A structural MRI study in transgender persons on cross-sex hormone therapy

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Abstract

Background: To date, research findings are inconsistent about whether neuroanatomy in transgender persons resembles that of their natal sex or their gender identity. Moreover, few studies have examined the effects of long-term, cross-sex hormonal treatment on neuroanatomy in this cohort. The purpose of the present study was to examine neuroanatomical differences in transgender persons after prolonged cross-sex hormone therapy.

Methods: Eighteen transgender men (female-to-male), 17 transgender women (male-to-female), 30 non-transgender men (natal men), and 27 non-transgender women (natal women) completed a high-resolution structural MRI scan at 3Tesla. Eligibility criteria for transgender persons were gender affirming surgery and at least 2 years of cross-sex hormone therapy. Exclusion criteria for non-transgender persons were presence of psychiatric or neurological disorder.

Results: Mean neuroanatomical volume for the amygdala, putamen and corpus callosum differed between transgender women and natal women but not between transgender women and natal men. Differences between transgender men and natal men were found in several brain structures, including the medial temporal lobe structures and cerebellum. Differences between transgender men and natal women were found in the medial temporal lobe, nucleus accumbens, and 3rd ventricle. Sexual dimorphism between non-transgender men and women included larger cerebellar volumes and smaller anterior corpus callosum in natal men relative to natal women. The results remained stable after correcting for additional factors including age, total intracranial volume, anxiety, and depressive symptoms.

Conclusions: Neuroanatomical differences were region-specific between transgender persons and their natal sex as well as their gender identity suggesting localized influence of sex hormones on neuroanatomy.

Introduction

Sexual dimorphism is widespread in the brain. Such dimorphism suggests for example that cerebellar, putamen, amygdala, and hippocampal volumes are larger in men versus women, whereas women have larger thalamic nuclei, lateral frontal gyri, and insular cortices than men [1]. However, the relationship between brain structure and gender identity is less clear. Presently, findings are inconsistent about whether the neuroanatomy of transgender persons resembles that of their natal sex or their gender identity (for recent review see [2]). One central question that remains to be determined is whether cross-sex hormone treatment "reverses" neuroanatomical sexual dimorphism, resulting in neuroanatomical features characteristic of gender identity rather than natal sex. Currently, however, studies on the neuroanatomical changes in transgender persons after prolonged cross-sex hormone treatment are too few in number to examine the putative effects of hormone therapy on neuroanatomy.

A post-mortem study in a small sample of hormonally-treated transgender women (TW, male-to-female) found that the bed nucleus of the stria terminalis [3] was similar in size to that typically found in non-transgender females, an effect that might have been partly driven by cross-sex hormone exposure. More recent studies evaluated the effects of testosterone treatment in transgender men (TM, female-to-male) and estrogen and antiandrogen treatment in TW [4-6]. Although one of these studies found cortical thickness was more characteristic of participants' gender identity than their natal sex in TM receiving androgens and TW receiving antiandrogens and estrogens [4], the findings contradict a study with an opposite pattern of cortical thickness in non-treated TW in the same areas [7]. Likewise, although one study reported a decrease in hypothalamus volume in TW with no changes in TM after treatment [5], another [6] cross-sex hormone study documented increases in TM in this region. Moreover, findings in transgender persons before they received hormone treatment are also difficult to interpret. Such studies have documented either a larger [8] or a smaller [9] putamen volume in TW relative to that of natal men, and some studies [10] could not find differences in other sexually dimorphic structures such as the corpus callosum [11]. Thus, current findings are inconsistent, and more complementary and confirmatory evidence is needed.

