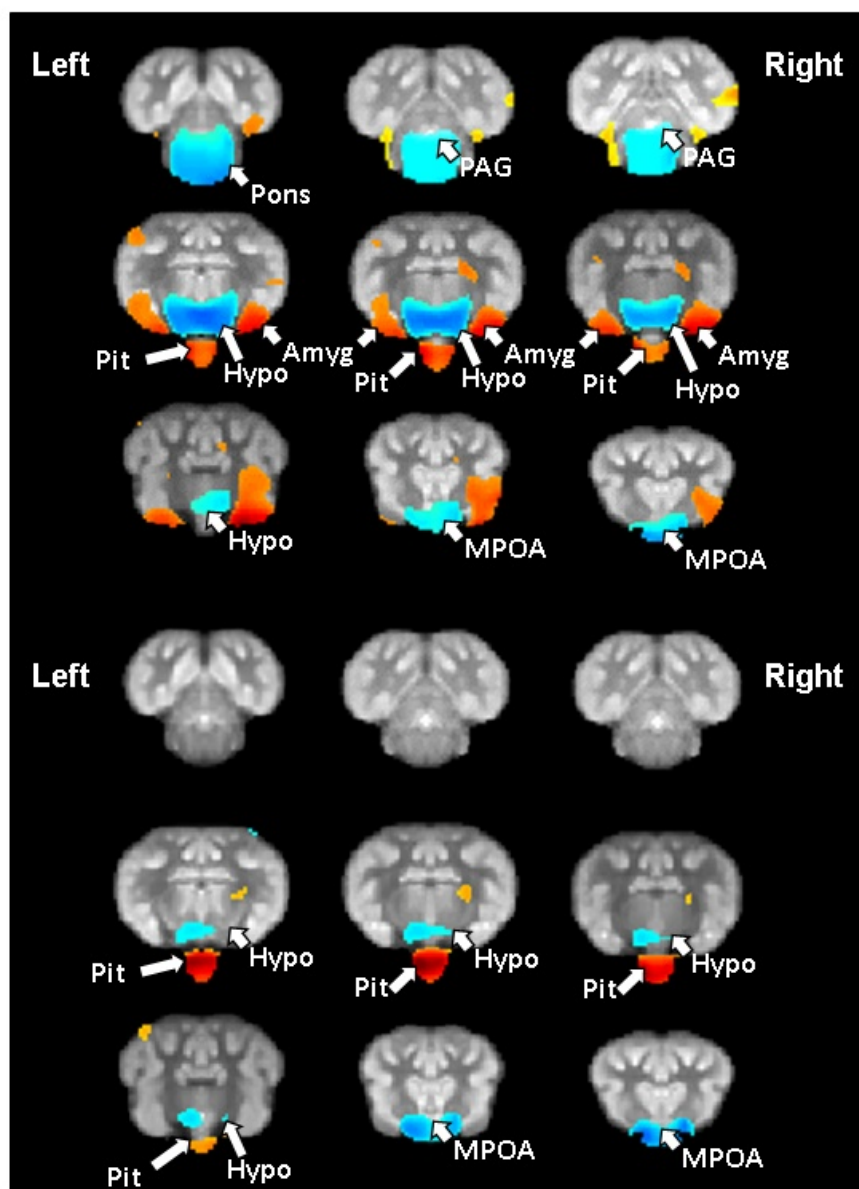
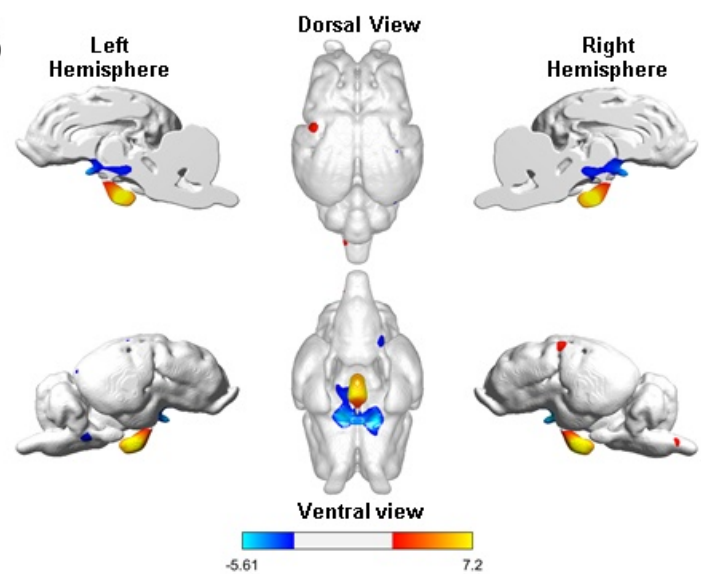
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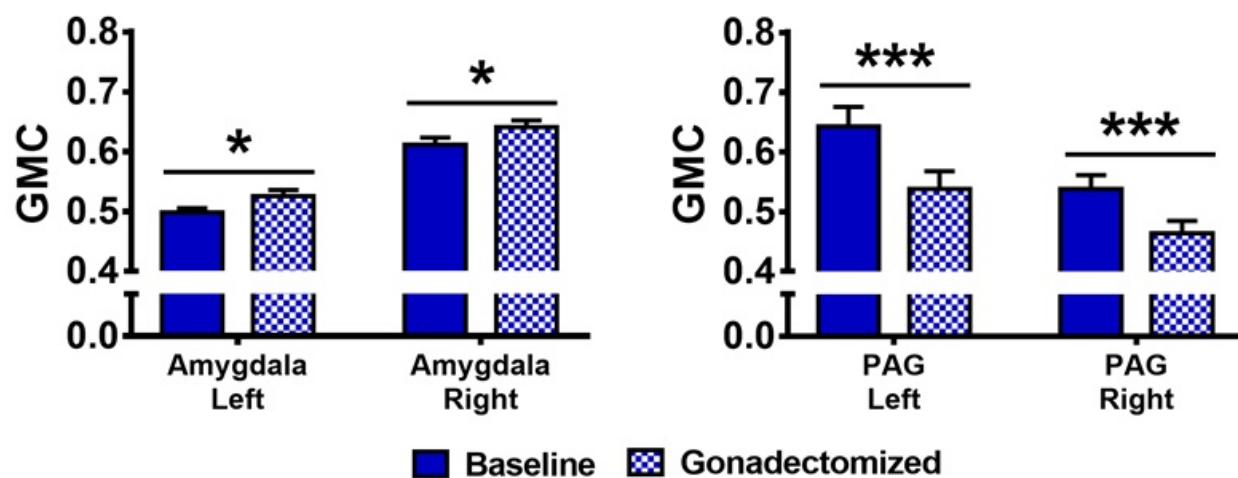
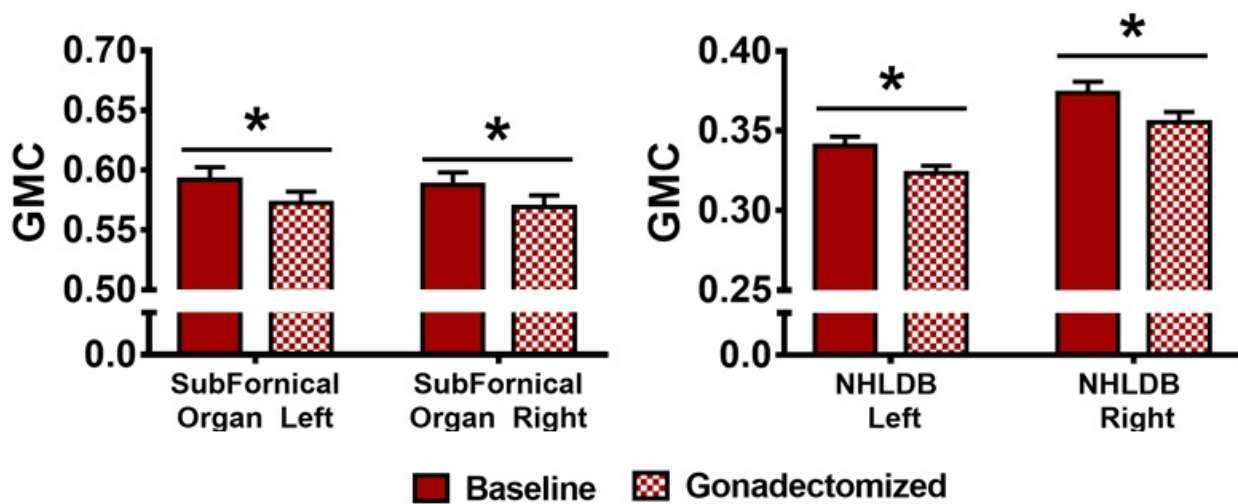


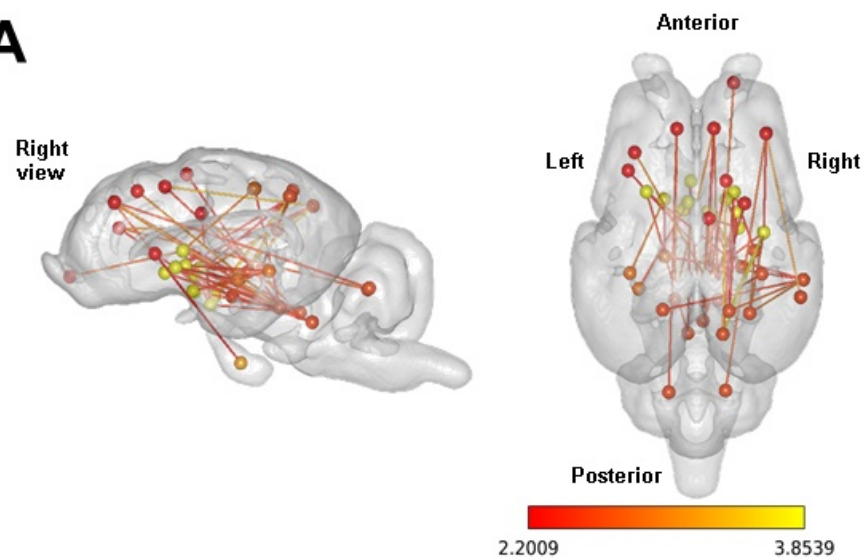
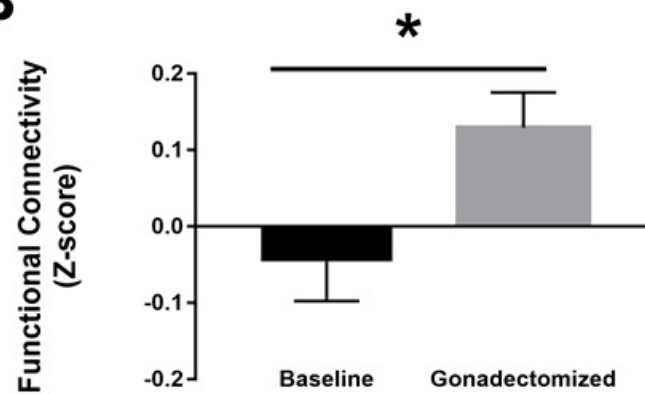
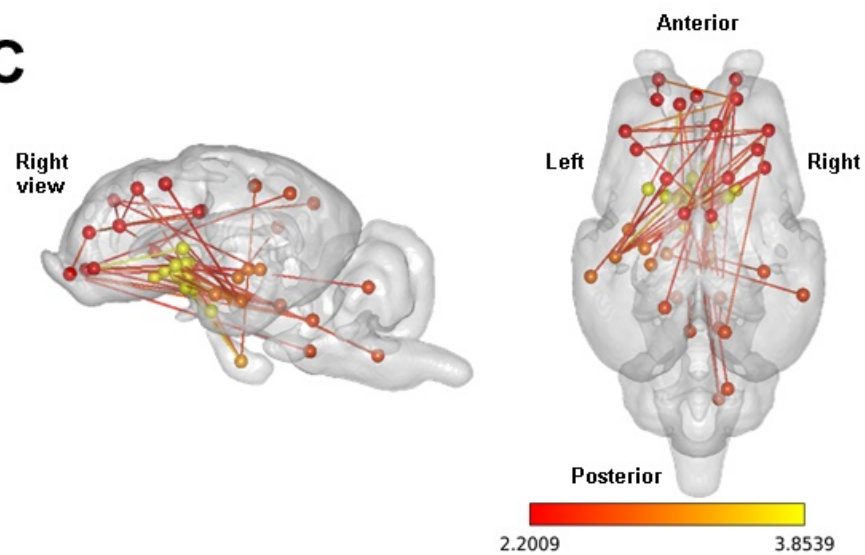
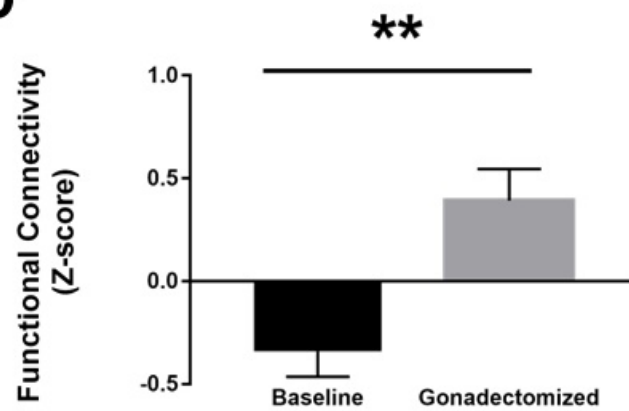
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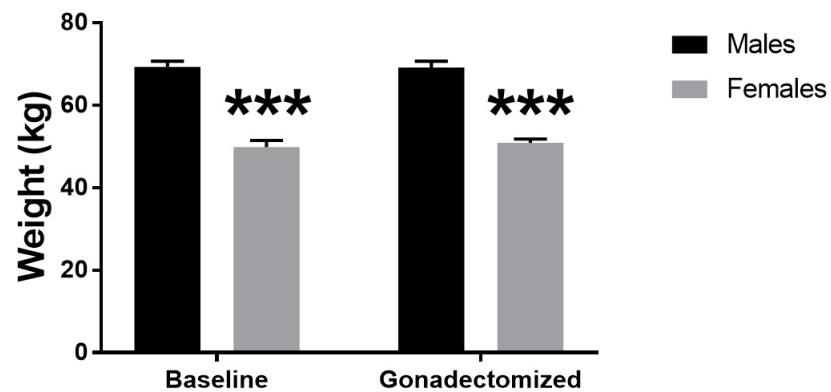
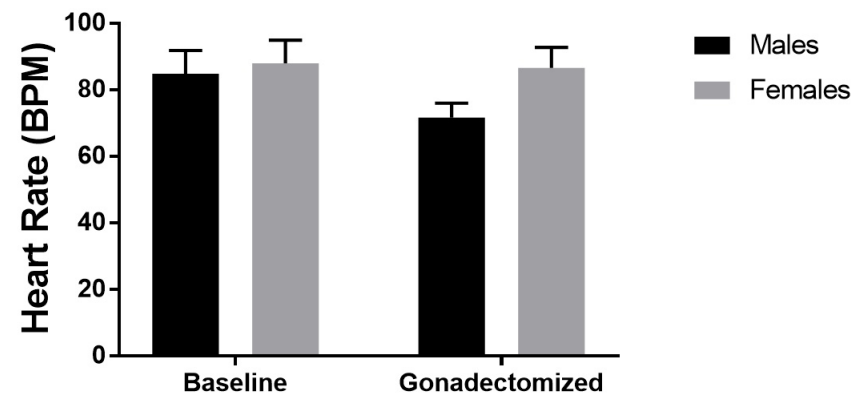
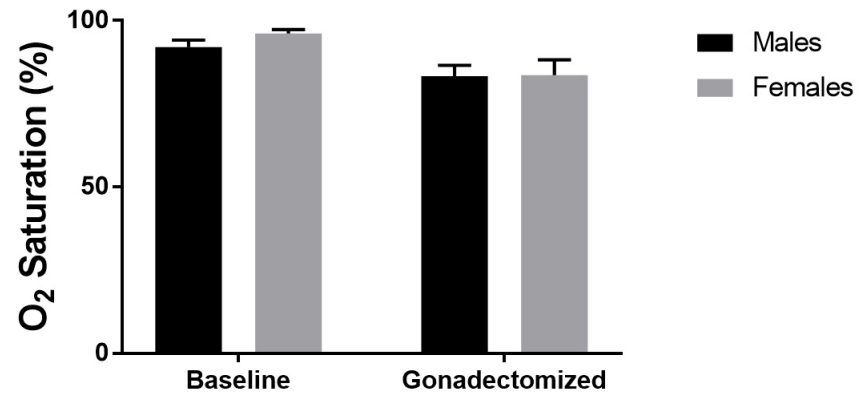
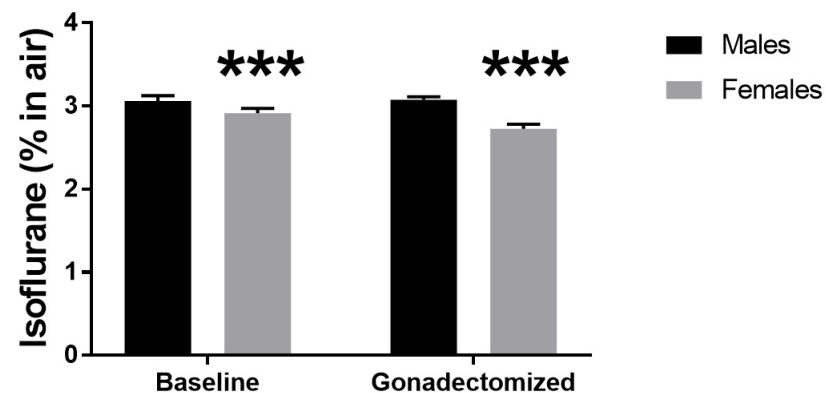
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**A****B**

