DIFFERENCE OF THE CORPUS CALLOSUM ON MIDSAGITTAL PLANE BETWEEN NORMAL MALE, FEMALE AND TRANSSEXUALS

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Abstract: We investigated differences in corpus callosum shapes at the midsagittal plane using MRI for different subjects: normal males, normal females, and subjects with gender identity disorder (GID). We first represented callosal shapes using Fourier descriptors of callosal contours. Using linear support vector machines (SVM) with soft-margin, we then determined a hyperplane that separates normal males and females most optimally in the vector space spanned by Fourier descriptors. We then proposed a measure that has prominent sex difference: it is defined as the coordinate of a callosal shape on the subspace orthogonal to the obtained hyperplane. We further showed that the value of the measure for GID more strongly reflects subjects' mental sex, i.e. gender, than their physical sex. We concluded that the measure found in this study has no sex-related differences, but does have gender-related differences. It is therefore useful as an objective measure for GID diagnoses.

Introduction

Diagnoses for gender identity disorder (GID) [1] and transsexualism are based on subjective observations by two or more psychiatrists [2]. Some objective measures to distinguish GID and transsexualism from normal males and females have been sought to avoid erroneous diagnoses that often result from purely subjective observation [3]. Discovery of such an objective measure is also important from the viewpoint of elucidating the causes and mechanisms of GID development.

Over the past few decades, numerous studies have been examined whether or not the corpus callosum (CC), which interconnects the two cerebral hemispheres, has sex-related differences [4], [5], [6], [7]. The callosal shape might have not only sex-related differences, but also some gender-related differences. Furthermore, because such differences are visible non-invasively, as by MRI, gender-related differences in callosal shape are useful as an objective measure for GID diagnoses.

Our goal is to discover gender-related differences in the callosal shape that can be measured non-invasively on the midsagittal plane using MRI. We then first quantitatively represent callosal shape on the midsagittal plane measured using MRI with Fourier descriptors [8]. Using linear support vector machines (SVM) with soft-margin [9], we next identify the component that reflects sex-related differences most strongly in the callosal shape represented with Fourier descriptors. After analyzing the magnitude of the component for callosal shape of persons with GID, we show that persons with FTM[1] have a magnitude that resembles that for normal males and that persons with MTF have a magnitude that resembles that for normal females. It suggests that the component in the callosal shape does not reflect sex, but rather gender.

Materials and Methods

This study examined midsagittal MRI scans of the heads of 422 normal subjects (211 males, 211 females) and 57 persons (24 MTFs, 33 FTMs) who had been diagnosed with GID or transsexualism by psychiatrists. These MRIs were recorded using a 1.5 Tesla super-conducting MRI system.

Callosal shapes extracted from MRI images for all subjects were normalized by both their size and orientation to investigate differences of callosal shape independent of size and orientation between normal males and females. Fourier descriptors [8] were employed to quantitatively represent callosal shape, the callosal contour, at the midsagittal plane. The Fourier descriptor represents a given contour as a multi-resolution expression, i.e. coarse to fine components of the original contour. Hence, the Fourier descriptor up to Kth order approximates the original contour with the coarsest K components. Figure 1 shows examples of callosal shapes approximated with various order K of Fourier descriptors. Figure 1 also indicates that a Fourier descriptor up to approximately K=9th order is necessary to represent callosal shapes.

The callosal shape for each subject is represented as a point in $4K$-dimensional vector space because the Fourier descriptor up to Kth order is equivalent to a $4K$-dimensional real vector. Callosal shapes for all subjects distribute in the $4K$-dimensional vector space.

We next determined the ($4K$–1)-dimensional hyperplane that separates the points for normal males

[1] A transsexual is classified as either a male-to-female transsexual (MTF), i.e. a male who wants to become female, or conversely, a female-to-male transsexual (FTM) [10]

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and those for normal females most optimally in the 4*K*-dimensional vector space. Linear SVM with soft-margins [9] were employed to determine such a hyperplane. Let *Vc* be the one-dimensional subspace that is orthogonal to the obtained hyperplane in 4*K*-dimensional vector space. Subspace *Vc* can be considered as the most sensitive one-dimensional subspace to differences of callosal shape between normal males and females. Let a_c be the coordinate on subspace *Vc* for a given callosal shape. The value a_c, which refers to the characteristic value, is expected to differ between normal males and females most prominently.