Despite the small number of structural MRI studies in transgender persons, parallel neuroimaging work in endocrine conditions of gonadal hormone perturbations might aid in predicting which brain regions are sensitive to sex steroid fluctuations [12-15]. The commonly found larger amygdala and hippocampal volumes in males relative to females are reduced in androgen deficiency [15]. Likewise, both androgen deficiency in Klinefelter Syndrome patients and antiandrogen treatment in TW appear to reduce cortical thickness in temporal cortex and increase ventricle size [4, 5, 14]. Finally, similar to striatal changes in transgender persons [8, 9], boys with early androgen excess have larger putamen volume and an enlarged medial temporal lobe (MTL) relative to unaffected comparisons [16]. Taken together, these converging lines of evidence indicate sensitivity to sex hormone fluctuations in several regions including the medial temporal lobe (MTL), the striatum, and the ventricles. However, data regarding specific associations of these structures with hormonal treatment in transgender persons are scarce.

This study examined whether the neuroanatomy in transgender persons receiving cross-sex hormone therapy resembled that of their natal sex or their gender identity in regions sensitive to gonadal hormone fluctuations. Additionally, global brain changes including total and subcortical grey matter volume (GMV), cerebellum, and corpus callosum size were also examined. To this end, we used a comprehensive morphometric analysis, analyzing not only volume but also cortical thickness and surface area. Based on the limited evidence available [4, 6-9, 16], we hypothesized patterns consistent with gender identity rather than natal sex in transgender persons.

********** Table 1 about here please**********

Methods

Participants

Eighteen transgender men (TM, M age = 37.22 years, SD = 8.29), 17 transgender women (TW, M age = 41.47, SD = 6.86), 27 non-transgender women (NTW, M age = 32.63, SD = 10.02) and 30 non-transgender men (NTM, M age = 31.50, SD = 8.52) participated in the study. Originally, another 7

participants were recruited but had to be excluded due to missing values on the anxiety and depression questionnaires. All transgender participants had undergone gender affirming surgery and been receiving cross-sex hormone therapy for at least 2 years. Thus, the final sample consisted of 92 participants in total (Table1). The sample differed significantly in age ($F(3,88) = 5.82$, $p = .001$) as well as depression ($F(3,88) = 6.32$, $p=.001$) and trait anxiety ($F(3,88)= 4.14$, $p=.009$). Age, depression, and trait anxiety were consequently used as covariates of no interest in all subsequent analyses. Transgender persons were recruited through flyers and the Department of Endocrinology of Ghent University Hospital and scanned on a 3T Siemens Trio (Siemens, Erlangen, Germany) MRI Scanner on site. Comparison participants were recruited through word of mouth and flyers. Exclusion criteria were present neurological or psychiatric disorders, or usage of psychotropic medication. The study was approved by the Medical Ethical Committee of Ghent University Hospital. All participants signed an informed consent prior to the study.

Screening questionnaires

Previous studies have acknowledged presence of mood and anxiety problems in transgender persons [17]. To be able to covary for potential differences in depression or anxiety, all participants completed the Beck Depression Inventory (BDI, [18]) and the Spielberger State/Trait Anxiety Inventory (STAI, [19]).

MRI acquisition

A high-resolution T1-weighted MPRAGE anatomical image was acquired (duration = 5:14 min) in ascending order with a FOV = 256 mm^2, slice thickness 1 x 1 x1 mm, TR = 2250 ms, TE = 2.52 ms, flip angle = 9 deg.

MRI processing and analysis

The original images were first visually inspected for artifacts and abnormal clinical findings that would lead to exclusion. Data were analysed with freesurfer (release 4.3.0, Martinos Center for Biomedical Imaging, Charlestown, MA; http://surfer.nmr.mgh.harvard.edu, [20, 21]) using an

automated procedure. Briefly, images were registered to a common stereotaxic space using affine transforms, normalized with respect to intensity, and skull stripped. Quality control was performed on a semi-automated basis checking for outliers and visual inspection after each processing step.