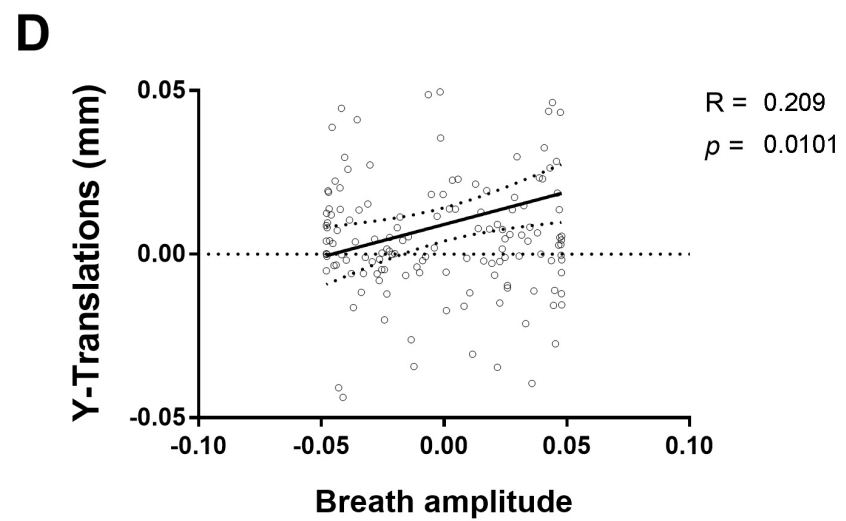
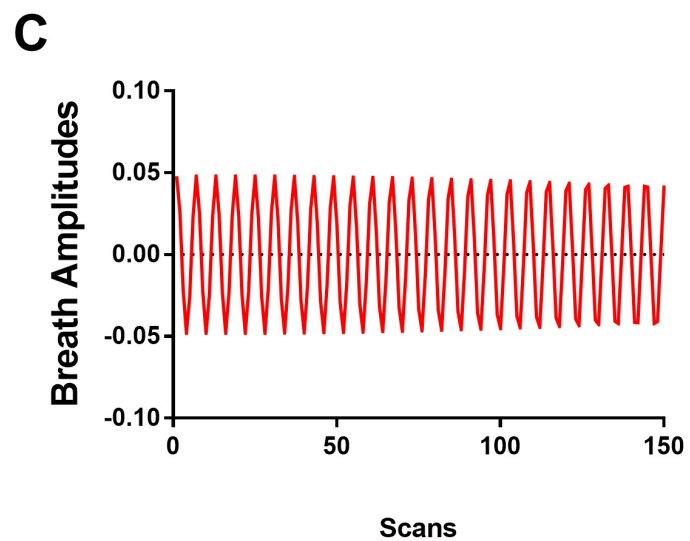
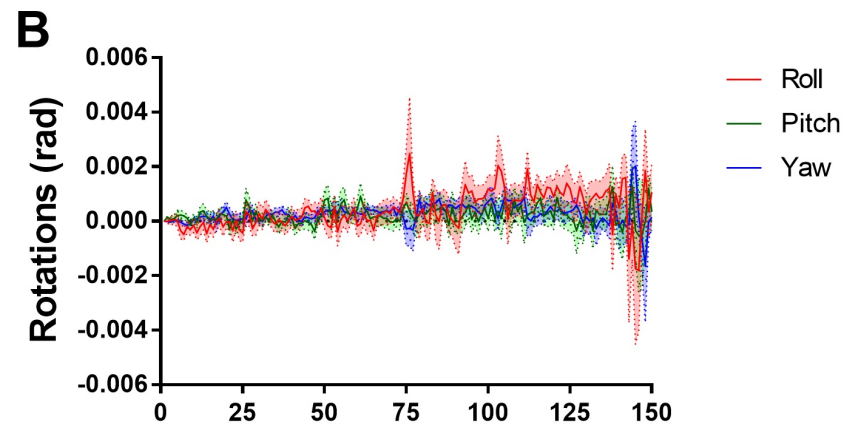
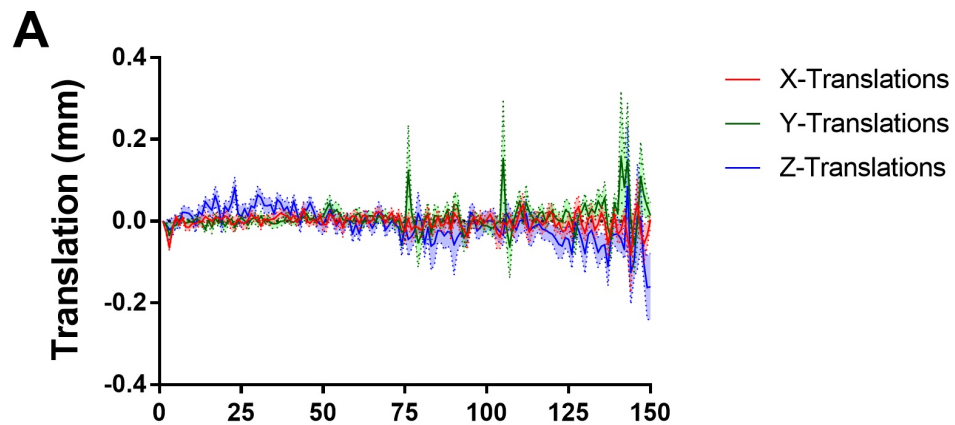


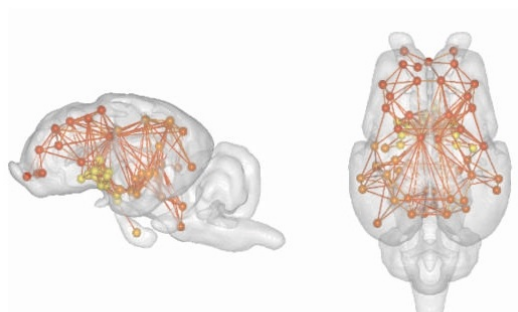
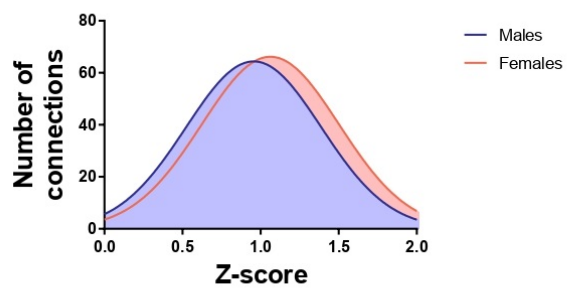
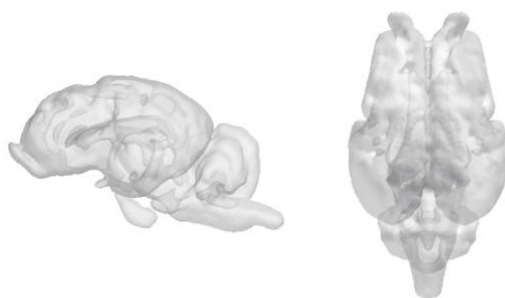
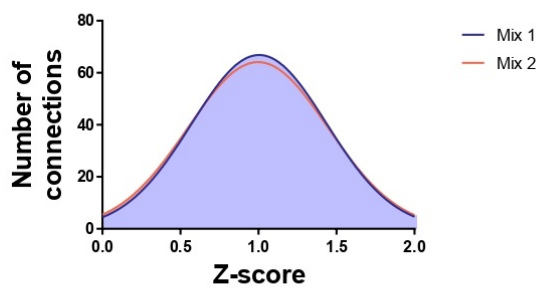
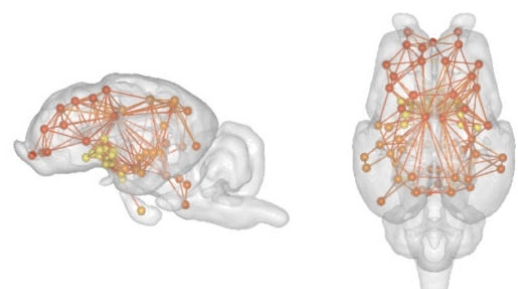
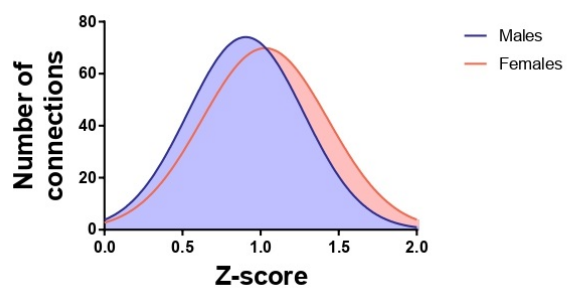
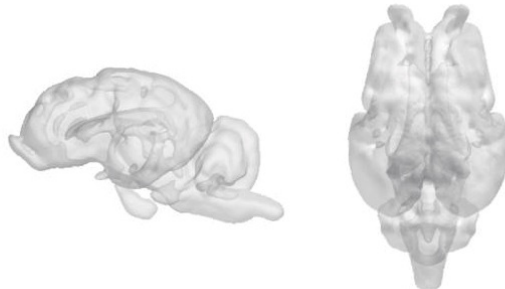
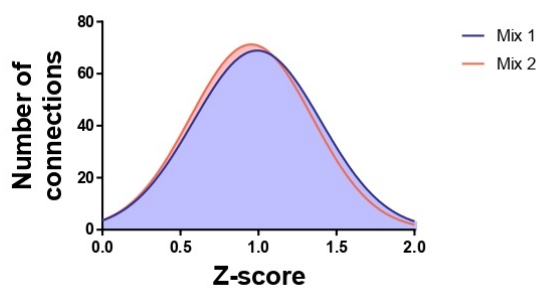
**A****B**

**A****B****C****D**

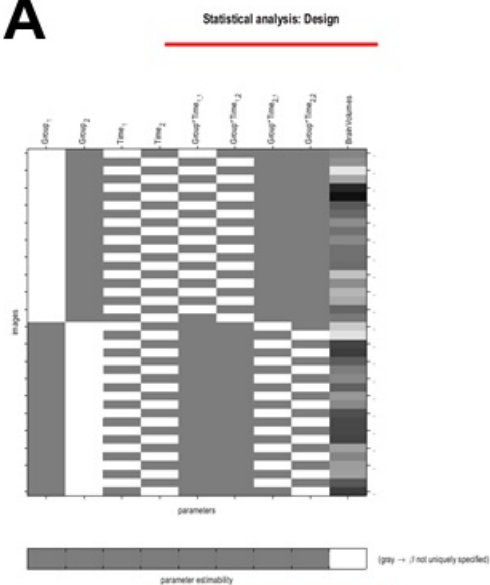
**A****B****C****D**





**A****B****C****D**

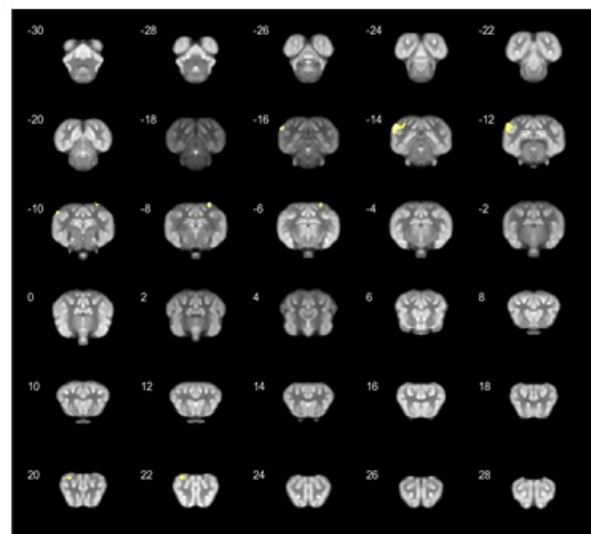
# A



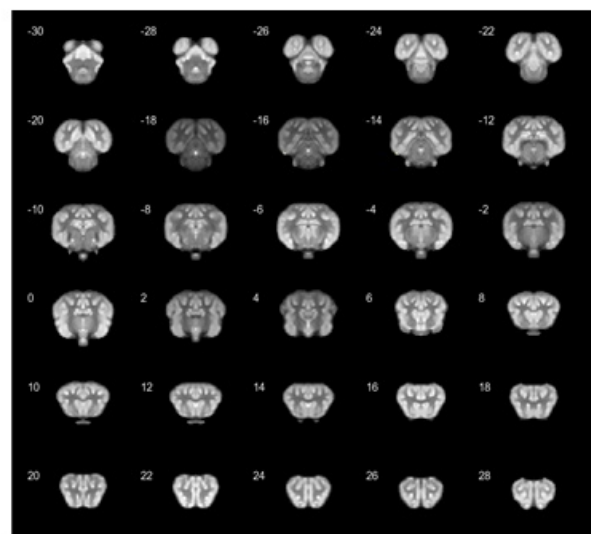
Design description...

- Design : Factorial factorial
- Global calculation : omit
- Grand mean scaling : no grand Mean scaling
- Global normalisation : no global normalisation
- Parameters : 8 condition, +1 covariate, +0 block, +0 nuisance
- 9 total, having 5 degrees of freedom
- leaving 35 degrees of freedom from 40 images

# B



# C



| Comparison                                      | Mean Males | Mean Females | Mean Diff  | 95,00% CI of diff     | t       | Individual P Value | Summary |
|-------------------------------------------------|------------|--------------|------------|-----------------------|---------|--------------------|---------|
| <b>Amygdala Right</b>                           |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,4821     | 0,5064       | -0,02427   | -0,04726 to -0,001285 | 2,071   | 0,0385             | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,4952     | 0,501        | -0,005836  | -0,0279 to 0,01623    | 0,5188  | 0,6039             | ns      |
| <b>Cingulate Cortex Left</b>                    |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,3795     | 0,4087       | -0,02927   | -0,05226 to -0,006284 | 2,497   | 0,0126             | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,3748     | 0,394        | -0,01917   | -0,04124 to 0,002891  | 1,704   | 0,0885             | ns      |
| <b>Hippocampus Left</b>                         |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,4393     | 0,4659       | -0,02663   | -0,04819 to -0,005069 | 2,422   | 0,0155             | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,4602     | 0,4692       | -0,008939  | -0,0305 to 0,01262    | 0,813   | 0,4163             | ns      |
| <b>Hippocampus Right</b>                        |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,5447     | 0,5915       | -0,04677   | -0,06976 to -0,02378  | 3,99    | <0,0001            | ****    |
| Males Gonadectomized vs. Females Gonadectomized | 0,5856     | 0,588        | -0,002384  | -0,02445 to 0,01968   | 0,2119  | 0,8322             | ns      |
| <b>Gyrus Rectus Right</b>                       |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,3713     | 0,3986       | -0,0273    | -0,05029 to -0,00431  | 2,329   | 0,02               | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,3729     | 0,3903       | -0,01737   | -0,03944 to 0,004689  | 1,545   | 0,1226             | ns      |
| <b>Medial Mamillary Nucleus Left</b>            |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,4145     | 0,3754       | 0,03906    | 0,0175 to 0,06063     | 3,553   | 0,0004             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,3778     | 0,3596       | 0,0182     | -0,003361 to 0,03976  | 1,655   | 0,098              | ns      |
| <b>Medial Mamillary Nucleus Right</b>           |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,3979     | 0,3599       | 0,03801    | 0,01644 to 0,05957    | 3,457   | 0,0006             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,3647     | 0,3474       | 0,01731    | -0,004256 to 0,03887  | 1,574   | 0,1156             | ns      |
| <b>Parahippocampal Cortex Left</b>              |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,2995     | 0,3216       | -0,02207   | -0,04506 to 0,0009229 | 1,883   | 0,05               | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,314      | 0,322        | -0,008038  | -0,0301 to 0,01403    | 0,7145  | 0,475              | ns      |
| <b>Parahippocampal Cortex Right</b>             |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,4254     | 0,4559       | -0,03051   | -0,0535 to -0,00752   | 2,603   | 0,0093             | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,4503     | 0,4543       | -0,004017  | -0,02608 to 0,01805   | 0,3571  | 0,7211             | ns      |
| <b>Pituitary Gland Left</b>                     |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,1744     | 0,1472       | 0,02718    | 0,005614 to 0,04874   | 2,657   | 0,015              | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,1798     | 0,1653       | 0,01447    | -0,007096 to 0,03603  | 1,236   | 0,1984             | ns      |
| <b>Pituitary Gland Right</b>                    |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,1923     | 0,1631       | 0,02925    | 0,007684 to 0,05081   | 2,76    | 0,0069             | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,1971     | 0,1832       | 0,0139     | -0,007664 to 0,03546  | 1,64    | 0,1963             | ns      |
| <b>Putamen Right</b>                            |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,3928     | 0,4173       | -0,02443   | -0,04741 to -0,001435 | 2,084   | 0,0373             | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,4033     | 0,416        | -0,01274   | -0,0348 to 0,009325   | 1,132   | 0,2576             | ns      |
| <b>Suprasylvian Gyrus Right</b>                 |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,415      | 0,4498       | -0,03488   | -0,05787 to -0,01189  | 2,976   | 0,003              | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,4467     | 0,4477       | -0,0009936 | -0,02306 to 0,02107   | 0,08833 | 0,9296             | ns      |
| <b>Medial Mamillary Nucleus Left</b>            |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,4145     | 0,3754       | 0,03906    | 0,0175 to 0,06063     | 3,553   | 0,0004             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,3778     | 0,3596       | 0,0182     | -0,003361 to 0,03976  | 1,655   | 0,098              | ns      |
| <b>Medial Mamillary Nucleus Right</b>           |            |              |            |                       |         |                    |         |
| Males Baseline vs. Females Baseline             | 0,3979     | 0,3599       | 0,03801    | 0,01644 to 0,05957    | 3,457   | 0,0006             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,3647     | 0,3474       | 0,01731    | -0,004256 to 0,03887  | 1,574   | 0,1156             | ns      |