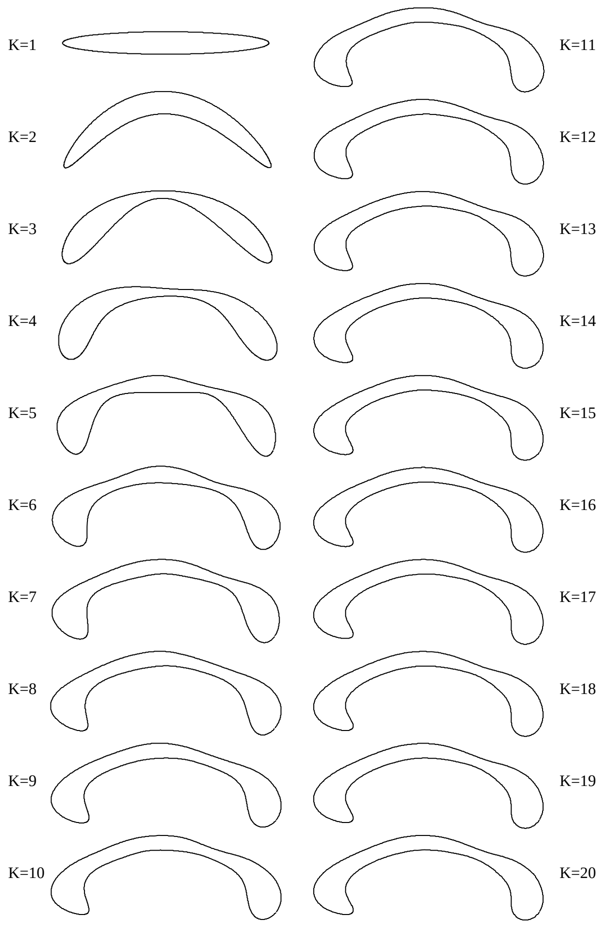

Figure 1: Examples of callosal shapes approximated with various order *K* of Fourier descriptors

Results

We determined the subspace *Vc* that is most sensitive to the difference of callosal shapes between normal males and females. Characteristic values a_c for all normal males and females were estimated from the obtained subspace *Vc*. The respective mean$\pm$standard deviation of the characteristic values a_c for normal males and females are 0.7361 ± 0.0845 and 0.6567 ± 0.0920. Figures 2(a) and 2(b) respectively portray histograms of characteristic values a_c for normal males and females. These figures show that the characteristic values a_c differ markedly between normal males and females. Student's t-test for two independent groups reveals that the characteristic value a_c differs significantly among normal males and females ($p < 10^{-17}$).