Structural neuroanatomy was characterized at three levels: 1) Grey matter volume (GMV) of subcortical brain structures, 2) cortical thickness, and 3) surface area size. Based on prior structural MRI findings [4, 7, 9, 22], and to reduce the chance of false positive findings, this study focused specifically on *a priori* regions of interest (ROIs), namely the MTL (amygdala, hippocampus, parahippocampus, fusiform gyrus) and the striatum (caudate nucleus, putamen, nucleus accumbens). In addition, major global volumetric effects (i.e., cortical and subcortical total GMV), cerebellum size, ventricle (3^{rd}, 4^{th}, 5^{th}) size, and corpus callosum volume (anterior/middle/posterior) were also investigated. Data were analysed using SPSS V.21 (alpha = .05, two-tailed). Multivariate analysis of variance (MANOVA) were used with Group as the between-subjects factor (TM, TW, NTM, NTW) and the following *covariates of no interest* age, total intracranial volume (TICV), total depressive symptoms (BDI), total trait anxiety symptoms (STAI Trait). Of note, given that total intracranial volume was covaried for, all differences in size have to be interpreted as being relative rather than absolute. To correct for multiple comparison testing, follow-up tests of significant effects were corrected using a step-down Bonferroni (Holm) procedure, $p < .05_{corrected}$, two tailed. To provide a more comprehensive picture of the results than normally given by p-values, upper and lower limits of the 95% CI are also presented in the tables [23].

********** Table 2 about here please**********

Results

Medial temporal lobe (MTL)

In MTL, a main effect of group was found for the left ($F(3,84) = 3.68$, $p = .02$) and right ($F(3,84) = 2.81$, $p = .045$) amygdala. After correction, follow-up tests indicated a larger left amygdala volume for TW relative to NTW ($p_{corr.} = .018$). Follow-up tests in the right amygdala did not survive statistical correction. A main effect in the right fusiform gyrus volume ($F(3,84) = 2.76$, $p = .047$) revealed a

significantly smaller volume in TM relative to both NTW ($p_{corr.}$ =0.048) and NTM ($p_{corr.}$ = 0.053)(Figure1). In addition, right fusiform area was also significantly different among the groups (F(3,83) = 4.74, p = .004). Here, NTM and NTW relative to TM had a larger surface area ($p_{corr.}$ =.042 and $p_{corr.}$ = 0.06, respectively). A main effect of group in the right parahippocampal area (F(3,84) = 3.08, p =.03) did not result in significant effects after correction.

********** Table 3 about here please**********

********** Figure 1 about here please**********

Striatum

In the striatum, a significant effect of group was found in the right putamen volume (F(3,84) = 3.63, p = .02) indicating larger volume for TW relative to NTW ($p_{corr.}$ = .042). No other effect survived correction. Follow-up tests to a main effect in the right accumbens (F(3,84) = 2.68, p = .05) indicated larger volume in TM relative to NTW ($p_{corr.}$ = .024)(Figure 1, Table 3).

********** Table 4 about here please**********

Global effects

Global analyses revealed significant group differences in the left (F(3,84) = 5.34, p=.002) and right (F(3,84) = 5.67, p = .001) cerebellum. Specifically, in the left cerebellum, corrected follow-up tests indicated larger relative left cerebellar volume in NTM relative to NTW ($p_{corr.}$ = .006) and TM ($p_{corr.}$ = .02). The same effect was present for the right cerebellum showing larger volume in NTM relative to NTW ($p_{corr.}$ = .006) and TM ($p_{corr.}$ = .006)(Table 4). A group effect in the anterior corpus callosum (F(3,83) = 4.70, p = .004) indicated that this region was larger in NTW than NTM ($p_{corr.}$ = .045) and TW ($p_{corr.}$ < .001). A similar effect in the posterior corpus callosum (F(3,83) = 3.40, p = .02)(Figure1)

revealed larger volume for NTW and TM than TW ($p_{corr.}$ = .01 for both comparisons). A different pattern was observed for the 3rd ventricle (F3,84) = 3.99, p = .01). It was smaller 3rd in TM relative to TW ($p_{corr.}$ = .035) and NTW ($p_{corr.}$ = .03)(Table 4).