| Comparison                                      | Mean Males | Mean Females | Mean Diff | 95,00% CI of diff     | t     | Individual P Value | Summary |
|-------------------------------------------------|------------|--------------|-----------|-----------------------|-------|--------------------|---------|
| <b>AnteriorSigmoides Gyrus Right</b>            |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,2171     | 0,1821       | 0,03498   | 0,01199 to 0,05797    | 2,984 | 0,0029             | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,2073     | 0,1791       | 0,02817   | 0,006102 to 0,05023   | 2,504 | 0,0124             | *       |
| <b>Cerebellum Left</b>                          |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,5363     | 0,5033       | 0,03296   | 0,009972 to 0,05595   | 2,812 | 0,005              | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,5331     | 0,4969       | 0,03621   | 0,01415 to 0,05827    | 3,219 | 0,0013             | **      |
| <b>Cerebellum Right</b>                         |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,452      | 0,4275       | 0,0245    | 0,00151 to 0,04749    | 2,09  | 0,0368             | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,4499     | 0,4211       | 0,0288    | 0,006735 to 0,05086   | 2,56  | 0,0106             | *       |
| <b>Ectolateralis Gyrus Left</b>                 |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4044     | 0,4461       | -0,04163  | -0,06462 to -0,01864  | 3,552 | 0,0004             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,3992     | 0,4382       | -0,03897  | -0,06104 to -0,01691  | 3,465 | 0,0005             | ***     |
| <b>Ectolateralis Gyrus Right</b>                |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4137     | 0,4663       | -0,05258  | -0,07557 to -0,02959  | 4,486 | <0,0001            | ****    |
| Males Gonadectomized vs. Females Gonadectomized | 0,4047     | 0,4428       | -0,03806  | -0,06013 to -0,016    | 3,384 | 0,0007             | ***     |
| <b>Entolateral Gyrus Left</b>                   |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,433      | 0,4709       | -0,03788  | -0,06087 to -0,01489  | 3,232 | 0,0013             | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,4318     | 0,4572       | -0,02542  | -0,04748 to -0,003356 | 2,26  | 0,024              | *       |
| <b>Entolateral Gyrus Right</b>                  |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4938     | 0,5382       | -0,04439  | -0,06738 to -0,0214   | 3,787 | 0,0002             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,4909     | 0,5205       | -0,02962  | -0,05169 to -0,007559 | 2,633 | 0,0085             | **      |
| <b>Insula Right</b>                             |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4799     | 0,5232       | -0,04335  | -0,06634 to -0,02036  | 3,698 | 0,0002             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,4853     | 0,5159       | -0,03066  | -0,05272 to -0,008596 | 2,725 | 0,0065             | **      |
| <b>Lateral Gyrus Left</b>                       |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4826     | 0,5276       | -0,045    | -0,06799 to -0,02201  | 3,839 | 0,0001             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,4804     | 0,5171       | -0,03669  | -0,05876 to -0,01463  | 3,262 | 0,0011             | **      |
| <b>Lateral Gyrus Right</b>                      |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4761     | 0,5282       | -0,05214  | -0,07513 to -0,02915  | 4,448 | <0,0001            | ****    |
| Males Gonadectomized vs. Females Gonadectomized | 0,4725     | 0,5081       | -0,03556  | -0,05763 to -0,0135   | 3,162 | 0,0016             | **      |
| <b>Medial Mamillary Nucleus Left</b>            |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,3947     | 0,3483       | 0,04637   | 0,02338 to 0,06936    | 3,956 | <0,0001            | ****    |
| Males Gonadectomized vs. Females Gonadectomized | 0,3615     | 0,3369       | 0,02457   | 0,002504 to 0,04663   | 2,184 | 0,0291             | *       |
| <b>Medial Mamillary Nucleus Right</b>           |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,3758     | 0,3316       | 0,04415   | 0,02116 to 0,06714    | 3,767 | 0,0002             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,346      | 0,3228       | 0,02318   | 0,001121 to 0,04525   | 2,061 | 0,0395             | *       |
| <b>Medial Septal Nucleus Left</b>               |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,3558     | 0,3852       | -0,02944  | -0,05243 to -0,006455 | 2,512 | 0,0121             | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,3612     | 0,385        | -0,02386  | -0,04592 to -0,001795 | 2,121 | 0,0341             | *       |
| <b>Occipital Lobe Left</b>                      |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4001     | 0,443        | -0,04296  | -0,06595 to -0,01997  | 3,665 | 0,0003             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,3982     | 0,4349       | -0,03663  | -0,0587 to -0,01457   | 3,257 | 0,0011             | **      |
| <b>Occipital Lobe Right</b>                     |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4175     | 0,4589       | -0,04142  | -0,06441 to -0,01844  | 3,534 | 0,0004             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,4182     | 0,4438       | -0,0256   | -0,04766 to -0,003535 | 2,276 | 0,023              | *       |
| <b>Olfactory Bulb Right</b>                     |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,2664     | 0,3154       | -0,04899  | -0,07198 to -0,026    | 4,18  | <0,0001            | ****    |
| Males Gonadectomized vs. Females Gonadectomized | 0,2749     | 0,3135       | -0,03868  | -0,06074 to -0,01661  | 3,438 | 0,0006             | ***     |
| <b>Orbital Gyrus Right</b>                      |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4071     | 0,4407       | -0,03356  | -0,05655 to -0,01058  | 2,864 | 0,0042             | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,4101     | 0,4337       | -0,02368  | -0,04574 to -0,001613 | 2,105 | 0,0355             | *       |
| <b>PostCruciate Gyrus Left</b>                  |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4971     | 0,4549       | 0,04219   | 0,0192 to 0,06518     | 3,6   | 0,0003             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,4891     | 0,4472       | 0,04187   | 0,01981 to 0,06393    | 3,722 | 0,0002             | ***     |
| <b>Posterior Sygmoideus Gyrus Left</b>          |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,3077     | 0,2794       | 0,02831   | 0,005325 to 0,0513    | 2,416 | 0,0158             | *       |
| Males Gonadectomized vs. Females Gonadectomized | 0,3027     | 0,274        | 0,02874   | 0,006673 to 0,0508    | 2,555 | 0,0107             | *       |
| <b>Posterior Sygmoideus Gyrus Right</b>         |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,3678     | 0,337        | 0,03078   | 0,007788 to 0,05377   | 2,626 | 0,0087             | **      |
| Males Gonadectomized vs. Females Gonadectomized | 0,363      | 0,3274       | 0,03554   | 0,01347 to 0,0576     | 3,159 | 0,0016             | **      |
| <b>Posterior Sylvian Gyrus Right</b>            |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4803     | 0,5318       | -0,05155  | -0,07454 to -0,02856  | 4,398 | <0,0001            | ****    |
| Males Gonadectomized vs. Females Gonadectomized | 0,4782     | 0,515        | -0,03686  | -0,05892 to -0,0148   | 3,277 | 0,0011             | **      |
| <b>Sylvian Gyrus Right</b>                      |            |              |           |                       |       |                    |         |
| Males Baseline vs. Females Baseline             | 0,4623     | 0,5024       | -0,0402   | -0,06318 to -0,01721  | 3,429 | 0,0006             | ***     |
| Males Gonadectomized vs. Females Gonadectomized | 0,4597     | 0,4886       | -0,02888  | -0,05094 to -0,006813 | 2,567 | 0,0103             | *       |

| Brain Region 1                        | Brain Region 2                                            | Mean functional connectivity Male baseline (Z score) | Mean functional connectivity Female baseline (Z score) |
|---------------------------------------|-----------------------------------------------------------|------------------------------------------------------|--------------------------------------------------------|
| Amygdala Left                         | Substantia Nigra Left                                     | 1,311                                                | 3,452                                                  |
| Amygdala Left                         | Globus Pallidum Left                                      | 2,148                                                | 1,805                                                  |
| Amygdala Right                        | Parahippocampal Cortex Right                              | 1,223                                                | 1,021                                                  |
| Amygdala Right                        | Substantia Nigra Right                                    | 0,845                                                | 1,507                                                  |
| Amygdala Right                        | Globus Pallidum Right                                     | 0,732                                                | -0,067                                                 |
| AnteriorSigmoides Gyrus Left          | Orbitofrontal Gyrus Left                                  | 1,446                                                | 1,935                                                  |
| AnteriorSigmoides Gyrus Left          | Precruciate Gyrus Left                                    | 0,622                                                | 1,501                                                  |
| AnteriorSigmoides Gyrus Left          | PostCruciate Gyrus Left                                   | 0,887                                                | 1,685                                                  |
| AnteriorSigmoides Gyrus Left          | Posterior Sygmoideus Gyrus Left                           | 0,372                                                | 0,703                                                  |
| AnteriorSigmoides Gyrus Right         | Cingulate Cortex Right                                    | 1,019                                                | 0,960                                                  |
| AnteriorSigmoides Gyrus Right         | Orbital Gyrus Right                                       | 0,585                                                | -0,354                                                 |
| AnteriorSigmoides Gyrus Right         | Orbitofrontal Gyrus Right                                 | 1,163                                                | 1,868                                                  |
| AnteriorSigmoides Gyrus Right         | Caudate Right                                             | 1,276                                                | 1,075                                                  |
| AnteriorSigmoides Gyrus Right         | Precruciate Gyrus Right                                   | 1,159                                                | 1,125                                                  |
| AnteriorSigmoides Gyrus Right         | Putamen Right                                             | 1,245                                                | 0,960                                                  |
| AnteriorSigmoides Gyrus Right         | Claustrocortex(Insula) Right                              | 1,213                                                | 1,599                                                  |
| AnteriorSigmoides Gyrus Right         | PostCruciate Gyrus Right                                  | 1,360                                                | 1,512                                                  |
| AnteriorSigmoides Gyrus Right         | Posterior Sygmoideus Gyrus Right                          | 1,141                                                | 0,650                                                  |
| AnteriorSigmoides Gyrus Right         | Sylvian Gyrus Right                                       | 1,070                                                | 0,855                                                  |
| Bed Nucleus of Stria Terminalis Left  | Lateral Septal Nucleus Left                               | 1,017                                                | 1,913                                                  |
| Bed Nucleus of Stria Terminalis Left  | Medial Septal Nucleus Left                                | 1,292                                                | 1,638                                                  |
| Bed Nucleus of Stria Terminalis Left  | Septum Left                                               | 1,054                                                | 1,776                                                  |
| Bed Nucleus of Stria Terminalis Left  | Preoptic Hypothalamic Area Left                           | 2,034                                                | 2,103                                                  |
| Bed Nucleus of Stria Terminalis Left  | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 1,773                                                | 2,092                                                  |
| Bed Nucleus of Stria Terminalis Left  | Caudate Left                                              | 0,523                                                | 1,668                                                  |
| Bed Nucleus of Stria Terminalis Left  | Globus Pallidum Left                                      | 1,194                                                | 0,931                                                  |
| Bed Nucleus of Stria Terminalis Left  | Putamen Left                                              | 0,329                                                | 0,977                                                  |
| Bed Nucleus of Stria Terminalis Left  | PostCruciate Gyrus Left                                   | 0,265                                                | 1,088                                                  |
| Bed Nucleus of Stria Terminalis Left  | SubFornical Organ Right                                   | 1,246                                                | 1,844                                                  |
| Bed Nucleus of Stria Terminalis Left  | Bed Nucleus of Stria Terminalis Right                     | 1,285                                                | 1,735                                                  |
| Bed Nucleus of Stria Terminalis Left  | Lateral Septal Nucleus Right                              | 0,629                                                | 1,532                                                  |
| Bed Nucleus of Stria Terminalis Left  | Septum Right                                              | 0,525                                                | 1,376                                                  |
| Bed Nucleus of Stria Terminalis Left  | Preoptic Hypothalamic Area Right                          | 1,542                                                | 1,735                                                  |
| Bed Nucleus of Stria Terminalis Right | Lateral Septal Nucleus Right                              | 1,154                                                | 1,660                                                  |
| Bed Nucleus of Stria Terminalis Right | Medial Septal Nucleus Right                               | 1,414                                                | 1,780                                                  |
| Bed Nucleus of Stria Terminalis Right | Septum Right                                              | 0,319                                                | 1,519                                                  |
| Bed Nucleus of Stria Terminalis Right | Preoptic Hypothalamic Area Right                          | 1,955                                                | 1,896                                                  |
| Bed Nucleus of Stria Terminalis Right | Caudate Right                                             | -0,261                                               | 1,093                                                  |
| Bed Nucleus of Stria Terminalis Right | Globus Pallidum Right                                     | 0,327                                                | 1,601                                                  |
| Bed Nucleus of Stria Terminalis Right | Putamen Right                                             | -0,336                                               | 1,525                                                  |
| Caudate Left                          | Globus Pallidum Left                                      | 1,302                                                | 0,969                                                  |
| Caudate Left                          | Putamen Left                                              | 1,533                                                | 2,379                                                  |
| Caudate Left                          | Claustrocortex(Insula) Left                               | 1,290                                                | 0,011                                                  |
| Caudate Left                          | PostCruciate Gyrus Left                                   | 0,753                                                | 0,528                                                  |
| Caudate Left                          | SubFornical Organ Right                                   | -0,954                                               | 0,930                                                  |
| Caudate Left                          | Bed Nucleus of Stria Terminalis Right                     | -0,289                                               | 0,981                                                  |
| Caudate Left                          | Septum Right                                              | 1,279                                                | 0,922                                                  |
| Caudate Left                          | Preoptic Hypothalamic Area Right                          | 0,543                                                | 1,115                                                  |
| Caudate Left                          | Caudate Right                                             | 1,047                                                | 0,867                                                  |
| Caudate Right                         | Globus Pallidum Right                                     | 0,759                                                | 1,362                                                  |
| Caudate Right                         | Precruciate Gyrus Right                                   | 0,821                                                | 0,779                                                  |
| Caudate Right                         | Putamen Right                                             | 1,591                                                | 2,012                                                  |
| Caudate Right                         | Claustrocortex(Insula) Right                              | 1,075                                                | 1,534                                                  |
| Caudate Right                         | PostCruciate Gyrus Right                                  | 1,159                                                | 1,515                                                  |
| Caudate Right                         | Posterior Sygmoideus Gyrus Right                          | 0,868                                                | 1,505                                                  |
| Caudate Right                         | Suprasylvian Gyrus Right                                  | 0,306                                                | 0,854                                                  |
| Caudate Right                         | Sylvian Gyrus Right                                       | 0,759                                                | 1,408                                                  |
| Cingulate Cortex Left                 | Orbitofrontal Gyrus Left                                  | 1,292                                                | 0,549                                                  |
| Cingulate Cortex Left                 | Hippocampus Left                                          | 0,163                                                | 1,108                                                  |
| Cingulate Cortex Left                 | Caudate Left                                              | 1,008                                                | 1,235                                                  |
| Cingulate Cortex Left                 | Precruciate Gyrus Left                                    | 1,605                                                | 2,187                                                  |
| Cingulate Cortex Left                 | Putamen Left                                              | 0,853                                                | 1,227                                                  |
| Cingulate Cortex Left                 | Thalamus Left                                             | 0,705                                                | 0,804                                                  |
| Cingulate Cortex Left                 | Lateral Gyrus Left                                        | 0,225                                                | 1,482                                                  |
| Cingulate Cortex Left                 | PostCruciate Gyrus Left                                   | 1,231                                                | 1,063                                                  |
| Cingulate Cortex Left                 | Posterior Sygmoideus Gyrus Left                           | 0,594                                                | 0,885                                                  |
| Cingulate Cortex Left                 | Suprasylvian Gyrus Left                                   | 0,763                                                | 0,684                                                  |
| Cingulate Cortex Left                 | Ectolateralis Gyrus Left                                  | -0,157                                               | 1,349                                                  |
| Cingulate Cortex Left                 | Entolateral Gyrus Left                                    | 1,118                                                | 0,943                                                  |
| Cingulate Cortex Left                 | Bed Nucleus of Stria Terminalis Right                     | -0,209                                               | 0,266                                                  |
| Cingulate Cortex Left                 | Medial Septal Nucleus Right                               | -0,468                                               | -0,210                                                 |
| Cingulate Cortex Left                 | Pineal Gland Right                                        | 0,595                                                | 0,551                                                  |
| Cingulate Cortex Left                 | Septum Right                                              | 1,042                                                | 1,050                                                  |
| Cingulate Cortex Left                 | Preoptic Hypothalamic Area Right                          | 0,636                                                | 0,395                                                  |
| Cingulate Cortex Left                 | AnteriorSigmoides Gyrus Right                             | 1,054                                                | 0,830                                                  |
| Cingulate Cortex Left                 | Cingulate Cortex Right                                    | 1,249                                                | 2,113                                                  |
| Cingulate Cortex Left                 | Orbitofrontal Gyrus Right                                 | 1,107                                                | 1,375                                                  |
| Cingulate Cortex Left                 | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 0,845                                                | 0,728                                                  |
| Cingulate Cortex Left                 | Caudate Right                                             | 1,055                                                | 1,130                                                  |
| Cingulate Cortex Left                 | Precruciate Gyrus Right                                   | 1,376                                                | 1,479                                                  |
| Cingulate Cortex Left                 | Putamen Right                                             | 0,917                                                | 0,268                                                  |
| Cingulate Cortex Left                 | Claustrocortex(Insula) Right                              | 0,988                                                | 1,079                                                  |
| Cingulate Cortex Left                 | Lateral Gyrus Right                                       | 0,592                                                | 0,787                                                  |
| Cingulate Cortex Left                 | PostCruciate Gyrus Right                                  | 1,013                                                | 1,285                                                  |
| Cingulate Cortex Left                 | Suprasylvian Gyrus Right                                  | 0,754                                                | 0,628                                                  |
| Cingulate Cortex Right                | Orbitofrontal Gyrus Right                                 | 1,230                                                | 1,517                                                  |
| Cingulate Cortex Right                | Hippocampus Right                                         | 1,173                                                | 1,344                                                  |
| Cingulate Cortex Right                | Caudate Right                                             | 1,049                                                | 1,066                                                  |
| Cingulate Cortex Right                | Precruciate Gyrus Right                                   | 1,385                                                | 1,673                                                  |
| Cingulate Cortex Right                | Putamen Right                                             | 0,949                                                | 0,301                                                  |
| Cingulate Cortex Right                | Thalamus Right                                            | 0,810                                                | 0,863                                                  |
| Cingulate Cortex Right                | Claustrocortex(Insula) Right                              | 1,150                                                | 1,390                                                  |
| Cingulate Cortex Right                | Lateral Gyrus Right                                       | 0,955                                                | 1,556                                                  |
| Cingulate Cortex Right                | PostCruciate Gyrus Right                                  | 1,244                                                | 1,282                                                  |
| Cingulate Cortex Right                | Posterior Sygmoideus Gyrus Right                          | 1,112                                                | 1,288                                                  |
| Cingulate Cortex Right                | Suprasylvian Gyrus Right                                  | 1,048                                                | 1,272                                                  |
| Cingulate Cortex Right                | Sylvian Gyrus Right                                       | 1,048                                                | 1,015                                                  |
| Cingulate Cortex Right                | Ectolateralis Gyrus Right                                 | 0,939                                                | 1,796                                                  |