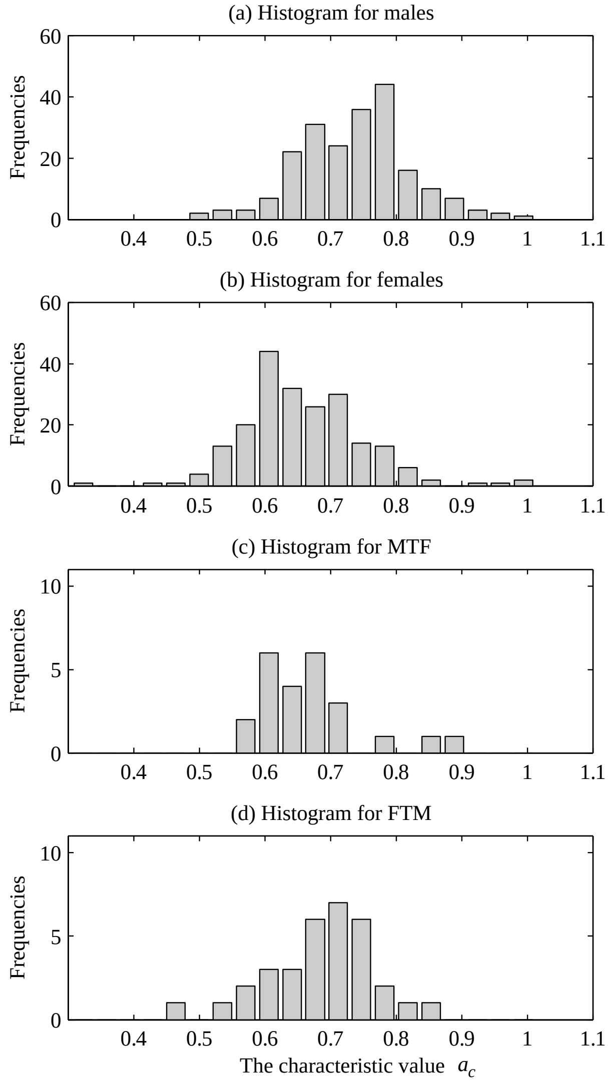

Figure 2: Histograms of characteristic values a_c for normal males, normal females, MTF, and FTM

Subspace *Vc* can be considered as the most sensitive one-dimensional subspace to differences of callosal shape between normal males and females. In other words, subspace *Vc* most includes the sex-related component extracted from the original callosal shape. Therefore, the characteristic value a_c, the coordinate on the subspace *Vc* for a given callosal shape, indicates the amount of the sex-related component. Figures 2(a) and 2(b) show that callosal shapes with larger values of a_c are considered to be more masculine; smaller values are more feminine.

The callosal shapes that correspond to various characteristic values of a_c yield an intuitive illustration of the sex-related component. Figure 3 shows callosal shapes at characteristic values a_c=0.32, 0.70, 0.98, which corresponds to the smallest value among normal

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females, the averaged value over all normal subjects, and the largest value in normal males, respectively. Terminologies of important areas of the CC are designated in the figure. Figure 3 reveals that: splenia of females are more bulbous than males', but not larger; females' isthmus are thicker, and males' anterior truncus are slightly more tumid than females'.

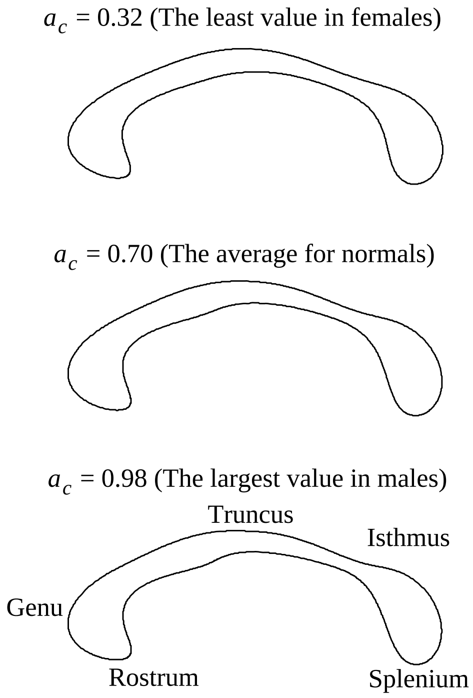

Figure 3: Callosal shapes at various a_c

We next examined how characteristic values a_c of GID subjects compared to those of the normal subjects. Figures 2(c) and 2(d) respectively depict histograms of the characteristic values a_c for persons with MTF and FTM in GID. Figures 2(a)–2(d) show that the histogram for MTF differs from that for normal males; it seems rather closer to that for normal females. Otherwise, the histogram for FTM appears to be swept toward larger a_c, i.e. closer distribution to that for normal males than that for normal females. Consequently, it can be concluded that persons with GID have characteristic values a_c closer to their mental sex, i.e. gender, than to their physical sex. We therefore refer the component *Vc* to the gender-related component.