In summary, neuroanatomical differences between transgender women and non-transgender women were found in the left amygdala, right putamen, and anterior/posterior corpus callosum. No differences were found in any measure between transgender women and non-transgender men. Differences between transgender men and non-transgender men were detected in fusiform gyrus volume and surface area, and the cerebellum. Transgender men differed from non-transgender women in right accumbens and fusiform gyrus volume/surface area, and 3rd ventricle size. Transgender men differed from transgender women in posterior corpus callosum. Sexually dimorphic effects indicated larger cerebellar volumes in natal men relative to natal women but a larger anterior corpus callosum for natal women.

Discussion

The present study examined differences in neuroanatomy between cross-sex hormone treated transgender men and transgender women. Based on prior work in transgender persons [4, 6, 8, 9] and in patients who had endocrine conditions with gonadal hormone perturbations [12, 15, 16], group differences were expected in the MTL, striatum, and ventricles. Three main findings pertinent to the study hypotheses were found: 1) Consistent with their natal sex, TW did not differ from non-transgender men and showed differences relative to non-transgender women in corpus callosum, putamen, and amygdala, 2) Consistent with their gender identity, transgender men differed from non-transgender women in the 3rd ventricle and the nucleus accumbens, 3) Transgender men differed from both natal men and natal women in fusiform volume.

Much of the brain is sexually dimorphic, especially the MTL given 1) larger amygdala and hippocampus volume in men relative to women [1], 2) high sex steroid receptor density in the MTL

[24], and 3) volumetric alterations of these structures in endocrine conditions of gonadal hormone perturbations [12]. To date, findings in transgender persons are highly inconsistent. Whereas some [9] have documented altered hippocampal volumes in transgender women before hormone treatment, others [4] could not replicate this effect. Associations in the present study indicated that amygdala volume in transgender women was consistent with the their natal sex rather than their gender identity. However, one surprising finding was that volume and area size in the fusiform gyrus were smaller in transgender men relative to both NTM and NTW, a finding that has not been reported previously. By comparison, no group differences were present in the hippocampus. Thus, although some differences might exist pre-treatment [9], the present findings and those of others [4] indicate that the amygdala and hippocampus volumes do not reverse to mirror gender identity after hormone treatment.

Based on prior work in endocrine conditions [16] and transgender persons [4], we had also hypothesized significant group differences in the striatum. Prior work has noted volumetric differences in the dorsal striatum (putamen) in transgender persons [8, 9] and endocrine disorders of androgen excess [16] albeit with mixed results to date. Whereas Savic & Arver [9] reported reduced putamen volume in TW relative to NTM and NTW, the opposite finding, namely a larger putamen in TW relative to NTM was found by Luders and colleagues [8]. The present finding of larger putamen volume in TW relative to NTW is thus largely consistent with that latter study. Given that the participants in the study by Luders et al. were transgender women who had not received hormone treatment and our participants were already receiving hormones for more than 2 years, the current data suggest that the putamen effect is stable and does also not change with cross-sex hormone therapy. Instead it might indicate pre-existing group differences. One interesting, previously not reported, association concerned the ventral striatum, i.e., the nucleus accumbens. Here, TM showed an effect consistent with their gender identity rather than their natal sex.

Finally, the present study also revealed associations between gender identity and global volumetric effects. Previous studies have documented larger ventricles in transgender women [4] but reductions in transgender men after cross-sex hormone therapy [5]. Consistent with the latter investigation [5], transgender men in the present study also had significantly smaller 3rd ventricles with no differences in 4th or 5th ventricles relative to both transgender women and non-transgender women.

In agreement with their suggestion [5], such a ventricular change might be due to a volumetric change in the structures surrounding the 3rd ventricle. Although further consistent with a sexually dimorphic pattern [11], the larger corpus callosum in TM and NTW relative to TW and NTM would indicate no change in this structure with cross-sex hormone treatment. Supplementing this finding, prior work to date has failed to identify differences in pre-hormone treated transgender persons in this structure [10]. Therefore, although 3rd ventricle size may be sensitive to hormonal treatment in transgender men, the corpus callosum does not appear to be responsive indicating regional sensitivity to hormone therapy.