|                                                          |                                                           |        |        |
|----------------------------------------------------------|-----------------------------------------------------------|--------|--------|
| Claustrocortex(Insula) Left                              | Sylvian Gyrus Left                                        | 0,944  | 0,346  |
| Claustrocortex(Insula) Right                             | Sylvian Gyrus Right                                       | 1,381  | 1,561  |
| Ectolateralis Gyrus Left                                 | Entolateral Gyrus Left                                    | -0,267 | 1,271  |
| Ectolateralis Gyrus Left                                 | Occipital Lobe Left                                       | 2,657  | 1,682  |
| Ectolateralis Gyrus Left                                 | Lateral Gyrus Right                                       | -0,085 | 0,948  |
| Geniculate Nucleus Left                                  | Thalamus Left                                             | 1,797  | 2,872  |
| Geniculate Nucleus Left                                  | Midbrain Left                                             | 0,203  | 1,025  |
| Geniculate Nucleus Right                                 | Thalamus Right                                            | 1,801  | 0,225  |
| Globus Pallidum Left                                     | Putamen Left                                              | 0,621  | 1,291  |
| Globus Pallidum Right                                    | Putamen Right                                             | 0,485  | 1,770  |
| Gyrus Rectus Left                                        | Olfactory Bulb Left                                       | 2,989  | 2,483  |
| Gyrus Rectus Left                                        | Gyrus Rectus Right                                        | 2,883  | 2,094  |
| Gyrus Rectus Right                                       | Olfactory Bulb Right                                      | 2,231  | 2,710  |
| Hippocampus Left                                         | Parahippocampal Cortex Left                               | -0,225 | 1,241  |
| Hippocampus Left                                         | Geniculate Nucleus Left                                   | 1,009  | 2,304  |
| Hippocampus Left                                         | Thalamus Left                                             | 0,455  | 2,052  |
| Hippocampus Left                                         | Lateral Gyrus Left                                        | 0,524  | 1,795  |
| Hippocampus Left                                         | Suprasylvian Gyrus Left                                   | 0,572  | 2,436  |
| Hippocampus Left                                         | Ectolateralis Gyrus Left                                  | 0,528  | 1,865  |
| Hippocampus Left                                         | Midbrain Left                                             | -0,702 | 1,017  |
| Hippocampus Left                                         | Pineal Gland Right                                        | -0,915 | 0,854  |
| Hippocampus Left                                         | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 0,175  | 1,284  |
| Hippocampus Left                                         | Periaqueductal Grey Substance Right                       | -1,578 | -0,655 |
| Hippocampus Right                                        | Parahippocampal Cortex Right                              | 0,858  | 1,224  |
| Hippocampus Right                                        | Geniculate Nucleus Right                                  | 1,061  | 0,727  |
| Hippocampus Right                                        | Periaqueductal Grey Substance Right                       | 1,602  | 0,235  |
| Hippocampus Right                                        | Thalamus Right                                            | 0,940  | 0,796  |
| Hippocampus Right                                        | Suprasylvian Gyrus Right                                  | 1,143  | 1,893  |
| Lateral Gyrus Left                                       | Suprasylvian Gyrus Left                                   | 0,877  | 1,772  |
| Lateral Gyrus Left                                       | Ectolateralis Gyrus Left                                  | 2,332  | 2,461  |
| Lateral Gyrus Left                                       | Entolateral Gyrus Left                                    | 0,144  | 2,306  |
| Lateral Gyrus Left                                       | Occipital Lobe Left                                       | 2,382  | 1,454  |
| Lateral Gyrus Left                                       | Pineal Gland Right                                        | 1,109  | 0,802  |
| Lateral Gyrus Left                                       | Lateral Gyrus Right                                       | 0,158  | 0,756  |
| Lateral Gyrus Right                                      | Suprasylvian Gyrus Right                                  | 1,306  | 1,849  |
| Lateral Septal Nucleus Left                              | Medial Septal Nucleus Left                                | 1,060  | 2,146  |
| Lateral Septal Nucleus Left                              | Septum Left                                               | -0,136 | 0,654  |
| Lateral Septal Nucleus Left                              | Preoptic Hypothalamic Area Left                           | 1,236  | 1,554  |
| Lateral Septal Nucleus Left                              | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 2,579  | 2,331  |
| Lateral Septal Nucleus Left                              | Substantia Nigra Left                                     | 1,295  | 0,142  |
| Lateral Septal Nucleus Left                              | Globus Pallidum Left                                      | -0,012 | 1,548  |
| Lateral Septal Nucleus Left                              | Medial Mamillary Nucleus Right                            | 1,400  | 0,503  |
| Lateral Septal Nucleus Left                              | SubFornical Organ Right                                   | 2,200  | 1,703  |
| Lateral Septal Nucleus Left                              | Bed Nucleus of Stria Terminalis Right                     | 1,220  | 1,082  |
| Lateral Septal Nucleus Left                              | Lateral Septal Nucleus Right                              | 2,345  | 1,966  |
| Lateral Septal Nucleus Left                              | Preoptic Hypothalamic Area Right                          | 0,751  | 0,933  |
| Lateral Septal Nucleus Right                             | Medial Septal Nucleus Right                               | 1,650  | 1,786  |
| Lateral Septal Nucleus Right                             | Preoptic Hypothalamic Area Right                          | 0,654  | 1,188  |
| Lateral Septal Nucleus Right                             | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | -0,590 | -0,473 |
| Lateral Septal Nucleus Right                             | Substantia Nigra Right                                    | 0,394  | 1,001  |
| Lateral Septal Nucleus Right                             | Globus Pallidum Right                                     | -0,520 | 0,729  |
| Medial Mamillary Nucleus Left                            | Lateral Septal Nucleus Left                               | 1,344  | 1,154  |
| Medial Mamillary Nucleus Left                            | Medial Septal Nucleus Left                                | 0,295  | 1,242  |
| Medial Mamillary Nucleus Left                            | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 0,756  | 0,803  |
| Medial Mamillary Nucleus Left                            | Substantia Nigra Left                                     | 1,705  | 1,286  |
| Medial Mamillary Nucleus Left                            | Medial Mamillary Nucleus Right                            | 2,064  | 2,104  |
| Medial Mamillary Nucleus Right                           | Lateral Septal Nucleus Right                              | 1,502  | 1,414  |
| Medial Mamillary Nucleus Right                           | Substantia Nigra Right                                    | 1,079  | 0,993  |
| Medial Mamillary Nucleus Right                           | Pituitary Gland Right                                     | 1,235  | 1,002  |
| Medial Septal Nucleus Left                               | Preoptic Hypothalamic Area Left                           | 1,645  | 1,393  |
| Medial Septal Nucleus Left                               | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 1,009  | 1,581  |
| Medial Septal Nucleus Left                               | Substantia Nigra Left                                     | 0,551  | 1,268  |
| Medial Septal Nucleus Left                               | Caudate Left                                              | 0,253  | 0,218  |
| Medial Septal Nucleus Left                               | Globus Pallidum Left                                      | 1,230  | 2,072  |
| Medial Septal Nucleus Left                               | SubFornical Organ Right                                   | 0,540  | 0,456  |
| Medial Septal Nucleus Left                               | Lateral Septal Nucleus Right                              | 0,646  | 0,673  |
| Medial Septal Nucleus Left                               | Medial Septal Nucleus Right                               | -0,039 | 0,861  |
| Medial Septal Nucleus Left                               | Preoptic Hypothalamic Area Right                          | -0,213 | 0,185  |
| Medial Septal Nucleus Right                              | Preoptic Hypothalamic Area Right                          | 0,210  | 1,479  |
| Medial Septal Nucleus Right                              | Substantia Nigra Right                                    | -0,246 | -0,336 |
| Medial Septal Nucleus Right                              | Caudate Right                                             | -1,551 | 0,448  |
| Medial Septal Nucleus Right                              | Globus Pallidum Right                                     | -0,243 | 1,625  |
| Medial Septal Nucleus Right                              | Putamen Right                                             | -1,611 | 0,781  |
| Midbrain Left                                            | Pineal Gland Right                                        | 1,446  | 1,172  |
| Midbrain Left                                            | Pons Right                                                | 1,269  | -0,536 |
| Midbrain Left                                            | Hippocampus Right                                         | 1,305  | 0,155  |
| Midbrain Left                                            | Periaqueductal Grey Substance Right                       | 1,311  | -1,194 |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Globus Pallidum Left                                      | 0,679  | 1,534  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Putamen Left                                              | -0,790 | 0,040  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | SubFornical Organ Right                                   | 1,741  | 1,597  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Bed Nucleus of Stria Terminalis Right                     | 0,689  | 1,267  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Lateral Septal Nucleus Right                              | 1,639  | 1,392  |
| Olfactory Bulb Left                                      | Gyrus Rectus Right                                        | 2,658  | 2,390  |
| Orbital Gyrus Left                                       | Orbitofrontal Gyrus Left                                  | 0,935  | 0,824  |
| Orbital Gyrus Left                                       | Precruciate Gyrus Left                                    | 0,657  | -0,021 |
| Orbital Gyrus Left                                       | Gyrus Rectus Left                                         | 2,899  | 0,806  |
| Orbital Gyrus Left                                       | Claustrocortex(Insula) Left                               | 0,824  | 2,944  |
| Orbital Gyrus Right                                      | Orbitofrontal Gyrus Right                                 | 0,362  | -0,001 |
| Orbital Gyrus Right                                      | Precruciate Gyrus Right                                   | 1,012  | 1,563  |
| Orbital Gyrus Right                                      | Gyrus Rectus Right                                        | 0,967  | 1,447  |
| Orbital Gyrus Right                                      | Olfactory Bulb Right                                      | 0,333  | 0,547  |
| Orbital Gyrus Right                                      | Claustrocortex(Insula) Right                              | 0,168  | -0,086 |
| Orbitofrontal Gyrus Left                                 | Precruciate Gyrus Left                                    | 0,680  | 1,103  |
| Orbitofrontal Gyrus Left                                 | Claustrocortex(Insula) Left                               | 1,596  | 2,134  |
| Orbitofrontal Gyrus Right                                | Precruciate Gyrus Right                                   | 1,236  | 1,380  |
| Orbitofrontal Gyrus Right                                | Claustrocortex(Insula) Right                              | 1,170  | 0,891  |
| Parahippocampal Cortex Left                              | Thalamus Left                                             | 0,160  | 1,725  |
| Parahippocampal Cortex Left                              | Suprasylvian Gyrus Left                                   | 0,071  | 1,348  |
| Parahippocampal Cortex Left                              | Sylvian Gyrus Left                                        | 1,144  | 1,953  |
| Parahippocampal Cortex Left                              | Ectolateralis Gyrus Left                                  | -1,481 | 1,166  |
| Parahippocampal Cortex Left                              | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 1,831  | 2,215  |



|                                    |                                                          |        |        |
|------------------------------------|----------------------------------------------------------|--------|--------|
| Parahippocampal Cortex Right       | Substantia Nigra Right                                   | 0.353  | -0.863 |
| Parahippocampal Cortex Right       | Suprasylvian Gyrus Right                                 | 1.003  | 1.346  |
| Parahippocampal Cortex Right       | Sylvian Gyrus Right                                      | 1.128  | 1.667  |
| Periaqueductal Grey Substance Left | Midbrain Left                                            | 0.484  | -1.438 |
| Periaqueductal Grey Substance Left | Pons Right                                               | 1.159  | 0.518  |
| Periaqueductal Grey Substance Left | Periaqueductal Grey Substance Right                      | 1.084  | 2.084  |
| Pineal Gland Left                  | Pons Left                                                | -0.010 | 0.497  |
| Pineal Gland Left                  | Cingulate Cortex Left                                    | -0.045 | 0.549  |
| Pineal Gland Left                  | Hippocampus Left                                         | -0.236 | 1.357  |
| Pineal Gland Left                  | Geniculate Nucleus Left                                  | 0.412  | 1.156  |
| Pineal Gland Left                  | Periaqueductal Grey Substance Left                       | 0.092  | -0.240 |
| Pineal Gland Left                  | Thalamus Left                                            | 0.542  | 0.987  |
| Pineal Gland Left                  | Lateral Gyrus Left                                       | 1.494  | 1.237  |
| Pineal Gland Left                  | Entolateral Gyrus Left                                   | -0.625 | 1.246  |
| Pineal Gland Left                  | Midbrain Left                                            | 0.762  | 1.728  |
| Pineal Gland Left                  | Pineal Gland Right                                       | 1.881  | 2.681  |
| Pineal Gland Left                  | Hippocampus Right                                        | 0.905  | 0.545  |
| Pineal Gland Left                  | Periaqueductal Grey Substance Right                      | 1.296  | -0.870 |
| Pineal Gland Right                 | Hippocampus Right                                        | 1.176  | 0.669  |
| Pineal Gland Right                 | Periaqueductal Grey Substance Right                      | 1.504  | -0.585 |
| Pituitary Gland Left               | Pituitary Gland Right                                    | 2.314  | 2.184  |
| Pons Left                          | Periaqueductal Grey Substance Left                       | 1.573  | 1.460  |
| Pons Left                          | Midbrain Left                                            | 0.343  | 0.017  |
| Pons Left                          | Pons Right                                               | 1.044  | 1.526  |
| Pons Left                          | Periaqueductal Grey Substance Right                      | 0.817  | 1.364  |
| Pons Right                         | Periaqueductal Grey Substance Right                      | 1.849  | 0.564  |
| PostCruciate Gyrus Left            | Posterior Sygmoideus Gyrus Left                          | 1.150  | 1.807  |
| PostCruciate Gyrus Left            | Septum Right                                             | 0.993  | 0.885  |
| PostCruciate Gyrus Left            | Preoptic Hypothalamic Area Right                         | 0.376  | 0.876  |
| PostCruciate Gyrus Right           | Posterior Sygmoideus Gyrus Right                         | 1.255  | 1.142  |
| PostCruciate Gyrus Right           | Sylvian Gyrus Right                                      | 1.030  | 0.823  |
| Posterior Sygmoideus Gyrus Left    | Sylvian Gyrus Left                                       | 0.864  | 0.986  |
| Posterior Sygmoideus Gyrus Left    | Posterior Sygmoideus Gyrus Right                         | 0.766  | 0.446  |
| Posterior Sygmoideus Gyrus Right   | Sylvian Gyrus Right                                      | 1.355  | 1.173  |
| Posterior Sylvian Gyrus Left       | Hippocampus Left                                         | 1.009  | 0.836  |
| Posterior Sylvian Gyrus Left       | Parahippocampal Cortex Left                              | -0.483 | -0.249 |
| Posterior Sylvian Gyrus Left       | Suprasylvian Gyrus Left                                  | 0.798  | 1.657  |
| Posterior Sylvian Gyrus Left       | Ectolateralis Gyrus Left                                 | 0.437  | 0.279  |
| Posterior Sylvian Gyrus Right      | Temporal Lobe Right                                      | 1.423  | 2.239  |
| Posterior Sylvian Gyrus Right      | Suprasylvian Gyrus Right                                 | 1.078  | 1.773  |
| Precruciate Gyrus Left             | Claustrocortex(Insula) Left                              | 0.981  | 0.668  |
| Precruciate Gyrus Left             | Precruciate Gyrus Right                                  | 1.373  | 1.764  |
| Precruciate Gyrus Right            | Gyrus Rectus Right                                       | 0.480  | 1.524  |
| Precruciate Gyrus Right            | Claustrocortex(Insula) Right                             | 1.020  | 0.722  |
| Precruciate Gyrus Right            | PostCruciate Gyrus Right                                 | 1.044  | 0.376  |
| Preoptic Hypothalamic Area Left    | Nucleus Of The Horizontal Limb Of The Diagonal Band Left | 1.691  | 1.901  |
| Preoptic Hypothalamic Area Left    | Caudate Left                                             | 0.298  | 1.499  |
| Preoptic Hypothalamic Area Left    | Globus Pallidum Left                                     | 0.627  | 1.494  |
| Preoptic Hypothalamic Area Left    | Putamen Left                                             | -0.081 | 1.118  |
| Preoptic Hypothalamic Area Left    | PostCruciate Gyrus Left                                  | 0.141  | 0.619  |
| Preoptic Hypothalamic Area Left    | Medial Mamillary Nucleus Right                           | -0.011 | 0.471  |
| Preoptic Hypothalamic Area Left    | SubFornical Organ Right                                  | 1.523  | 1.668  |
| Preoptic Hypothalamic Area Left    | Bed Nucleus of Stria Terminalis Right                    | 0.845  | 1.355  |
| Preoptic Hypothalamic Area Left    | Lateral Septal Nucleus Right                             | 1.056  | 1.406  |
| Preoptic Hypothalamic Area Left    | Medial Septal Nucleus Right                              | 0.426  | 1.718  |
| Preoptic Hypothalamic Area Left    | Septum Right                                             | 0.079  | 0.627  |
| Preoptic Hypothalamic Area Left    | Preoptic Hypothalamic Area Right                         | 1.662  | 1.834  |
| Preoptic Hypothalamic Area Left    | Caudate Right                                            | -0.121 | 0.465  |
| Preoptic Hypothalamic Area Left    | Globus Pallidum Right                                    | 0.046  | 0.830  |
| Preoptic Hypothalamic Area Right   | Cingulate Cortex Right                                   | -0.149 | 0.599  |
| Preoptic Hypothalamic Area Right   | Substantia Nigra Right                                   | -0.064 | 0.370  |
| Preoptic Hypothalamic Area Right   | Caudate Right                                            | 0.525  | 1.290  |
| Preoptic Hypothalamic Area Right   | Globus Pallidum Right                                    | 0.497  | 1.647  |
| Preoptic Hypothalamic Area Right   | Putamen Right                                            | 0.405  | 1.669  |
| Preoptic Hypothalamic Area Right   | PostCruciate Gyrus Right                                 | 0.035  | 1.466  |
| Putamen Left                       | Claustrocortex(Insula) Left                              | 1.313  | 1.129  |
| Putamen Left                       | PostCruciate Gyrus Left                                  | 0.294  | -0.109 |
| Putamen Left                       | Bed Nucleus of Stria Terminalis Right                    | -0.539 | 0.429  |
| Putamen Left                       | Septum Right                                             | 1.212  | 0.013  |
| Putamen Right                      | Claustrocortex(Insula) Right                             | 0.999  | 1.157  |
| Putamen Right                      | PostCruciate Gyrus Right                                 | 1.025  | 0.706  |
| Putamen Right                      | Sylvian Gyrus Right                                      | 0.692  | 0.431  |
| Septum Left                        | Preoptic Hypothalamic Area Left                          | 1.030  | 1.526  |
| Septum Left                        | Nucleus Of The Horizontal Limb Of The Diagonal Band Left | 0.172  | 1.259  |
| Septum Left                        | Caudate Left                                             | 1.230  | 1.777  |
| Septum Left                        | Globus Pallidum Left                                     | 0.554  | 0.156  |
| Septum Left                        | Putamen Left                                             | 1.126  | 1.397  |
| Septum Left                        | PostCruciate Gyrus Left                                  | 0.750  | 1.134  |
| Septum Left                        | SubFornical Organ Right                                  | 0.366  | 1.492  |
| Septum Left                        | Bed Nucleus of Stria Terminalis Right                    | 1.460  | 1.609  |
| Septum Left                        | Lateral Septal Nucleus Right                             | -0.217 | 1.235  |
| Septum Left                        | Medial Septal Nucleus Right                              | -0.383 | 0.888  |
| Septum Left                        | Septum Right                                             | 1.631  | 2.003  |
| Septum Left                        | Preoptic Hypothalamic Area Right                         | 1.909  | 1.622  |
| Septum Left                        | Caudate Right                                            | 1.054  | 1.662  |
| Septum Left                        | Globus Pallidum Right                                    | 0.162  | 0.609  |
| Septum Left                        | Putamen Right                                            | 0.953  | 1.309  |
| Septum Right                       | Preoptic Hypothalamic Area Right                         | 1.163  | 1.236  |
| Septum Right                       | Caudate Right                                            | 1.320  | 1.918  |
| Septum Right                       | Globus Pallidum Right                                    | 0.165  | 0.551  |
| Septum Right                       | Putamen Right                                            | 1.248  | 1.385  |
| SubFornical Organ Left             | Bed Nucleus of Stria Terminalis Left                     | 1.501  | 1.934  |
| SubFornical Organ Left             | Lateral Septal Nucleus Left                              | 2.153  | 2.226  |
| SubFornical Organ Left             | Medial Septal Nucleus Left                               | 1.178  | 1.707  |
| SubFornical Organ Left             | Septum Left                                              | -0.013 | 1.324  |
| SubFornical Organ Left             | Preoptic Hypothalamic Area Left                          | 1.836  | 2.001  |
| SubFornical Organ Left             | Nucleus Of The Horizontal Limb Of The Diagonal Band Left | 2.280  | 2.176  |
| SubFornical Organ Left             | Caudate Left                                             | -0.668 | 1.164  |
| SubFornical Organ Left             | Globus Pallidum Left                                     | 0.049  | 1.127  |
| SubFornical Organ Left             | Medial Mamillary Nucleus Right                           | 0.813  | 0.308  |
| SubFornical Organ Left             | SubFornical Organ Right                                  | 2.676  | 2.205  |