We performed a principal component analysis to precisely examine the relationship between distribution of the callosal shapes for normal subjects in the 4*K* dimensional vector space and the subspace *Vc* obtained in this study. Figure 4(a) shows all eigenvalues for the covariance matrix of callosal shapes for normal subjects in descending order. Let *Vi* be the *N*-dimensional subspace spanned by the *N* eigenvectors corresponding to the largest *N* eigenvalues. Subspace *Vi* represents the principal components of callosal shape variation for normal subjects – the components that have the largest individuality. Figure 4(b) shows angles between subspace *Vi* and subspace *Vc* as a function of *N*. Figures 4(a) and 4(b) show that the obtained subspace *Vc*, the gender-related component, makes an angle of 90 (deg) with subspace *Vi*, the largest idiosyncratic component; in other words, these subspaces are mutually orthogonal. Figures 4(a) and 4(b) also show that the magnitude of the gender-related component is much smaller than those of idiosyncratic components. Therefore, the gender-related component is considered to be extremely difficult to detect.

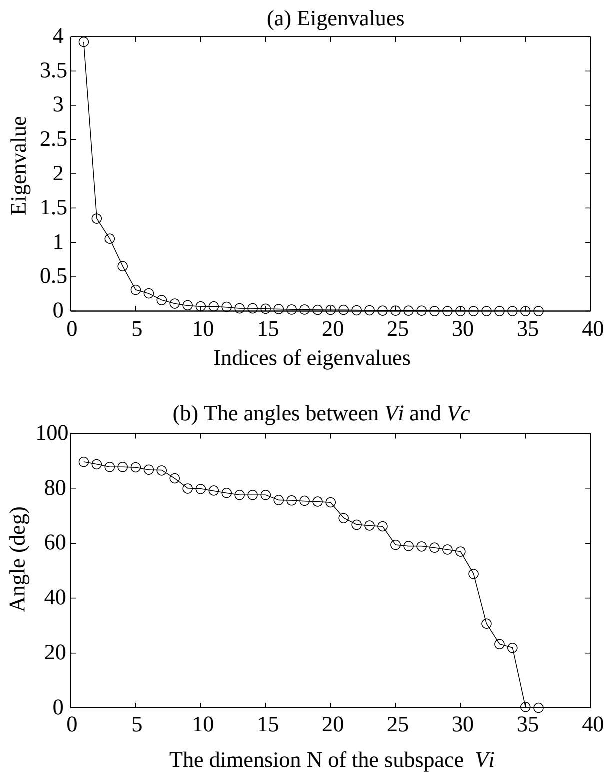

Figure 4: Eigenvalues of callosal shapes for normal subjects and the angles between the subspace *Vc* and *Vi*

Discussion

Over the past few decades, many studies have been conducted to investigate whether or not callosal shapes have sex-related differences. In 1982, Lacoste-Utamsing and Holloway [6] originally reported the existence of sex differences in the splenium of the CC. Investigating the midsagittal sliced splenia of normal brains (male=9, female=5) by autopsy, they argued that females tended to have both a more bulbous and larger splenium than males. On the other hand, Allen et al. refuted that the areas of both overall CC and its subdivisions showed no sexual dimorphism by measuring the midsagittal scanned CC by MRI of 73 age-matched pairs of males and females [4]. Nevertheless, they also reported that females had a significantly more bulbous splenium than males. Measuring the midsagittal MRI scans of the CCs of 20 control males, 20 control females, 10 MTF transsexuals, and 10 FTM transsexuals, Emory et al. [7] reported a slight tendency for females to have a more bulbous splenium than males, but asserted that the

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callosal shapes did not differ significantly among the four groups. Steinmetz et al. investigated the area, normalized with the callosal overall area, of various segments of the CC for 26 males and the same number of females [11]. They reported that the normalized area corresponding to the isthmus was larger in females than in males. Clarke and Zaidel maintained that sex differences were found for measures of the posterior body (i.e. isthmus) of the CC in 60 healthy young adults [12]. Bishop et al. reviewed 49 studies that included almost all studies published before 1994 regardless of whether the CC was measured at autopsy or by MRI. That study concluded that CC exhibited neither size nor shape differences attributable to sex [5].

Whether the shape of CC has sex-related or gender-related differences remains controversial. Figure 4 depicts the cause of the controversy: the magnitude of the gender-related component is considerably smaller than those of the idiosyncratic components. However, we have isolated the gender-related component shown in Fig. 3, which supports the inferences of Allen et al. [4], Steinmetz et al. [11], and Clarke and Zaidel [12].