The precise clinical relevance of neuroanatomical changes after hormone therapy remains to be determined. However, characterizing the different changes associated with cross-sex hormone treatment is important. For example, ventricular enlargement has not only been associated with grey matter reduction due to ageing [26], but has also been identified as a putative marker for progression of Alzheimer's Disease [27] or a risk factor for psychopathology [28]. Hulshof Pol [5] observed a final 3rd ventricle size in transgender women on hormonal therapy that was larger after treatment than the ventricle size observed in both natal men and women. Although the mechanisms and clinical implications of such effects are unknown, they deserve further study given reports of physiological risk with hormonal treatment [25] and prevalence of psychopathology [17] in transgender persons. Much more complementary information on the physiological and neurological changes with hormonal treatment is therefore needed.

Some limitations of the present study require discussion. First, the relatively small sample size of patients needs to be acknowledged. However, the sample size of the present study was within the range of prior work (e.g., [4, 8, 10, 22]). The second limitation concerns the fact that although all participants had received gender affirming surgery and had already been taking cross-sex hormone therapy for a minimum of 2 years, MRI scans from before the genital surgery were lacking. Thus, we cannot make any statements regarding causality of treatment and merely report associations. However, we nonetheless believe these data worthwhile to be reported for the following reasons. First, with the exception of four prior studies, three in-vivo [4-6]) and one post-mortem [3], the majority of earlier morphometric work has examined structural brain differences in transgender persons who had not received hormone treatment. Moreover, these prior studies were characterized by relatively small

sample size requiring independent replication. Second, our study included both TM and TW whereas a few prior studies only included TW [3, 7-9] or TM [6] thus enabling a more comprehensive comparison. Third, in the present study, subthreshold mood and anxiety symptoms were taken into consideration. This has not been examined in prior work although it may have played an important role in their findings. Although it could be criticized that such differences in mood and anxiety only occurred in our sample, we believe this to be unlikely given convincing documentation of depressive and anxious symptoms in transgender persons [17]. This would suggest that our sample is representative of transgender persons living in their gender identity. Fourth and finally, direct sex differences between natal men and natal women were few and limited to the cerebellum and the corpus callosum. However, due to the large variability among the population, large-scale studies (e.g.,[1, 11]) are needed to make definitive statements. Therefore, the findings should be considered relative to the transgender groups rather than displaying a lack of normal sexual dimorphism.

Broadly speaking, the findings of the present study are largely consistent with prior work [4-6] in that they suggest some plasticity of the brain even during adulthood with cross-sex hormone treatment. However, they also appear to indicate regionally-specific changes, such that some, but not all, investigated structures transition towards gender identity. Future studies are needed to replicate these findings and examine in a next step whether these neuroanatomical differences are associated with functional or cognitive changes of the subserved brain regions.

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Conflict of interest: The authors have nothing to disclose.

Captions

Figure 1. Figure displays mean and 95% CI of the volumetric analyses for the four groups. Horizontal lines indicate significant differences ($p<.05_{corr}$) between groups after correction for multiple comparisons.

Table 1. Demographic information for each of the four groups, comparison men (CM), comparison women (CW), trans men (TM), trans women (TW).

Table 2. Results of morphometric analyses for each of the groups in the medial temporal lobe. Results are mean values with the 95% CI in square brackets underneath. For volume, values are mm^3 for area they are mm^2 and for thickness are mm.

Table 3. Results of morphometric analyses of the striatum for each of the groups. Results are mean values with the 95% CI in square brackets underneath. Volumetric values are mm^3.

Table 4. Results of global volumetric analyses for each of the groups. Results are mean values with the 95% CI in square brackets underneath. Values are mm^3.