|                          |                                                           |        |        |
|--------------------------|-----------------------------------------------------------|--------|--------|
| SubFornical Organ Left   | Bed Nucleus of Stria Terminalis Right                     | 1,896  | 1,799  |
| SubFornical Organ Left   | Lateral Septal Nucleus Right                              | 2,306  | 1,928  |
| SubFornical Organ Left   | Medial Septal Nucleus Right                               | 1,501  | 1,644  |
| SubFornical Organ Left   | Septum Right                                              | -0,558 | 0,896  |
| SubFornical Organ Left   | Preoptic Hypothalamic Area Right                          | 1,509  | 1,775  |
| SubFornical Organ Left   | Globus Pallidum Right                                     | -0,005 | 0,713  |
| SubFornical Organ Right  | Bed Nucleus of Stria Terminalis Right                     | 2,571  | 2,014  |
| SubFornical Organ Right  | Lateral Septal Nucleus Right                              | 2,459  | 2,110  |
| SubFornical Organ Right  | Medial Septal Nucleus Right                               | 1,842  | 1,882  |
| SubFornical Organ Right  | Septum Right                                              | -0,581 | 1,120  |
| SubFornical Organ Right  | Preoptic Hypothalamic Area Right                          | 1,568  | 1,854  |
| SubFornical Organ Right  | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | -0,588 | -0,140 |
| SubFornical Organ Right  | Globus Pallidum Right                                     | -0,135 | 1,102  |
| Substantia Nigra Left    | Globus Pallidum Left                                      | 0,643  | 1,423  |
| Substantia Nigra Right   | Globus Pallidum Right                                     | 0,262  | -0,682 |
| Suprasylvian Gyrus Left  | Sylvian Gyrus Left                                        | 0,452  | 1,061  |
| Suprasylvian Gyrus Left  | Ectolateralis Gyrus Left                                  | 1,257  | 1,904  |
| Suprasylvian Gyrus Left  | Occipital Lobe Left                                       | 1,074  | 0,944  |
| Suprasylvian Gyrus Right | Sylvian Gyrus Right                                       | 1,099  | 1,058  |
| Temporal Lobe Left       | Hippocampus Left                                          | -0,132 | 1,036  |
| Temporal Lobe Left       | Parahippocampal Cortex Left                               | 1,329  | 1,377  |
| Temporal Lobe Left       | Suprasylvian Gyrus Left                                   | 0,478  | 1,050  |
| Temporal Lobe Left       | Sylvian Gyrus Left                                        | 1,117  | 1,016  |
| Temporal Lobe Left       | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 1,324  | 1,307  |
| Temporal Lobe Right      | Hippocampus Right                                         | 0,866  | 1,823  |
| Temporal Lobe Right      | Parahippocampal Cortex Right                              | 0,647  | 1,359  |
| Temporal Lobe Right      | Suprasylvian Gyrus Right                                  | 0,977  | 1,320  |
| Temporal Lobe Right      | Sylvian Gyrus Right                                       | 1,124  | 1,638  |
| Thalamus Left            | Midbrain Left                                             | 0,631  | 0,983  |
| Thalamus Left            | Pineal Gland Right                                        | 0,591  | 0,787  |
| Thalamus Left            | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 0,632  | 1,585  |
| Thalamus Left            | Thalamus Right                                            | 1,512  | -0,166 |

| Brain Region 1                        | Brain Region 2                                            | Mean functional connectivity Male castrated (Z score) | Mean functional connectivity Female castrated (Z score) |
|---------------------------------------|-----------------------------------------------------------|-------------------------------------------------------|---------------------------------------------------------|
| Amygdala Left                         | Parahippocampal Cortex Left                               | 1.151                                                 | 0.229                                                   |
| Amygdala Left                         | Substantia Nigra Left                                     | 1.986                                                 | 1.828                                                   |
| Amygdala Left                         | Globus Pallidum Left                                      | 1.519                                                 | 1.450                                                   |
| Amygdala Right                        | Parahippocampal Cortex Right                              | 0.955                                                 | 1.265                                                   |
| Amygdala Right                        | Substantia Nigra Right                                    | 2.025                                                 | 0.577                                                   |
| Amygdala Right                        | Globus Pallidum Right                                     | 1.151                                                 | -0.136                                                  |
| AnteriorSigmoides Gyrus Left          | Orbitofrontal Gyrus Left                                  | 0.899                                                 | 2.907                                                   |
| AnteriorSigmoides Gyrus Left          | Precruciate Gyrus Left                                    | 1.270                                                 | 1.522                                                   |
| AnteriorSigmoides Gyrus Left          | PostCruciate Gyrus Left                                   | 1.643                                                 | 0.513                                                   |
| AnteriorSigmoides Gyrus Right         | Cingulate Cortex Right                                    | 1.106                                                 | 0.836                                                   |
| AnteriorSigmoides Gyrus Right         | Orbital Gyrus Right                                       | -0.446                                                | 0.401                                                   |
| AnteriorSigmoides Gyrus Right         | Orbitofrontal Gyrus Right                                 | 1.382                                                 | 1.759                                                   |
| AnteriorSigmoides Gyrus Right         | Precruciate Gyrus Right                                   | 1.852                                                 | 1.174                                                   |
| AnteriorSigmoides Gyrus Right         | Putamen Right                                             | 0.011                                                 | 0.213                                                   |
| AnteriorSigmoides Gyrus Right         | Claustrocortex(Insula) Right                              | -0.775                                                | 1.323                                                   |
| AnteriorSigmoides Gyrus Right         | PostCruciate Gyrus Right                                  | 1.712                                                 | 1.891                                                   |
| AnteriorSigmoides Gyrus Right         | Posterior Symgmoideus Gyrus Right                         | 1.060                                                 | 1.902                                                   |
| AnteriorSigmoides Gyrus Right         | Sylvian Gyrus Right                                       | -0.290                                                | 0.801                                                   |
| Bed Nucleus of Stria Terminalis Left  | Lateral Septal Nucleus Left                               | 1.548                                                 | 1.599                                                   |
| Bed Nucleus of Stria Terminalis Left  | Medial Septal Nucleus Left                                | 1.510                                                 | 1.430                                                   |
| Bed Nucleus of Stria Terminalis Left  | Septum Left                                               | 1.871                                                 | 2.347                                                   |
| Bed Nucleus of Stria Terminalis Left  | Preoptic Hypothalamic Area Left                           | 1.725                                                 | 2.130                                                   |
| Bed Nucleus of Stria Terminalis Left  | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 1.895                                                 | 2.243                                                   |
| Bed Nucleus of Stria Terminalis Left  | Caudate Left                                              | 1.023                                                 | 1.906                                                   |
| Bed Nucleus of Stria Terminalis Left  | Globus Pallidum Left                                      | 0.672                                                 | 1.561                                                   |
| Bed Nucleus of Stria Terminalis Left  | Putamen Left                                              | 0.628                                                 | 1.166                                                   |
| Bed Nucleus of Stria Terminalis Left  | SubFormical Organ Right                                   | 1.160                                                 | 1.253                                                   |
| Bed Nucleus of Stria Terminalis Left  | Bed Nucleus of Stria Terminalis Right                     | 0.674                                                 | 1.683                                                   |
| Bed Nucleus of Stria Terminalis Left  | Lateral Septal Nucleus Right                              | 0.815                                                 | 0.452                                                   |
| Bed Nucleus of Stria Terminalis Left  | Septum Right                                              | 0.829                                                 | 1.310                                                   |
| Bed Nucleus of Stria Terminalis Left  | Preoptic Hypothalamic Area Right                          | 1.121                                                 | 1.786                                                   |
| Bed Nucleus of Stria Terminalis Right | Lateral Septal Nucleus Right                              | 1.851                                                 | 1.622                                                   |
| Bed Nucleus of Stria Terminalis Right | Medial Septal Nucleus Right                               | 1.735                                                 | 2.407                                                   |
| Bed Nucleus of Stria Terminalis Right | Septum Right                                              | 0.480                                                 | 1.670                                                   |
| Bed Nucleus of Stria Terminalis Right | Preoptic Hypothalamic Area Right                          | 1.934                                                 | 2.301                                                   |
| Bed Nucleus of Stria Terminalis Right | Caudate Right                                             | 0.604                                                 | 0.704                                                   |
| Bed Nucleus of Stria Terminalis Right | Globus Pallidum Right                                     | 0.329                                                 | 1.061                                                   |
| Bed Nucleus of Stria Terminalis Right | Putamen Right                                             | -0.239                                                | 0.583                                                   |
| Caudate Left                          | Globus Pallidum Left                                      | 1.131                                                 | 1.539                                                   |
| Caudate Left                          | Putamen Left                                              | 1.599                                                 | 1.993                                                   |
| Caudate Left                          | Thalamus Left                                             | 0.212                                                 | 0.142                                                   |
| Caudate Left                          | Claustrocortex(Insula) Left                               | 1.502                                                 | 0.480                                                   |
| Caudate Left                          | PostCruciate Gyrus Left                                   | 1.755                                                 | 1.303                                                   |
| Caudate Left                          | Bed Nucleus of Stria Terminalis Right                     | 1.222                                                 | 0.843                                                   |
| Caudate Left                          | Septum Right                                              | 0.347                                                 | 0.734                                                   |
| Caudate Left                          | Preoptic Hypothalamic Area Right                          | 1.453                                                 | 1.063                                                   |
| Caudate Left                          | Cingulate Cortex Right                                    | 0.640                                                 | 0.188                                                   |
| Caudate Left                          | Caudate Right                                             | 1.026                                                 | 0.352                                                   |
| Caudate Right                         | Globus Pallidum Right                                     | 1.365                                                 | 2.068                                                   |
| Caudate Right                         | Putamen Right                                             | 2.242                                                 | 2.444                                                   |
| Caudate Right                         | Claustrocortex(Insula) Right                              | 0.457                                                 | 2.147                                                   |
| Caudate Right                         | PostCruciate Gyrus Right                                  | 1.425                                                 | 0.287                                                   |
| Caudate Right                         | Posterior Symgmoideus Gyrus Right                         | 0.992                                                 | 1.625                                                   |
| Caudate Right                         | Sylvian Gyrus Right                                       | 1.023                                                 | 0.390                                                   |
| Cingulate Cortex Left                 | Orbital Gyrus Left                                        | 1.032                                                 | -0.108                                                  |
| Cingulate Cortex Left                 | Orbitofrontal Gyrus Left                                  | 0.824                                                 | -0.392                                                  |
| Cingulate Cortex Left                 | Hippocampus Left                                          | 1.069                                                 | 0.263                                                   |
| Cingulate Cortex Left                 | Caudate Left                                              | 0.565                                                 | 0.581                                                   |
| Cingulate Cortex Left                 | Precruciate Gyrus Left                                    | 1.347                                                 | 1.104                                                   |
| Cingulate Cortex Left                 | Putamen Left                                              | 0.556                                                 | 0.203                                                   |
| Cingulate Cortex Left                 | Gyrus Rectus Left                                         | 0.756                                                 | 1.257                                                   |
| Cingulate Cortex Left                 | Geniculate Nucleus Left                                   | 0.038                                                 | -1.093                                                  |
| Cingulate Cortex Left                 | Thalamus Left                                             | 0.154                                                 | -0.522                                                  |
| Cingulate Cortex Left                 | Claustrocortex(Insula) Left                               | 0.779                                                 | 0.414                                                   |
| Cingulate Cortex Left                 | Lateral Gyrus Left                                        | 0.749                                                 | -0.309                                                  |
| Cingulate Cortex Left                 | PostCruciate Gyrus Left                                   | 1.210                                                 | 0.965                                                   |
| Cingulate Cortex Left                 | Posterior Symgmoideus Gyrus Left                          | 1.402                                                 | -0.454                                                  |
| Cingulate Cortex Left                 | Suprasylvian Gyrus Left                                   | 0.887                                                 | 0.019                                                   |
| Cingulate Cortex Left                 | Sylvian Gyrus Left                                        | 0.037                                                 | -0.727                                                  |
| Cingulate Cortex Left                 | Ectolateralis Gyrus Left                                  | 0.750                                                 | -0.370                                                  |
| Cingulate Cortex Left                 | Entolateral Gyrus Left                                    | 1.809                                                 | 0.731                                                   |
| Cingulate Cortex Left                 | Midbrain Left                                             | 0.413                                                 | 0.200                                                   |
| Cingulate Cortex Left                 | Septum Right                                              | 0.624                                                 | 0.682                                                   |
| Cingulate Cortex Left                 | AnteriorSigmoides Gyrus Right                             | -0.213                                                | 1.076                                                   |
| Cingulate Cortex Left                 | Cingulate Cortex Right                                    | 1.854                                                 | 1.689                                                   |
| Cingulate Cortex Left                 | Orbital Gyrus Right                                       | 0.773                                                 | -0.117                                                  |
| Cingulate Cortex Left                 | Orbitofrontal Gyrus Right                                 | 1.258                                                 | 1.006                                                   |
| Cingulate Cortex Left                 | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 0.648                                                 | 0.057                                                   |
| Cingulate Cortex Left                 | Caudate Right                                             | 0.125                                                 | 0.705                                                   |
| Cingulate Cortex Left                 | Precruciate Gyrus Right                                   | 0.107                                                 | 1.094                                                   |
| Cingulate Cortex Left                 | Putamen Right                                             | 0.439                                                 | -0.015                                                  |
| Cingulate Cortex Left                 | Claustrocortex(Insula) Right                              | 0.601                                                 | 1.431                                                   |
| Cingulate Cortex Left                 | Lateral Gyrus Right                                       | 0.046                                                 | 0.120                                                   |
| Cingulate Cortex Left                 | PostCruciate Gyrus Right                                  | -0.408                                                | 1.267                                                   |
| Cingulate Cortex Left                 | Posterior Symgmoideus Gyrus Right                         | -0.308                                                | 0.190                                                   |
| Cingulate Cortex Left                 | Sylvian Gyrus Right                                       | 0.523                                                 | 0.414                                                   |
| Cingulate Cortex Left                 | Entolateral Gyrus Right                                   | 0.612                                                 | 0.800                                                   |
| Cingulate Cortex Right                | Orbital Gyrus Right                                       | 0.250                                                 | 0.954                                                   |
| Cingulate Cortex Right                | Orbitofrontal Gyrus Right                                 | 1.485                                                 | 0.833                                                   |
| Cingulate Cortex Right                | Hippocampus Right                                         | 0.643                                                 | 0.991                                                   |
| Cingulate Cortex Right                | Caudate Right                                             | 0.727                                                 | 0.600                                                   |
| Cingulate Cortex Right                | Precruciate Gyrus Right                                   | 1.329                                                 | 1.380                                                   |
| Cingulate Cortex Right                | Putamen Right                                             | 0.640                                                 | -0.206                                                  |
| Cingulate Cortex Right                | Periaqueductal Grey Substance Right                       | 0.440                                                 | 0.908                                                   |
| Cingulate Cortex Right                | Claustrocortex(Insula) Right                              | 0.000                                                 | 1.130                                                   |
| Cingulate Cortex Right                | Lateral Gyrus Right                                       | 1.330                                                 | 0.945                                                   |
| Cingulate Cortex Right                | PostCruciate Gyrus Right                                  | 0.888                                                 | 1.840                                                   |
| Cingulate Cortex Right                | Posterior Symgmoideus Gyrus Right                         | 0.831                                                 | 0.654                                                   |
| Cingulate Cortex Right                | Suprasylvian Gyrus Right                                  | 1.086                                                 | 0.628                                                   |
| Cingulate Cortex Right                | Sylvian Gyrus Right                                       | -0.079                                                | 1.163                                                   |
| Cingulate Cortex Right                | Ectolateralis Gyrus Right                                 | 1.158                                                 | 0.835                                                   |
| Cingulate Cortex Right                | Entolateral Gyrus Right                                   | 1.442                                                 | 1.453                                                   |
| Cingulate Cortex Right                | Occipital Lobe Right                                      | 0.460                                                 | 0.954                                                   |
| Claustrocortex(Insula) Left           | Sylvian Gyrus Left                                        | 1.339                                                 | 0.174                                                   |
| Claustrocortex(Insula) Left           | Gyrus Rectus Right                                        | 0.306                                                 | -1.244                                                  |
| Claustrocortex(Insula) Right          | PostCruciate Gyrus Right                                  | -1.257                                                | 0.311                                                   |
| Claustrocortex(Insula) Right          | Posterior Symgmoideus Gyrus Right                         | -1.668                                                | 0.485                                                   |
| Claustrocortex(Insula) Right          | Sylvian Gyrus Right                                       | 1.262                                                 | 0.109                                                   |
| Ectolateralis Gyrus Left              | Entolateral Gyrus Left                                    | 1.437                                                 | 1.544                                                   |
| Ectolateralis Gyrus Left              | Occipital Lobe Left                                       | 1.144                                                 | 1.391                                                   |
| Ectolateralis Gyrus Right             | Entolateral Gyrus Right                                   | 2.633                                                 | 1.226                                                   |
| Ectolateralis Gyrus Right             | Occipital Lobe Right                                      | 1.282                                                 | 1.255                                                   |
| Ectolateralis Gyrus Left              | Entolateral Gyrus Right                                   | 1.902                                                 | 1.293                                                   |
| Entolateral Gyrus Right               | Occipital Lobe Right                                      | 0.894                                                 | 1.183                                                   |