Although the gender-related component is much smaller than those of the idiosyncratic components, the gender-related component is clearly distinguishable from the other once subspace *Vc* is identified because they are mutually orthogonal. Consequently, it is considered that the characteristic value a_c identified in this study is a candidate of objective measures for GID diagnoses.

Sexual differentiation of the human nervous system begins from the sixth week after fertilization. In the process of the CC development in the order of genu, truncus, splenium and rostrum during viviparity of 8–20 weeks, the developing direction of the CC might depend on both temporal and spatial relationships with other regions in the brain, such as the cortex and limbic system. Future research should specifically examine how the callosal characteristic value a_c relates to the several hormones that affect the growth of other brain regions. Furthermore, investigations into what regions of the human brain control, and are affected by, gender and sex are necessary for elucidating the cross-relationship between the human brain and gender.

Conclusions

We quantitatively represented callosal shape at the midsagittal plane on MRI using Fourier descriptors. Using linear SVM with soft-margins, we found a component in the callosal shape; the component most strongly reflects sex-related differences between normal males and females. We showed that the magnitudes of the components for MTF and FTM persons are closer to their mental sex, i.e. gender, rather than their physical sex. We then proposed the magnitude of the component as a criterion to evaluate gender. The criterion is useful for objective and quantitative diagnoses of GID. Use of the criterion in combination with the other objective criteria might markedly increase the certainty of diagnoses after more detailed examination.

References

[1] American Psychiatric Association (1994): 'Gender Identity Disorders', in Frances A. (Ed): '*Diagnostic and Statistical Manual of Mental Disorders, 4th ed., (DSM-IV)*', (APA, Washington DC), pages 532–538.
[2] The Second Special Committee on Gender Identity Disorder, the Japanese Society of Psychiatry and Neurology (2002): 'The guideline of diagnoses and cure on gender identity disorder', *Magazine for Psychiatrists and Neurologists*, 104:618–632.
[3] KAMEYA Y. and NARITA Y. (1999): 'A clinical and psycho-sociological case study on gender identity disorder', *J. Clin. Psychiatry*, 28:563–573.
[4] ALLEN L. S., RICHEY M. F., CHAI Y. M., and GORSKI R. A. (1991): 'Sex differences in the corpus callosum of the living human being', *J. Neurosci*., 11:933–942.
[5] BISHOP K. M. and WAHLSTEN D. (1997): 'Sex differences in the human corpus callosum: myth or reality? ', *Neurosci. Biobehav. Rev*., 21(5):581–601.
[6] DE LACOSTE-UTAMSING C. and HOLLOWAY R. L. (1982): 'Sexual dimorphism in the human corpus callosum', *Science*, 216:1431–1432.
[7] EMORY L. E., WILLIAMS D. H., COLE C. M., AMPARO E. G., and MEYER W. J. (1991): 'Anatomic variation of the corpus callosum in persons with gender dysphoria', *Arch. Sex. Behav.*, 20(4):409–417.
[8] GRANLUND G. H. (1972): 'Fourier preprocessing for hand print character recognition', *IEEE Trans. on Comput.*, C-21:195–201.
[9] CRISTIANINI N. and TAYLOR J. S. (2000): '*An Introduction to Support Vector Machines: and Other Kernel-Based Learning Methods*', (Cambridge Univ. Press, Cambridge).
[10] World Health Organization (1992): 'Gender Identity Disorders', in Sartorius N. (Ed): '*The ICD-10 Classification of Mental and Behavioural Disorders*', (WHO, Geneva), pages 215–217.
[11] STEINMETZ H., JÄNCKE L., KLEINSCHMIDT A., Schlaug G., Volkmann J., and Huang Y. (1992): 'Sex but no hand difference in the isthmus of the corpus callosum', *Neurology*, 42:749–752.
[12] CLARKE J. M. and ZAIDEL E. (1994): 'Anatomical-behavioral relationships: corpus callosum morphometry and hemispheric specialization', *Behav. Brain Research*, 64:185–202.