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Mean (SD)	NTM N=30	NTW N=27	TM N=18	TW N=17	Effect (Bonf. corrected)
Age in years	31.50 (8.52)	32.63 (10.02)	37.22 (8.29)	41.47 (6.86)	NTM,NTW<TW
BDI[a]	2.73 (3.57)	3.89 (4.96)	5.17 (5.62)	10.76 (11.02)	TW>NTM,NTW
STAI-Trait[b]	41.23 (8.83)	43.63 (8.72)	47.72 (3.44)	47.59 (5.23)	TW,TM>NTM
Testosterone[c] (ng/dl)	418.58 (214.49)	27.36 (10.31)	854.63 (658.36)	14.76 (5.26)	
Androstenedione[c] (ng/dl)	67.79 (33.28)	81.98 (36.94)	105.33 (50.62)	54.65 (18.92)	
LH[c] (mU/ml)	5.71 (2.40)	13.04 (13.97)	4.74 (7.44)	26.78 (16.12)	
E1[c] (pg/ml)	36.89 (31.25)	79.78 (64.67)	60.24 (21.91)	230.77 (441.19)	
E2[c] (pg/ml)	24.83 (21.40)	91.37 (98.11)	37.01 (16.42)	105.86 (129.12)	
Cortisol[c] (µg/dl)	9.96 (4.15)	7.94 (3.38)	7.89 (3.37)	8.56 (3.45)	

[a]BDI = Beck Depression Inventory

[b]STAI-Trait =Spielberger Trait Anxiety Inventory

[c]for hormonal analyses, only a subset of hormones was available in comparisons (n=16 for NTM and n=18 for NTW) while 3 assays could not be analyzed in the transgender group (n=16 for TM and N=16 for TW); LH = luteinizing hormone; E1 = estrone; E2 = estradiol

Medial temporal lobe	NTM N = 30	NTW N = 27	TM N = 18	TW N = 17	Effect (Bonf.. corrected)
L. Amygdala volume	1653.41 [1585 1721]	1517.15 [1447 1587]	1629.17 [1549 1709]	1702.23 [1612 1793]	TW>NTW
R. Amygdala volume	1619.64 [1556 1683]	1500.08 [1434 1566]	1549.82 [1475 1625]	1648.32 [1564 1733]	ns
L. HP volume	4227.24 [4058 4396]	4185.45 [4011 4360]	4352.58 [4154 4551]	4439.60 [4215 4664]	-
R. HP volume	4272.34 [4100 4444]	4275.46 [4098 4453]	4395.08 [4193 4597]	4491.71 [4263 4720]	-
L. PH volume	2288.18 [2170 2406]	2401.79 [2280 2523]	2553.02 [2414 2692]	2389.11 [2232 2546]	-
R. PH volume	2314.14 [2181 2447]	2186.24 [2049 2323]	2258.36 [2101 2415]	2212.57 [2036 2390]	-
L. PH thickness	2.70 [2.58 2.82]	2.93 [2.80 3.05]	3.03 [2.88 3.17]	2.88 [2.72 3.04]	ns
R. PH thickness	2.76 [2.64 2.88]	2.94 [2.81 3.06]	2.97 [2.83 3.11]	2.84 [2.68 3.00]	-
L. PH area	731.00 [699 763]	687.39 [654 721]	707.43 [669 746]	697.62 [654 741]	-
R. PH area	738.76 [701 776]	655.95 [617 694]	668.33 [624 712]	681.26 [631 731]	ns
L. FF volume	10557.87 [10029 11087]	9863.12 [9318 10408]	9988.88 [9367 10611]	10382.27 [9679 11086]	-
R. FF volume	10544.10 [10106 10982]	10220.28 [9769 10672]	9543.13 [9028 10058]	10307.10 [9724 10889]	NTM,NTW>TM
L. FF thickness	2.78 [2.73 2.83]	2.82 [2.76 2.87]	2.84 [2.78 2.90]	2.74 [2.67 2.81]	-
R. FF thickness	2.80 [2.75 2.85]	2.83 [2.78 2.88]	2.85 [2.79 2.91]	2.83 [2.77 2.90]	-