|                                                          |                                                           |        |        |
|----------------------------------------------------------|-----------------------------------------------------------|--------|--------|
| Geniculate Nucleus Left                                  | Thalamus Left                                             | 1.841  | 2.128  |
| Geniculate Nucleus Right                                 | Thalamus Right                                            | 2.113  | 1.617  |
| Globus Pallidum Left                                     | Putamen Left                                              | 1.808  | 1.553  |
| Globus Pallidum Right                                    | Putamen Right                                             | 2.096  | 2.359  |
| Gyrus Rectus Left                                        | Olfactory Bulb Left                                       | 2.738  | 1.484  |
| Gyrus Rectus Left                                        | Gyrus Rectus Right                                        | 2.850  | 1.757  |
| Gyrus Rectus Left                                        | Olfactory Bulb Right                                      | 2.339  | -0.370 |
| Gyrus Rectus Right                                       | Olfactory Bulb Right                                      | 2.348  | 1.383  |
| Hippocampus Left                                         | Parahippocampal Cortex Left                               | 1.608  | 1.460  |
| Hippocampus Left                                         | Geniculate Nucleus Left                                   | 1.324  | -0.135 |
| Hippocampus Left                                         | Lateral Gyrus Left                                        | 1.104  | 0.134  |
| Hippocampus Left                                         | Suprasylvian Gyrus Left                                   | 1.962  | 1.211  |
| Hippocampus Left                                         | Ectolateralis Gyrus Left                                  | 1.157  | -0.940 |
| Hippocampus Left                                         | Midbrain Left                                             | 1.379  | 1.457  |
| Hippocampus Left                                         | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 1.933  | 1.351  |
| Hippocampus Right                                        | Parahippocampal Cortex Right                              | 1.447  | 1.140  |
| Hippocampus Right                                        | Geniculate Nucleus Right                                  | 0.029  | 0.707  |
| Hippocampus Right                                        | Periaqueductal Grey Substance Right                       | 1.265  | 1.459  |
| Hippocampus Right                                        | Thalamus Right                                            | 0.760  | 1.004  |
| Hippocampus Right                                        | Suprasylvian Gyrus Right                                  | 0.516  | 0.699  |
| Hippocampus Right                                        | Ectolateralis Gyrus Right                                 | 0.131  | 1.343  |
| Hippocampus Right                                        | Midbrain Right                                            | 1.478  | 1.477  |
| Lateral Gyrus Left                                       | Suprasylvian Gyrus Left                                   | 1.506  | 0.293  |
| Lateral Gyrus Left                                       | Ectolateralis Gyrus Left                                  | 1.968  | 2.743  |
| Lateral Gyrus Left                                       | Entolateral Gyrus Left                                    | 1.976  | 1.816  |
| Lateral Gyrus Left                                       | Occipital Lobe Left                                       | -0.025 | 1.326  |
| Lateral Gyrus Left                                       | Lateral Gyrus Right                                       | 1.392  | 0.817  |
| Lateral Gyrus Right                                      | Suprasylvian Gyrus Right                                  | 1.392  | 0.833  |
| Lateral Gyrus Right                                      | Ectolateralis Gyrus Right                                 | 2.711  | 1.810  |
| Lateral Gyrus Right                                      | Entolateral Gyrus Right                                   | 2.844  | 1.974  |
| Lateral Gyrus Right                                      | Occipital Lobe Right                                      | 1.443  | 1.373  |
| Lateral Septal Nucleus Left                              | Medial Septal Nucleus Left                                | 2.009  | 1.313  |
| Lateral Septal Nucleus Left                              | Preoptic Hypothalamic Area Left                           | 1.800  | 0.993  |
| Lateral Septal Nucleus Left                              | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 2.010  | 2.145  |
| Lateral Septal Nucleus Left                              | Substantia Nigra Left                                     | 0.779  | 0.129  |
| Lateral Septal Nucleus Left                              | Globus Pallidum Left                                      | 1.221  | 0.695  |
| Lateral Septal Nucleus Left                              | Medial Mamillary Nucleus Right                            | -0.127 | 0.451  |
| Lateral Septal Nucleus Left                              | SubFornical Organ Right                                   | 1.665  | 0.960  |
| Lateral Septal Nucleus Left                              | Bed Nucleus Of Stria Terminalis Right                     | 0.944  | 0.544  |
| Lateral Septal Nucleus Left                              | Lateral Septal Nucleus Right                              | 1.643  | 1.132  |
| Lateral Septal Nucleus Left                              | Preoptic Hypothalamic Area Right                          | 1.539  | 0.595  |
| Lateral Septal Nucleus Right                             | Medial Septal Nucleus Right                               | 1.894  | 1.916  |
| Lateral Septal Nucleus Right                             | Preoptic Hypothalamic Area Right                          | 1.562  | 1.518  |
| Lateral Septal Nucleus Right                             | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | -0.105 | 1.216  |
| Lateral Septal Nucleus Right                             | Substantia Nigra Right                                    | 0.459  | 0.969  |
| Lateral Septal Nucleus Right                             | Globus Pallidum Right                                     | 0.268  | 0.047  |
| Medial Mamillary Nucleus Left                            | Lateral Septal Nucleus Left                               | 1.162  | 1.682  |
| Medial Mamillary Nucleus Left                            | Medial Septal Nucleus Left                                | 1.166  | -0.177 |
| Medial Mamillary Nucleus Left                            | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 0.951  | 2.205  |
| Medial Mamillary Nucleus Left                            | Substantia Nigra Left                                     | 0.959  | -0.462 |
| Medial Mamillary Nucleus Left                            | Globus Pallidum Left                                      | 1.350  | -0.582 |
| Medial Mamillary Nucleus Left                            | Medial Mamillary Nucleus Right                            | 0.390  | 1.526  |
| Medial Mamillary Nucleus Left                            | Lateral Septal Nucleus Right                              | 0.575  | -0.159 |
| Medial Mamillary Nucleus Right                           | SubFornical Organ Right                                   | -0.957 | 0.043  |
| Medial Mamillary Nucleus Right                           | Bed Nucleus Of Stria Terminalis Right                     | -1.299 | -0.255 |
| Medial Mamillary Nucleus Right                           | Lateral Septal Nucleus Right                              | 0.505  | 0.958  |
| Medial Mamillary Nucleus Right                           | Medial Septal Nucleus Right                               | 0.237  | 0.239  |
| Medial Mamillary Nucleus Right                           | Preoptic Hypothalamic Area Right                          | -0.650 | 0.037  |
| Medial Mamillary Nucleus Right                           | Substantia Nigra Right                                    | 1.888  | 1.594  |
| Medial Mamillary Nucleus Right                           | Pituitary Gland Right                                     | -1.985 | 1.360  |
| Medial Septal Nucleus Left                               | Preoptic Hypothalamic Area Left                           | 1.904  | 2.000  |
| Medial Septal Nucleus Left                               | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 1.736  | 1.643  |
| Medial Septal Nucleus Left                               | Substantia Nigra Left                                     | 0.458  | 0.773  |
| Medial Septal Nucleus Left                               | Caudate Left                                              | 1.322  | 1.286  |
| Medial Septal Nucleus Left                               | Globus Pallidum Left                                      | 1.012  | 2.008  |
| Medial Septal Nucleus Left                               | SubFornical Organ Right                                   | 1.807  | 1.322  |
| Medial Septal Nucleus Left                               | Lateral Septal Nucleus Right                              | 1.689  | 0.803  |
| Medial Septal Nucleus Left                               | Medial Septal Nucleus Right                               | 1.337  | 0.950  |
| Medial Septal Nucleus Left                               | Preoptic Hypothalamic Area Right                          | 1.589  | 1.488  |
| Medial Septal Nucleus Right                              | Preoptic Hypothalamic Area Right                          | 1.638  | 1.900  |
| Medial Septal Nucleus Right                              | Substantia Nigra Right                                    | 0.585  | 0.110  |
| Medial Septal Nucleus Right                              | Caudate Right                                             | 0.752  | 0.683  |
| Medial Septal Nucleus Right                              | Globus Pallidum Right                                     | 1.684  | 1.266  |
| Medial Septal Nucleus Right                              | Putamen Right                                             | 0.551  | 0.493  |
| Midbrain Left                                            | Pineal Gland Right                                        | 1.109  | 1.480  |
| Midbrain Left                                            | Pons Right                                                | 1.073  | 1.393  |
| Midbrain Left                                            | Hippocampus Right                                         | 1.091  | 1.672  |
| Midbrain Left                                            | Periaqueductal Grey Substance Right                       | 1.924  | 1.486  |
| Midbrain Left                                            | Midbrain Right                                            | 1.588  | 1.531  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Substantia Nigra Left                                     | 0.742  | -0.476 |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Globus Pallidum Left                                      | 1.362  | 1.675  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Putamen Left                                              | 0.961  | 0.896  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | SubFornical Organ Right                                   | 1.292  | 0.150  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Bed Nucleus Of Stria Terminalis Right                     | 0.659  | 0.536  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left | Lateral Septal Nucleus Right                              | 0.870  | -0.285 |
| Olfactory Bulb Left                                      | Gyrus Rectus Right                                        | 2.892  | 1.154  |
| Orbital Gyrus Left                                       | Orbitofrontal Gyrus Left                                  | 0.668  | 1.946  |
| Orbital Gyrus Left                                       | Precruciate Gyrus Left                                    | 1.728  | 1.149  |
| Orbital Gyrus Left                                       | Gyrus Rectus Left                                         | 1.681  | 0.430  |
| Orbital Gyrus Left                                       | Olfactory Bulb Left                                       | 1.911  | 0.784  |
| Orbital Gyrus Left                                       | Claustrocortex(Insula) Left                               | 0.264  | 0.971  |
| Orbital Gyrus Left                                       | Gyrus Rectus Right                                        | 2.002  | -1.310 |
| Orbital Gyrus Right                                      | Precruciate Gyrus Right                                   | 1.871  | 1.857  |
| Orbital Gyrus Right                                      | Gyrus Rectus Right                                        | 1.903  | 1.659  |
| Orbital Gyrus Right                                      | Olfactory Bulb Right                                      | 1.966  | 0.857  |
| Orbitofrontal Gyrus Left                                 | Precruciate Gyrus Left                                    | 0.777  | 1.469  |
| Orbitofrontal Gyrus Left                                 | Claustrocortex(Insula) Left                               | 0.715  | 2.133  |
| Orbitofrontal Gyrus Right                                | Precruciate Gyrus Right                                   | -0.246 | 0.911  |
| Orbitofrontal Gyrus Right                                | Claustrocortex(Insula) Right                              | 0.262  | 1.429  |
| Parahippocampal Cortex Left                              | Substantia Nigra Left                                     | 0.741  | 0.925  |
| Parahippocampal Cortex Left                              | Thalamus Left                                             | 1.694  | 0.645  |
| Parahippocampal Cortex Left                              | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 2.155  | 1.731  |
| Parahippocampal Cortex Right                             | Substantia Nigra Right                                    | 0.152  | 0.735  |
| Parahippocampal Cortex Right                             | Caudate Right                                             | 1.449  | 0.617  |
| Parahippocampal Cortex Right                             | Globus Pallidum Right                                     | 1.004  | 0.143  |
| Parahippocampal Cortex Right                             | Putamen Right                                             | 1.655  | 0.314  |
| Parahippocampal Cortex Right                             | Geniculate Nucleus Right                                  | -1.083 | -0.004 |
| Parahippocampal Cortex Right                             | Thalamus Right                                            | -0.905 | 0.264  |
| Parahippocampal Cortex Right                             | Claustrocortex(Insula) Right                              | 0.857  | 0.701  |
| Parahippocampal Cortex Right                             | Lateral Gyrus Right                                       | -0.545 | 0.222  |
| Parahippocampal Cortex Right                             | Suprasylvian Gyrus Right                                  | 0.139  | 0.319  |
| Parahippocampal Cortex Right                             | Sylvian Gyrus Right                                       | 1.414  | 0.160  |
| Parahippocampal Cortex Right                             | Ectolateralis Gyrus Right                                 | 0.184  | 0.083  |
| Parahippocampal Cortex Right                             | Occipital Lobe Right                                      | -0.517 | 0.851  |
| Parahippocampal Cortex Right                             | Midbrain Right                                            | 0.294  | 0.401  |
| Periaqueductal Grey Substance Left                       | Pons Right                                                | 1.505  | 1.333  |
| Periaqueductal Grey Substance Left                       | Periaqueductal Grey Substance Right                       | 1.880  | 1.523  |