L. FF area	3296.69 [3162 3431]	3061.25 [2923 3200]	3112.89 [2955 3271]	3271.21 [3093 3450]	-
R. FF area	3360.81 [3240 3482]	3190.07 [3065 3315]	2983.85 [2842 3126]	3225.74 [3065 3387]	NTM,NTW>TM

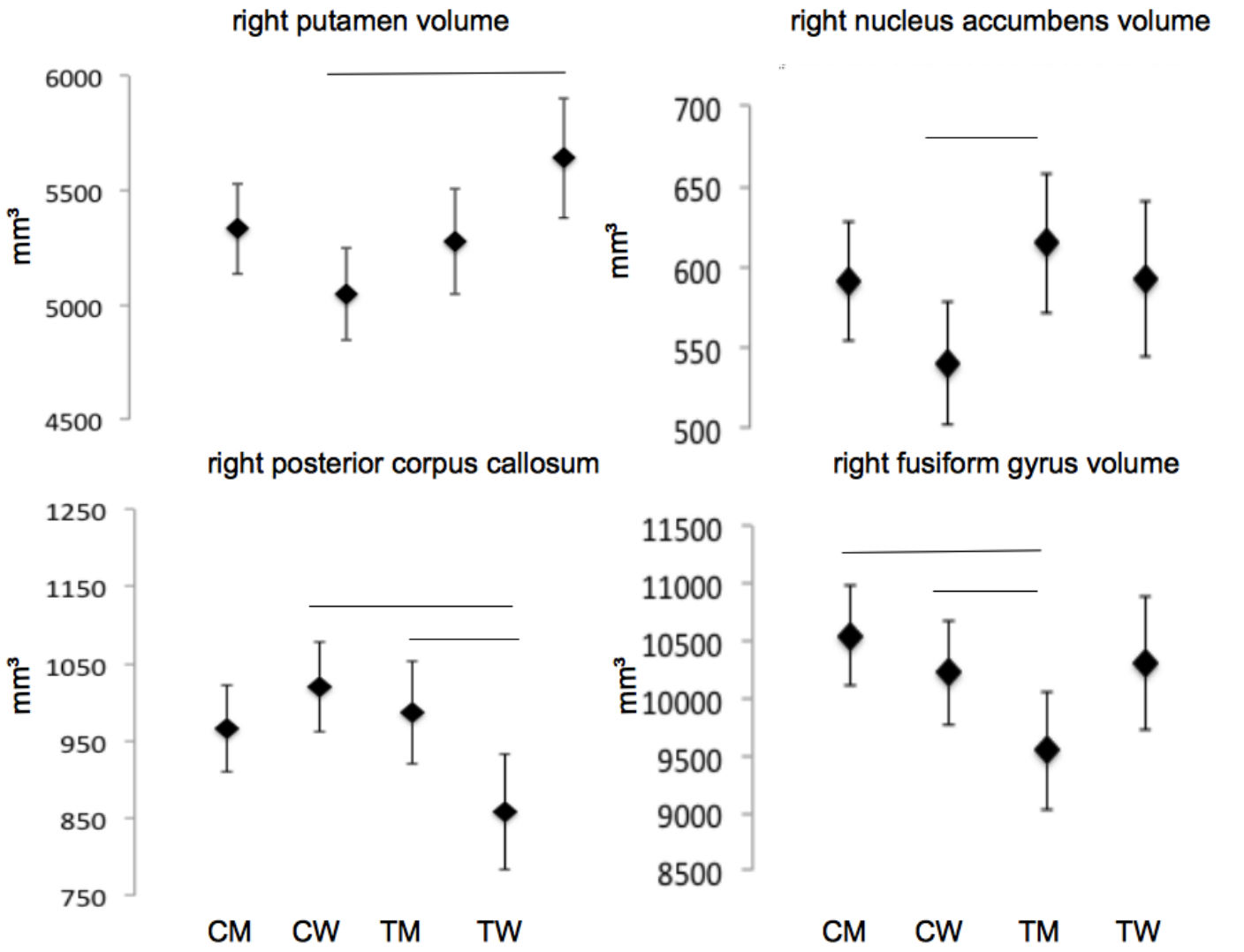
L. = left, R. = right; HP = Hippocampus; PH = parahippocampus; FF = fusiform; ns = not significant after follow-up; "-" no significant main effects of group

Striatum	NTM N = 30	NTW N = 27	TM N = 18	TW N = 17	Effect (Bonf. corrected)
L. Caudate volume	3698.01 [3533 3863]	3643.14 [3473 3813]	3718.87 [3525 3913]	3751.87 [3532 3971]	-
R. Caudate volume	3736.21 [3567 3905]	3757.99 [3584 3932]	3777.79 [3579 3977]	3792.14 [3567 4017]	-
L. Putamen volume	5650.38 [5415 5886]	5341.97 [5099 5585]	5662.87 [5386 5940]	5875.99 [5562 6190]	-
R. Putamen volume	5331.76 [5135 5528]	5048.15 [48 46 5251]	5277.10 [5046 5508]	5640.87 [5379 5902]	TW > NTW
L. Accumbens volume	504.07 [463 545]	448.58 [406 491]	501.78 [453 550]	500.71 [446 556]	-
R. Accumbens volume	591.05 [554 628]	540.20 [503 578]	614.77 [572 658]	592.78 [544 641]	TM > NTW

L. = left/R. = right; ns = not significant after follow-up; “-“ = no significant main effect

Global volumes	NTM N = 30	NTW N = 27	TM N = 18	TW N = 17	Effect (Bonf. corrected)
Total GMV	656994 [644039 669949]	641529 [628182 654877]	643721 [628485 658957]	665766 [648538 682994]	-
Cortical GMV	484854.03 [473591 496116]	479198.85 [467594 490803]	482071.37 [468825 495317]	493958.59 [478981 508936]	-
Subcortical GMV	59079.25 [57755 60403]	57080.06 [55716 58444]	58313.06 [56756 59870]	60250.41 [58489 62011]	-
L. cerebellum	56052.88 [54420 57685]	52027.63 [50345 53710]	51048.09 [49127 52968]	54561.48 [52390 56732]	NTM>NTW,TM
R. cerebellum	57689.51 [55981 59398]	53644.94 [51885 55405]	52697.74 [50689 54707]	57421.48 [55150 59693]	NTM>NTW,TM
3rd ventricle	993.77 [863 1123]	1003.31 [869 1137]	800.99 [648 953]	1190 [1017 1363]	TM<TW,NTW
4th ventricle	1828.36 [1593 2064]	2025.95 [1783 2269]	1574.04 [1301 1856]	1987.43 [1674 2301]	-
5th ventricle	6.06 [2 10]	8.59 [4 13]	6.75 [2 11]	4.00 [-1 9]	-
CC- Anterior	857.83 [807 908]	955.54 [903 1007]	910.33 [851 970]	788.13 [721 855]	NTW>NTM,TW
CC- Central	454.25 [419 489]	493.69 [457 530]	476.63 [435 518]	426.58 [380 473]	-
CC - Posterior	966.64 [910 1023]	1019.95 [962 1078]	987.21 [921 1054]	858.74 [784 934]	NTW,TM >TW

L.=left/R.=right; GMV – grey matter volume; CC = corpus callosum; ns = not significant after follow-up; "-" no significant main effect


right putamen volume
6000
5500
5000
4500
mm³
right nucleus accumbens volume
700
650
600
550
500
mm³
right posterior corpus callosum
1250
1150
1050
950
850
750
mm³
CM
CW
TM
TW
right fusiform gyrus volume
11500
11000
10500
10000
9500
9000
8500
mm³
CM
CW
TM
TW