|                                     |                                                           |        |        |
|-------------------------------------|-----------------------------------------------------------|--------|--------|
| Periaqueductal Grey Substance Right | Midbrain Right                                            | 1.079  | 1.524  |
| Pineal Gland Left                   | Hippocampus Left                                          | 1.684  | 0.835  |
| Pineal Gland Left                   | Geniculate Nucleus Left                                   | 0.690  | -0.182 |
| Pineal Gland Left                   | Midbrain Left                                             | 0.925  | 0.887  |
| Pineal Gland Left                   | Pineal Gland Right                                        | 3.477  | 1.567  |
| Pineal Gland Left                   | Hippocampus Right                                         | 0.454  | 0.825  |
| Pineal Gland Left                   | Midbrain Right                                            | 0.995  | 0.818  |
| Pineal Gland Right                  | Hippocampus Right                                         | 0.355  | 1.276  |
| Pineal Gland Right                  | Midbrain Right                                            | 0.368  | 1.304  |
| Pituitary Gland Left                | Pituitary Gland Right                                     | 2.126  | 2.046  |
| Pons Left                           | Periaqueductal Grey Substance Left                        | 2.554  | 1.781  |
| Pons Left                           | Pons Right                                                | 2.007  | 1.691  |
| Pons Right                          | Periaqueductal Grey Substance Right                       | 0.937  | 1.584  |
| PostCruciate Gyrus Left             | Posterior Symgmoideus Gyrus Left                          | 1.857  | 2.180  |
| PostCruciate Gyrus Left             | AnteriorSigmoides Gyrus Right                             | -0.997 | 0.319  |
| PostCruciate Gyrus Left             | PostCruciate Gyrus Right                                  | -0.363 | -0.292 |
| PostCruciate Gyrus Right            | Posterior Symgmoideus Gyrus Right                         | 1.940  | 2.105  |
| PostCruciate Gyrus Right            | Sylvian Gyrus Right                                       | -0.016 | 1.122  |
| Posterior Symgmoideus Gyrus Left    | Suprasylvian Gyrus Left                                   | -0.390 | 0.036  |
| Posterior Symgmoideus Gyrus Left    | Sylvian Gyrus Left                                        | -0.417 | 0.330  |
| Posterior Symgmoideus Gyrus Right   | Sylvian Gyrus Right                                       | -0.678 | 0.431  |
| Posterior Sylvian Gyrus Left        | Suprasylvian Gyrus Left                                   | 1.820  | 1.751  |
| Posterior Sylvian Gyrus Right       | Temporal Lobe Right                                       | 0.396  | 2.102  |
| Posterior Sylvian Gyrus Right       | Suprasylvian Gyrus Right                                  | -0.996 | 1.365  |
| Posterior Sylvian Gyrus Right       | Ectolateralis Gyrus Right                                 | -0.217 | 0.092  |
| Precruciate Gyrus Left              | Gyrus Rectus Left                                         | 1.076  | -0.913 |
| Precruciate Gyrus Left              | Claustrocortex(Insula) Left                               | 0.376  | 0.824  |
| Precruciate Gyrus Left              | Orbital Gyrus Right                                       | 1.376  | -1.059 |
| Precruciate Gyrus Left              | Precruciate Gyrus Right                                   | 1.178  | 1.971  |
| Precruciate Gyrus Right             | Gyrus Rectus Right                                        | 0.470  | 1.239  |
| Precruciate Gyrus Right             | PostCruciate Gyrus Right                                  | 0.636  | 0.427  |
| Preoptic Hypothalamic Area Left     | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 1.740  | 1.492  |
| Preoptic Hypothalamic Area Left     | Caudate Left                                              | 1.567  | 1.548  |
| Preoptic Hypothalamic Area Left     | Globus Pallidum Left                                      | 0.799  | 1.436  |
| Preoptic Hypothalamic Area Left     | Putamen Left                                              | 0.611  | 0.540  |
| Preoptic Hypothalamic Area Left     | Medial Mamillary Nucleus Right                            | 0.247  | 0.099  |
| Preoptic Hypothalamic Area Left     | SubFornical Organ Right                                   | 1.803  | 1.576  |
| Preoptic Hypothalamic Area Left     | Bed Nucleus of Stria Terminalis Right                     | 1.232  | 1.713  |
| Preoptic Hypothalamic Area Left     | Lateral Septal Nucleus Right                              | 1.634  | 0.889  |
| Preoptic Hypothalamic Area Left     | Medial Septal Nucleus Right                               | 1.461  | 1.548  |
| Preoptic Hypothalamic Area Left     | Septum Right                                              | -0.370 | 0.527  |
| Preoptic Hypothalamic Area Left     | Preoptic Hypothalamic Area Right                          | 1.908  | 2.433  |
| Preoptic Hypothalamic Area Left     | Substantia Nigra Right                                    | -0.096 | 0.179  |
| Preoptic Hypothalamic Area Left     | Globus Pallidum Right                                     | 0.220  | -0.248 |
| Preoptic Hypothalamic Area Right    | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | -0.255 | -0.039 |
| Preoptic Hypothalamic Area Right    | Substantia Nigra Right                                    | -0.515 | 0.212  |
| Preoptic Hypothalamic Area Right    | Caudate Right                                             | 1.008  | 0.298  |
| Preoptic Hypothalamic Area Right    | Globus Pallidum Right                                     | 0.415  | 0.407  |
| Preoptic Hypothalamic Area Right    | Putamen Right                                             | 0.126  | 0.004  |
| Putamen Left                        | Claustrocortex(Insula) Left                               | 2.184  | 1.342  |
| Putamen Left                        | Septum Right                                              | 0.609  | 0.087  |
| Putamen Right                       | Claustrocortex(Insula) Right                              | 1.379  | 1.469  |
| Putamen Right                       | PostCruciate Gyrus Right                                  | 0.225  | -0.985 |
| Putamen Right                       | Posterior Symgmoideus Gyrus Right                         | -0.233 | 0.931  |
| Putamen Right                       | Sylvian Gyrus Right                                       | 1.181  | -0.288 |
| Septum Left                         | Preoptic Hypothalamic Area Left                           | 1.812  | 1.756  |
| Septum Left                         | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 1.454  | 1.625  |
| Septum Left                         | Caudate Left                                              | 1.547  | 1.722  |
| Septum Left                         | Putamen Left                                              | 0.836  | 0.694  |
| Septum Left                         | SubFornical Organ Right                                   | 1.337  | 0.742  |
| Septum Left                         | Bed Nucleus of Stria Terminalis Right                     | 1.341  | 1.578  |
| Septum Left                         | Lateral Septal Nucleus Right                              | 1.088  | 0.253  |
| Septum Left                         | Septum Right                                              | 1.552  | 2.189  |
| Septum Left                         | Preoptic Hypothalamic Area Right                          | 1.723  | 1.874  |
| Septum Left                         | Caudate Right                                             | 1.341  | 1.210  |
| Septum Right                        | Preoptic Hypothalamic Area Right                          | -0.187 | 0.828  |
| Septum Right                        | Caudate Right                                             | 0.789  | 1.924  |
| Septum Right                        | Putamen Right                                             | 0.851  | 1.655  |
| SubFornical Organ Left              | Bed Nucleus of Stria Terminalis Left                      | 1.664  | 1.836  |
| SubFornical Organ Left              | Lateral Septal Nucleus Left                               | 1.810  | 1.982  |
| SubFornical Organ Left              | Medial Septal Nucleus Left                                | 1.964  | 1.961  |
| SubFornical Organ Left              | Septum Left                                               | 1.523  | 1.189  |
| SubFornical Organ Left              | Preoptic Hypothalamic Area Left                           | 1.864  | 2.070  |
| SubFornical Organ Left              | Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 1.686  | 1.380  |
| SubFornical Organ Left              | Globus Pallidum Left                                      | 0.879  | 1.288  |
| SubFornical Organ Left              | Medial Mamillary Nucleus Right                            | -0.222 | 0.274  |
| SubFornical Organ Left              | SubFornical Organ Right                                   | 2.332  | 2.206  |
| SubFornical Organ Left              | Bed Nucleus of Stria Terminalis Right                     | 1.645  | 1.905  |
| SubFornical Organ Left              | Lateral Septal Nucleus Right                              | 1.989  | 1.794  |
| SubFornical Organ Left              | Medial Septal Nucleus Right                               | 1.567  | 1.492  |
| SubFornical Organ Left              | Septum Right                                              | -0.738 | 0.263  |
| SubFornical Organ Left              | Preoptic Hypothalamic Area Right                          | 1.888  | 1.968  |
| SubFornical Organ Right             | Bed Nucleus of Stria Terminalis Right                     | 2.019  | 2.354  |
| SubFornical Organ Right             | Lateral Septal Nucleus Right                              | 2.304  | 2.120  |
| SubFornical Organ Right             | Medial Septal Nucleus Right                               | 1.709  | 1.936  |
| SubFornical Organ Right             | Septum Right                                              | -0.960 | 0.561  |
| SubFornical Organ Right             | Preoptic Hypothalamic Area Right                          | 1.936  | 2.157  |
| SubFornical Organ Right             | Globus Pallidum Right                                     | -0.253 | -0.148 |
| Substantia Nigra Left               | Globus Pallidum Left                                      | 1.557  | 0.780  |
| Substantia Nigra Right              | Globus Pallidum Right                                     | 0.908  | -0.197 |
| Suprasylvian Gyrus Left             | Sylvian Gyrus Left                                        | 0.557  | 1.659  |
| Suprasylvian Gyrus Left             | Ectolateralis Gyrus Left                                  | 1.921  | -0.031 |
| Suprasylvian Gyrus Right            | Ectolateralis Gyrus Right                                 | 2.095  | 1.129  |
| Temporal Lobe Left                  | Parahippocampal Cortex Left                               | 1.797  | 1.003  |
| Temporal Lobe Right                 | Hippocampus Right                                         | 0.226  | -0.041 |
| Temporal Lobe Right                 | Parahippocampal Cortex Right                              | 1.336  | 0.436  |
| Temporal Lobe Right                 | Suprasylvian Gyrus Right                                  | -0.979 | 0.279  |
| Temporal Lobe Right                 | Ectolateralis Gyrus Right                                 | -0.816 | -0.081 |
| Thalamus Left                       | Midbrain Left                                             | 1.757  | -0.094 |
| Thalamus Left                       | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 1.872  | 0.223  |
| Thalamus Right                      | Midbrain Right                                            | 0.886  | 0.803  |

| Regions Of Interest                 | Baseline | Gonadectomized | Mean Diff, | 95,00% CI of diff     | t     | Individual P Value | Summary |
|-------------------------------------|----------|----------------|------------|-----------------------|-------|--------------------|---------|
| Amygdala Left                       | 0,5747   | 0,5947         | -0,02003   | -0,0394 to -0,0006694 | 2,033 | 0,0426             | *       |
| Amygdala Right                      | 0,6125   | 0,6351         | -0,02259   | -0,04195 to -0,003222 | 2,293 | 0,0224             | *       |
| Cerebellum Left                     | 0,4168   | 0,3852         | 0,03157    | 0,0122 to 0,05093     | 3,204 | 0,0015             | **      |
| Clastrum Left                       | 0,4534   | 0,3776         | 0,07577    | 0,05641 to 0,09514    | 7,692 | <0,0001            | ****    |
| Clastrum Right                      | 0,4363   | 0,3628         | 0,07348    | 0,05412 to 0,09284    | 7,459 | <0,0001            | ****    |
| Ectolateralis Gyrus Left            | 0,6395   | 0,4975         | 0,1421     | 0,1227 to 0,1614      | 14,42 | <0,0001            | ****    |
| Ectolateralis Gyrus Right           | 0,6409   | 0,5043         | 0,1366     | 0,1173 to 0,156       | 13,87 | <0,0001            | ****    |
| Fornix Left                         | 0,4503   | 0,4237         | 0,02661    | 0,007247 to 0,04597   | 2,701 | 0,0072             | **      |
| Fornix Right                        | 0,4793   | 0,4462         | 0,03301    | 0,01365 to 0,05237    | 3,351 | 0,0009             | ***     |
| Geniculate Nucleus Left             | 0,179    | 0,1576         | 0,02133    | 0,001967 to 0,04069   | 2,165 | 0,0309             | *       |
| Hippocampus Left                    | 0,5206   | 0,5416         | -0,02107   | -0,04043 to -0,001703 | 2,138 | 0,033              | *       |
| Medial Mamillary Nucleus Left       | 0,3783   | 0,3503         | 0,02796    | 0,008596 to 0,04732   | 2,838 | 0,0048             | **      |
| Medial Mamillary Nucleus Right      | 0,3745   | 0,3433         | 0,03117    | 0,01181 to 0,05053    | 3,164 | 0,0017             | **      |
| Medial Septal Nucleus Right         | 0,4452   | 0,4234         | 0,02187    | 0,002503 to 0,04123   | 2,22  | 0,027              | *       |
| Medulla Oblongata Left              | 0,2755   | 0,211          | 0,06453    | 0,04516 to 0,08389    | 6,55  | <0,0001            | ****    |
| Medulla Oblongata Right             | 0,3083   | 0,2387         | 0,06954    | 0,05017 to 0,0889     | 7,059 | <0,0001            | ****    |
| Midbrain Left                       | 0,234    | 0,1787         | 0,05531    | 0,03594 to 0,07467    | 5,614 | <0,0001            | ****    |
| Midbrain Right                      | 0,2313   | 0,1792         | 0,05206    | 0,0327 to 0,07143     | 5,285 | <0,0001            | ****    |
| Orbital Gyrus Left                  | 0,468    | 0,492          | -0,024     | -0,04337 to -0,004639 | 2,436 | 0,0152             | *       |
| Periaqueductal Grey Substance Left  | 0,6429   | 0,538          | 0,1049     | 0,08554 to 0,1243     | 10,65 | <0,0001            | ****    |
| Periaqueductal Grey Substance Right | 0,5522   | 0,4744         | 0,07781    | 0,05845 to 0,09717    | 7,898 | <0,0001            | ****    |
| Pons Left                           | 0,4104   | 0,2825         | 0,1279     | 0,1086 to 0,1473      | 12,98 | <0,0001            | ****    |
| Pons Right                          | 0,3971   | 0,2762         | 0,1209     | 0,1015 to 0,1402      | 12,27 | <0,0001            | ****    |
| Preoptic Hypothalamic Area Left     | 0,442    | 0,4189         | 0,02306    | 0,003696 to 0,04242   | 2,341 | 0,0197             | *       |
| Preoptic Hypothalamic Area Right    | 0,4748   | 0,4432         | 0,03164    | 0,01228 to 0,051      | 3,212 | 0,0014             | **      |
| SubFornical Organ Right             | 0,5848   | 0,559          | 0,02578    | 0,006419 to 0,04515   | 2,617 | 0,0092             | **      |
| Suprasylvian Gyrus Right            | 0,3862   | 0,4068         | -0,02064   | -0,04 to -0,001274    | 2,095 | 0,0368             | *       |
| Thalamus Left                       | 0,3032   | 0,2707         | 0,03245    | 0,01309 to 0,05182    | 3,294 | 0,0011             | **      |
| Thalamus Right                      | 0,3102   | 0,2793         | 0,03091    | 0,01155 to 0,05028    | 3,138 | 0,0018             | **      |

| Regions Of Interest                                       | Baseline | Gonadectomized | Mean Diff, | 95,00% CI of diff     | t     | Individual P Value | Summary |
|-----------------------------------------------------------|----------|----------------|------------|-----------------------|-------|--------------------|---------|
| Clastrum Left                                             | 0,4085   | 0,3737         | 0,03473    | 0,02561 to 0,04385    | 7,489 | <0,0001            | ****    |
| Clastrum Right                                            | 0,4046   | 0,3703         | 0,03427    | 0,02515 to 0,0434     | 7,391 | <0,0001            | ****    |
| Ectolateralis Gyrus Right                                 | 0,4411   | 0,4165         | 0,02462    | 0,0155 to 0,03374     | 5,31  | <0,0001            | ****    |
| Subfornical Organ Left                                    | 0,4372   | 0,4115         | 0,0257     | 0,01658 to 0,03482    | 5,541 | <0,0001            | ****    |
| Subfornical Organ Right                                   | 0,4431   | 0,4166         | 0,02647    | 0,01734 to 0,03559    | 5,707 | <0,0001            | ****    |
| Globus Pallidum Left                                      | 0,2584   | 0,2484         | 0,01006    | 0,0009362 to 0,01918  | 2,169 | 0,0308             | *       |
| Globus Pallidum Right                                     | 0,2473   | 0,2372         | 0,01018    | 0,001057 to 0,0193    | 2,195 | 0,0289             | *       |
| Medial Mamillary Nucleus Left                             | 0,3348   | 0,3135         | 0,02131    | 0,01219 to 0,03043    | 4,595 | <0,0001            | ****    |
| Medial Mamillary Nucleus Right                            | 0,3335   | 0,3116         | 0,02195    | 0,01283 to 0,03107    | 4,733 | <0,0001            | ****    |
| Medulla Oblongata Right                                   | 0,1898   | 0,1649         | 0,02496    | 0,01584 to 0,03409    | 5,383 | <0,0001            | ****    |
| Midbrain Left                                             | 0,2078   | 0,1805         | 0,02727    | 0,01815 to 0,03639    | 5,881 | <0,0001            | ****    |
| Midbrain Right                                            | 0,2595   | 0,2321         | 0,02736    | 0,01824 to 0,03648    | 5,9   | <0,0001            | ****    |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | 0,2834   | 0,2678         | 0,01566    | 0,006534 to 0,02478   | 3,376 | 0,0008             | ***     |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 0,3093   | 0,2903         | 0,01902    | 0,009901 to 0,02814   | 4,102 | <0,0001            | ****    |
| Parahippocampal Cortex Right                              | 0,3541   | 0,323          | 0,03116    | 0,02204 to 0,04028    | 6,719 | <0,0001            | ****    |
| Pituitary Gland Left                                      | 0,04898  | 0,06561        | -0,01663   | -0,02575 to -0,007506 | 3,586 | 0,0004             | ***     |
| Pituitary Gland Right                                     | 0,05069  | 0,06808        | -0,01739   | -0,02651 to -0,008265 | 3,749 | 0,0002             | ***     |
| Preoptic Hypothalamic Area Left                           | 0,4288   | 0,4038         | 0,02504    | 0,01592 to 0,03416    | 5,4   | <0,0001            | ****    |
| Preoptic Hypothalamic Area Right                          | 0,4189   | 0,394          | 0,02485    | 0,01573 to 0,03397    | 5,358 | <0,0001            | ****    |
| Putamen Right                                             | 0,328    | 0,3159         | 0,01215    | 0,003031 to 0,02127   | 2,621 | 0,0092             | **      |
| Substantia Nigra Right                                    | 0,1451   | 0,1353         | 0,009719   | 0,0005973 to 0,01884  | 2,096 | 0,0368             | *       |
| Thalamus Left                                             | 0,3341   | 0,3113         | 0,0228     | 0,01368 to 0,03192    | 4,916 | <0,0001            | ****    |

| Brain Region 1                        | Brain Region 2                                           | Mean functional connectivity Male baseline (Z score) | Mean functional connectivity Male castrated (Z score) |
|---------------------------------------|----------------------------------------------------------|------------------------------------------------------|-------------------------------------------------------|
| AnteriorSigmoides Gyrus Left          | Caudate Left                                             | 0,022                                                | 0,900                                                 |
| AnteriorSigmoides Gyrus Left          | Gyrus Rectus Left                                        | 0,879                                                | 0,181                                                 |
| AnteriorSigmoides Gyrus Left          | Gyrus Rectus Right                                       | 0,391                                                | 0,293                                                 |
| Bed Nucleus of Stria Terminalis Left  | Orbital Gyrus Right                                      | 0,105                                                | -0,923                                                |
| Bed Nucleus of Stria Terminalis Left  | Orbitofrontal Gyrus Right                                | 0,211                                                | -0,207                                                |
| Bed Nucleus of Stria Terminalis Right | AnteriorSigmoides Gyrus Right                            | 0,727                                                | -0,791                                                |
| Bed Nucleus of Stria Terminalis Right | Orbital Gyrus Right                                      | -0,741                                               | -2,185                                                |
| Bed Nucleus of Stria Terminalis Right | Orbitofrontal Gyrus Right                                | 0,729                                                | -1,148                                                |
| Bed Nucleus of Stria Terminalis Right | Precluciate Gyrus Right                                  | -0,134                                               | -1,563                                                |
| Caudate Left                          | Occipital Lobe Left                                      | 0,488                                                | -1,465                                                |
| Cingulate Cortex Left                 | Bed Nucleus of Stria Terminalis Right                    | 0,542                                                | -0,209                                                |
| Gyrus Rectus Left                     | Entolateral Gyrus Left                                   | -1,063                                               | -1,000                                                |
| Gyrus Rectus Left                     | Lateral Septal Nucleus Right                             | -0,430                                               | -1,212                                                |
| Gyrus Rectus Left                     | Pineal Gland Right                                       | -0,554                                               | -2,254                                                |
| Gyrus Rectus Left                     | Periaqueductal Grey Substance Right                      | -0,088                                               | -2,178                                                |
| Hippocampus Left                      | Lateral Gyrus Left                                       | 1,104                                                | 0,524                                                 |
| Hippocampus Left                      | Thalamus Right                                           | 0,935                                                | -0,579                                                |
| Lateral Gyrus Left                    | Suprasylvian Gyrus Left                                  | 1,506                                                | 0,877                                                 |
| Medial Septal Nucleus Left            | PostCruciate Gyrus Left                                  | 1,009                                                | -0,131                                                |
| Medial Septal Nucleus Left            | PostCruciate Gyrus Right                                 | 0,287                                                | -0,464                                                |
| Medial Septal Nucleus Right           | Orbital Gyrus Right                                      | 0,223                                                | -0,890                                                |
| Occipital Lobe Left                   | Thalamus Right                                           | -0,014                                               | -1,364                                                |
| Orbital Gyrus Right                   | Globus Pallidum Right                                    | 0,936                                                | -0,657                                                |
| Parahippocampal Cortex Left           | Periaqueductal Grey Substance Left                       | 0,484                                                | -0,113                                                |
| Parahippocampal Cortex Left           | Cerebellum Left                                          | -0,686                                               | -0,987                                                |
| Parahippocampal Cortex Left           | Lateral Gyrus Left                                       | 1,258                                                | -1,429                                                |
| Parahippocampal Cortex Left           | Pons Right                                               | 0,886                                                | -0,569                                                |
| Parahippocampal Cortex Left           | Geniculate Nucleus Right                                 | 1,582                                                | -0,500                                                |
| Parahippocampal Cortex Left           | Lateral Gyrus Right                                      | 1,138                                                | 0,177                                                 |
| Parahippocampal Cortex Left           | Suprasylvian Gyrus Right                                 | 0,970                                                | 0,286                                                 |
| Parahippocampal Cortex Left           | Ectolateralis Gyrus Right                                | 0,668                                                | 0,493                                                 |
| Periaqueductal Grey Substance Left    | Periaqueductal Grey Substance Right                      | 1,880                                                | 1,084                                                 |
| Periaqueductal Grey Substance Right   | Midbrain Right                                           | 1,079                                                | 1,294                                                 |
| Pituitary Gland Left                  | Thalamus Left                                            | -0,054                                               | -0,006                                                |
| Pituitary Gland Left                  | Entolateral Gyrus Left                                   | 0,330                                                | -0,179                                                |
| Pituitary Gland Left                  | Septum Right                                             | 0,031                                                | -0,589                                                |
| Pituitary Gland Left                  | Putamen Right                                            | 0,614                                                | -0,440                                                |
| Pituitary Gland Left                  | Claustrocortex(Insula) Right                             | 0,073                                                | -0,661                                                |
| Pituitary Gland Left                  | Lateral Gyrus Right                                      | -0,111                                               | -0,555                                                |
| Pituitary Gland Left                  | Ectolateralis Gyrus Right                                | 0,326                                                | -0,731                                                |
| Pituitary Gland Left                  | Medulla Oblongata Right                                  | 0,428                                                | 0,144                                                 |
| Pons Left                             | Pons Right                                               | 2,007                                                | 1,044                                                 |
| PostCruciate Gyrus Left               | Medulla Oblongata Left                                   | 0,198                                                | -0,112                                                |
| PostCruciate Gyrus Left               | Medulla Oblongata Right                                  | 0,007                                                | 0,141                                                 |
| Posterior Sygmoideus Gyrus Left       | Medulla Oblongata Right                                  | 0,362                                                | 1,138                                                 |
| Posterior Sylvian Gyrus Left          | Substantia Nigra Left                                    | 0,153                                                | -2,259                                                |
| Posterior Sylvian Gyrus Left          | Septum Right                                             | 0,323                                                | -1,120                                                |
| Posterior Sylvian Gyrus Left          | Orbitofrontal Gyrus Right                                | 0,341                                                | -0,673                                                |
| Posterior Sylvian Gyrus Left          | Ectolateralis Gyrus Right                                | -0,392                                               | -0,094                                                |
| Preoptic Hypothalamic Area Right      | Orbital Gyrus Right                                      | -0,522                                               | -0,748                                                |
| Preoptic Hypothalamic Area Right      | Orbitofrontal Gyrus Right                                | 0,517                                                | -0,010                                                |
| Septum Left                           | Nucleus Of The Horizontal Limb Of The Diagonal Band Left | 1,454                                                | 0,172                                                 |
| Septum Left                           | PostCruciate Gyrus Left                                  | 1,290                                                | 0,750                                                 |
| Septum Left                           | Orbital Gyrus Right                                      | 0,147                                                | -0,865                                                |
| Septum Left                           | Orbitofrontal Gyrus Right                                | 0,713                                                | 0,414                                                 |
| Septum Right                          | AnteriorSigmoides Gyrus Right                            | 0,605                                                | 0,763                                                 |
| Septum Right                          | Orbital Gyrus Right                                      | 0,195                                                | -1,094                                                |
| SubFornical Organ Left                | Orbital Gyrus Right                                      | -0,705                                               | -0,449                                                |
| SubFornical Organ Left                | Orbitofrontal Gyrus Right                                | 0,576                                                | -0,881                                                |
| SubFornical Organ Right               | Orbital Gyrus Right                                      | -0,825                                               | -0,944                                                |
| SubFornical Organ Right               | Orbitofrontal Gyrus Right                                | 0,744                                                | -1,245                                                |
| Substantia Nigra Left                 | Posterior Sylvian Gyrus Right                            | 1,244                                                | -1,712                                                |
| Temporal Lobe Left                    | Periaqueductal Grey Substance Left                       | 0,725                                                | 0,428                                                 |
| Temporal Lobe Left                    | Pons Right                                               | 1,263                                                | 0,006                                                 |
| Temporal Lobe Left                    | Gyrus Rectus Right                                       | -0,660                                               | -0,144                                                |
| Temporal Lobe Left                    | Periaqueductal Grey Substance Right                      | 0,429                                                | -0,023                                                |



| Brain Region 1                                            | Brain Region 2                                            | Mean functional connectivity Female baseline (Z score) | Mean functional connectivity Female castrated (Z score) |
|-----------------------------------------------------------|-----------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------|
| Amygdala Left                                             | Globus Pallidum Left                                      | 1.450                                                  | 1.805                                                   |
| AnteriorSigmoides Gyrus Left                              | Gyrus Rectus Left                                         | -1.753                                                 | 0.239                                                   |
| AnteriorSigmoides Gyrus Left                              | Orbitofrontal Gyrus Right                                 | -0.017                                                 | 0.569                                                   |
| AnteriorSigmoides Gyrus Right                             | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | 0.258                                                  | 0.273                                                   |
| Bed Nucleus of Stria Terminalis Left                      | Lateral Septal Nucleus Left                               | 1.599                                                  | 1.913                                                   |
| Bed Nucleus of Stria Terminalis Left                      | Pituitary Gland Left                                      | -1.046                                                 | -0.106                                                  |
| Bed Nucleus of Stria Terminalis Left                      | Medial Mamillary Nucleus Right                            | -0.408                                                 | 0.313                                                   |
| Bed Nucleus of Stria Terminalis Left                      | Pituitary Gland Right                                     | -1.004                                                 | -0.466                                                  |
| Bed Nucleus of Stria Terminalis Left                      | Midbrain Right                                            | -0.529                                                 | -0.096                                                  |
| Bed Nucleus of Stria Terminalis Right                     | Pituitary Gland Right                                     | -0.560                                                 | 0.057                                                   |
| Caudate Left                                              | Gyrus Rectus Left                                         | 0.147                                                  | -0.087                                                  |
| Cingulate Cortex Left                                     | Orbital Gyrus Right                                       | -0.117                                                 | 0.374                                                   |
| Cingulate Cortex Left                                     | Orbitofrontal Gyrus Right                                 | 1.006                                                  | 1.375                                                   |
| Cingulate Cortex Left                                     | Claustrocortex(Insula) Right                              | 1.431                                                  | 1.079                                                   |
| Cingulate Cortex Left                                     | Sylvian Gyrus Right                                       | 0.414                                                  | 1.002                                                   |
| Cingulate Cortex Right                                    | Orbital Gyrus Right                                       | 0.954                                                  | 1.582                                                   |
| Cingulate Cortex Right                                    | Orbitofrontal Gyrus Right                                 | 0.833                                                  | 1.517                                                   |
| Cingulate Cortex Right                                    | Precurciate Gyrus Right                                   | 1.380                                                  | 1.673                                                   |
| Claustrocortex(Insula) Left                               | Pineal Gland Right                                        | -1.819                                                 | -0.527                                                  |
| Ectolateralis Gyrus Left                                  | Suprasylvian Gyrus Right                                  | -0.335                                                 | 0.272                                                   |
| Geniculate Nucleus Left                                   | Olfactory Bulb Right                                      | -0.632                                                 | 0.543                                                   |
| Gyrus Rectus Left                                         | Olfactory Bulb Left                                       | 1.484                                                  | 2.483                                                   |
| Gyrus Rectus Left                                         | Periaqueductal Grey Substance Left                        | -0.037                                                 | 0.782                                                   |
| Gyrus Rectus Left                                         | PostCruciate Gyrus Left                                   | 0.173                                                  | -1.528                                                  |
| Gyrus Rectus Left                                         | Orbital Gyrus Right                                       | 0.604                                                  | 1.130                                                   |
| Gyrus Rectus Left                                         | Precurciate Gyrus Right                                   | 0.657                                                  | 0.784                                                   |
| Lateral Gyrus Left                                        | Olfactory Bulb Right                                      | -0.732                                                 | -0.374                                                  |
| Lateral Septal Nucleus Left                               | SubFornical Organ Right                                   | 0.960                                                  | 1.703                                                   |
| Medial Mamillary Nucleus Left                             | AnteriorSigmoides Gyrus Right                             | -0.397                                                 | -0.404                                                  |
| Medial Septal Nucleus Left                                | Medulla Oblongata Right                                   | -0.925                                                 | -0.949                                                  |
| Medial Septal Nucleus Right                               | Pituitary Gland Right                                     | 0.346                                                  | -0.483                                                  |
| Medulla Oblongata Left                                    | Pineal Gland Right                                        | 0.849                                                  | 0.099                                                   |
| Midbrain Left                                             | Olfactory Bulb Right                                      | -0.560                                                 | -0.482                                                  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | Midbrain Left                                             | -1.287                                                 | -0.321                                                  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | Pituitary Gland Right                                     | -1.293                                                 | -0.716                                                  |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Left  | Midbrain Right                                            | -1.303                                                 | 0.564                                                   |
| Nucleus Of The Horizontal Limb Of The Diagonal Band Right | Claustrocortex(Insula) Right                              | -0.644                                                 | 0.332                                                   |
| Olfactory Bulb Left                                       | Periaqueductal Grey Substance Left                        | -1.022                                                 | 0.373                                                   |
| Olfactory Bulb Left                                       | Orbital Gyrus Right                                       | -1.102                                                 | 1.148                                                   |
| Orbital Gyrus Left                                        | Olfactory Bulb Left                                       | 0.784                                                  | 0.780                                                   |
| Orbitofrontal Gyrus Left                                  | Suprasylvian Gyrus Left                                   | -1.883                                                 | -0.474                                                  |
| Orbitofrontal Gyrus Left                                  | Cingulate Cortex Right                                    | -2.575                                                 | -0.288                                                  |
| Orbitofrontal Gyrus Left                                  | Orbital Gyrus Right                                       | -1.481                                                 | 1.601                                                   |
| Orbitofrontal Gyrus Left                                  | Orbitofrontal Gyrus Right                                 | -0.935                                                 | 0.861                                                   |
| Orbitofrontal Gyrus Left                                  | Precurciate Gyrus Right                                   | -0.624                                                 | 1.118                                                   |
| Orbitofrontal Gyrus Right                                 | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | -1.614                                                 | 0.049                                                   |
| Orbitofrontal Gyrus Right                                 | Entolateral Gyrus Right                                   | -0.748                                                 | 0.735                                                   |
| Parahippocampal Cortex Left                               | Putamen Left                                              | -0.318                                                 | -0.225                                                  |
| Parahippocampal Cortex Left                               | Claustrocortex(Insula) Left                               | -0.677                                                 | 1.192                                                   |
| Parahippocampal Cortex Left                               | PostCruciate Gyrus Left                                   | -1.375                                                 | 0.197                                                   |
| Parahippocampal Cortex Left                               | Posterior Sygmoideus Gyrus Left                           | -0.916                                                 | 1.433                                                   |
| Parahippocampal Cortex Left                               | Bed Nucleus of Stria Terminalis Right                     | -0.574                                                 | -0.465                                                  |
| Parahippocampal Cortex Left                               | Septum Right                                              | -1.430                                                 | -0.317                                                  |
| Parahippocampal Cortex Left                               | AnteriorSigmoides Gyrus Right                             | 0.556                                                  | -0.735                                                  |
| Parahippocampal Cortex Left                               | Orbitofrontal Gyrus Right                                 | -1.258                                                 | 0.102                                                   |
| Parahippocampal Cortex Left                               | Caudate Right                                             | -1.275                                                 | 0.276                                                   |
| Parahippocampal Cortex Left                               | Claustrocortex(Insula) Right                              | -0.818                                                 | -0.413                                                  |
| Parahippocampal Cortex Left                               | PostCruciate Gyrus Right                                  | 0.632                                                  | -0.639                                                  |
| Parahippocampal Cortex Left                               | Posterior Sygmoideus Gyrus Right                          | -0.588                                                 | 0.989                                                   |
| Periaqueductal Grey Substance Left                        | Olfactory Bulb Right                                      | -0.388                                                 | 0.598                                                   |
| Pineal Gland Left                                         | Pineal Gland Right                                        | 1.567                                                  | 2.681                                                   |
| Pituitary Gland Left                                      | Posterior Sylvian Gyrus Right                             | -1.618                                                 | 0.084                                                   |
| Pituitary Gland Left                                      | Medial Septal Nucleus Right                               | -0.724                                                 | -1.003                                                  |
| Pituitary Gland Left                                      | Sylvian Gyrus Right                                       | -0.107                                                 | -0.194                                                  |
| Pituitary Gland Right                                     | Suprasylvian Gyrus Right                                  | -1.205                                                 | 0.823                                                   |
| Pons Right                                                | Gyrus Rectus Right                                        | 0.227                                                  | 0.592                                                   |
| Pons Right                                                | Olfactory Bulb Right                                      | -0.091                                                 | 1.389                                                   |
| Posterior Sygmoideus Gyrus Left                           | Thalamus Right                                            | -1.079                                                 | 0.282                                                   |
| Precurciate Gyrus Left                                    | Olfactory Bulb Left                                       | 1.339                                                  | 1.082                                                   |
| Preoptic Hypothalamic Area Left                           | Gyrus Rectus Left                                         | -0.201                                                 | -0.290                                                  |
| Preoptic Hypothalamic Area Left                           | Medulla Oblongata Left                                    | -0.600                                                 | -0.107                                                  |
| Preoptic Hypothalamic Area Left                           | Medulla Oblongata Right                                   | -1.066                                                 | 0.564                                                   |
| Preoptic Hypothalamic Area Right                          | Pituitary Gland Right                                     | -0.026                                                 | 0.041                                                   |
| Preoptic Hypothalamic Area Right                          | Cerebellum Right                                          | -0.957                                                 | 1.223                                                   |
| Preoptic Hypothalamic Area Right                          | Medulla Oblongata Right                                   | -1.287                                                 | 1.184                                                   |
| Putamen Left                                              | Gyrus Rectus Left                                         | -0.020                                                 | -0.348                                                  |
| Putamen Left                                              | Substantia Nigra Right                                    | -1.607                                                 | 1.091                                                   |
| Putamen Left                                              | Gyrus Rectus Right                                        | -0.218                                                 | -0.535                                                  |
| Septum Left                                               | Amygdala Left                                             | -0.073                                                 | -0.751                                                  |
| Septum Left                                               | Parahippocampal Cortex Left                               | -1.055                                                 | -0.384                                                  |
| Septum Left                                               | Gyrus Rectus Left                                         | -0.005                                                 | -0.062                                                  |
| Septum Left                                               | Pituitary Gland Left                                      | -1.204                                                 | 0.739                                                   |
| Septum Left                                               | Pituitary Gland Right                                     | -0.880                                                 | 0.087                                                   |
| Septum Left                                               | Midbrain Right                                            | -0.887                                                 | -0.194                                                  |
| Septum Right                                              | Nucleus Of The Horizontal Limb Of The Diagonal Band Right | -1.401                                                 | 0.646                                                   |
| Septum Right                                              | Periaqueductal Grey Substance Right                       | -1.765                                                 | 0.544                                                   |
| Septum Right                                              | Midbrain Right                                            | -1.555                                                 | -0.130                                                  |
| SubFornical Organ Left                                    | Pituitary Gland Right                                     | -0.240                                                 | -0.374                                                  |
| SubFornical Organ Right                                   | Pituitary Gland Right                                     | -0.102                                                 | -0.056                                                  |
| Temporal Lobe Left                                        | Septum Right                                              | -1.371                                                 | -0.233                                                  |
| Temporal Lobe Left                                        | Precurciate Gyrus Right                                   | -1.495                                                 | -0.235                                                  |
| Thalamus Left                                             | Posterior Sylvian Gyrus Right                             | -1.023                                                 | -0.824                                                  |
| Thalamus Left                                             | Putamen Right                                             | -0.639                                                 | 0.336                                                   |
| Thalamus Left                                             | Claustrocortex(Insula) Right                              | -1.006                                                 | -0.675                                                  |



**Conflict of interest :**

The authors state that they have no conflict of interest.

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