Age-related Changes in White Matter Tracts Associated with Face Recognition System

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Summary

Objectives. Analyze anatomical connectivity and integrity of three white matter tracts involve in face recognition system in three age samples: children, young adults and elderly adults. *Background.* The neural circuit of face recognition has been well characterized in a wide age spectrum. However, anatomical connectivity changes across aging are still unclear. *Methods.* The variations in the connectivity of this circuit in three age samples (32 individuals, 8 to 78 years) are examined here, by focusing in three major association tracts: inferior frontal-occipital (IFOF), inferior longitudinal (ILF) and superior longitudinal fasciculi (SLF). These seem to be connectors between nodes of the face recognition system (occipital face area (OFA), face fusiform area (FFA) and superior temporal sulcus (STS), although little is known about SLF. Fiber tracking computations were performed using a deterministic method. *Results.* Fractional anisotropy (FA) and number of streamlines of the IFOF, ILF and SLF were estimated. Resulting FA values are similar across groups in ILF and SLF. However, the IFOF shows a decrease FA in elderly adults. In addition, children exhibit lower number of streamlines than young adults in all tracts, while elderly exhibit a selective decrease in the bilateral IFOF and a selective increase in SLF. *Conclusions.* Our study shows that the anatomical connectivity of the face recognition circuit remains similar. Aging produces a selective decrease in the occipito-frontal connectivity, preserving the connectivity with the temporal lobe.

Keywords: Aging, tractography, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus.

Cambios Relacionados a la Edad en los Tractos de la Sustancia Blanca Asociados al Sistema de Reconocimiento Facial

Resumen

Objetivo. Analizar la conectividad e integridad de tres tractos involucrados en el sistema de reconocimiento de caras en tres grupos de edad: niños, adultos jóvenes y adultos viejos. *Antecedente.* La actividad neural que subyace al reconocimiento de caras ha sido bien caracterizada en un amplio espectro de edades. Sin embargo, los cambios en la conectividad anatómica a través de las edades, aún no es claro. *Método.* Se examinaron las variaciones en la conectividad de este circuito en tres grupos con diferentes edades (32 participantes, entre los 8 y lo 78 años), enfocándose en tres fascículos de asociación: fascículo inferior frontal-occipital (IFOF), fascículo inferior longitudinal (ILF) y fascículo superior longitudinal (SLF). Estos parecen ser conectores entre nodos implicados en el reconocimiento de caras (área facial occipital (OFA) y circunvolución temporal superior (STS) aunque se sabe poco de la DLF. Utilizando un método determinístico se realizaron computaciones para el seguimiento de las fibras. *Resultados:* Se estimaron la anisotropía fraccional (FA) y el número de corrientes de IFOF, ILF y SLF. Los valores hallados FA son similares a través de los grupos en ILF y SLF. Sin embargo, la IFOF muestra un decremento en los adultos viejos. Además, los niños muestran un número menor de corrientes que los adultos en todos los tractos, en tanto que los adultos viejos muestran un decremento selectivo en OFOF bilateral y un incremento selectivo en SLF. *Conclusiones:* Nuestro estudio muestra que la conectividad anatómica en los circuitos que participan en el reconcomiendo de caras permanecen similares. En envejecimiento produce un decremento selectivo en la conectividad occipito-frontal, preservándose la conectividad con el lóbulo temporal

Palabras clave: Envejecimiento, fascículo fronto-occipital, fascículo longitudinal inferior, fascículo longitudinal superior.

Introduction

Occipito-temporal cortex in humans includes functionally defined regions that preferentially respond to faces. These regions have been reliably identified using functional magnetic resonance imaging (fMRI), revealing the “core” of face processing (Friston, Harrison, & Penny, 2003; Haxby, Hoffman, & Gobbini, 2002; Mountcastle, 1998). These “core” regions are the fusiform face area (FFA), located at fusiform gyrus, the occipital face area (OFA) and superior temporal sulcus (STS) and all they are involved in structural face perception, responding more to faces than to objects or scenes (especially in the right hemisphere) (Kanwisher, McDermott, & Chun, 1997; Li, Xue, Cui, & Wong, 2011). The extended system includes regions not exclusively devoted to face processing, that are optionally recruited according to task, such as posterior cingulate and orbitofrontal areas (Valdés-Sosa et al., 2011). The activation of these brain regions by faces has been replicated in many studies using various tasks (Friston et al., 2003).

Several studies have focused on different developmental trajectories of face processing area, revealing critical age-related differences in visual cortex function (Aylward, 2005; Golarai et al., 2007; Scherf, Behrmann, Humphreys, & Luna, 2007). However, ascertaining the change of neural circuitry underlying a cognitive process requires not only identifying the critical cortical nodes but also establishing their anatomical and functional links. Aging is associated with a reduction in white matter volume (Good et al., 2002; Young, 1993) that seems to be more pervasive at times than even the gray matter decline (Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003), and generally involve a reduction in the integrity of white matter tracts (Madden et al., 2009; Sullivan & Pfefferbaum, 2006). This decline of white matter tracts integrity, involved in connecting the critical cortical nodes, can be examined with Diffusion Tensor Imaging (DTI). Recent studies of this technique have started to uncover age-related microstructural changes in white matter (Jones et al., 2006; Pfefferbaum & Sullivan, 2003; Sullivan & Pfefferbaum, 2006). Several reports evince a global white matter volume increase from childhood to adultness (Courchesne et al., 2000; Lebel & Beaulieu, 2011), and a further declination after maturation (Ge et al., 2002).

It has been postulated the importance of two major association tracks in face processing circuitry connectivity: inferior longitudinal (ILF) and inferior fronto-occipital fascicule (IFOF). The IFOF connects inferior-lateral and dorso-lateral frontal cortex with posterior temporal cortex (Crosby, 1962; Gloor, 1997) and continues posteriorly before radiating to the occipital lobe (Catani, Howard, Pajevic, & Jones, 2002). The ILF passes along the lateral wall of the occipital and temporal horns of the lateral ventricle (Catani et al., 2002) and fibers project in the superior, middle, and inferior temporal and fusiform gyri and project to the lingula, cuneus, lateral surface of the occipital lobe and occipital pole (Crosby, 1962; Dejerine, 1895) These tracts are the most important connectors between occipito-temporal nodes (FFA and OFA) and the frontal lobe (Mori, Wakana, Van Zijl, & Nagae-Poetscher, 2005). Some studies have focused in these tracts, linking brain connectivity changes with face processing variables (Tavor et al., 2014; Thomas et al., 2008); and also a few studies have described changes in white matter connectivity cross life in children and (Scherf, Thomas, Doyle, & Behrmann, 2014; Thomas et al., 2008), in ILF and IFOF.

However, there is another major tract, the superior longitudinal fascicule (SLF) that could be associated with the face processing circuit. SLF stems from the caudal part of the superior temporal gyrus reaching the occipital and parietal lobes (Mori et al., 2008) and arches around the caudal end of the Sylvian fissure and extends to the lateral prefrontal cortex (Makris et al., 2005), thus it could be involved in connecting STS with frontal (Philippi, Mehta, Grabowski, Adolphs, & Rudrauf, 2009). Philippi et al. suggested the implication of SLF in other kinds of information conveyed by faces, such as the processing of emotional expression, lip speech, due to the relationship of this tract with STS (Philippi et al., 2009).

Recently Ethofer et al. (2013) in a study of functional responses and structural connections of cortical areas for processing faces and voices in STS have demonstrated that stronger connections in audiovisual integration areas running through the dorsal part of the SLF do exist. Thus, given the close relationship of this track with visual processing and its trajectory, reaching the superior temporal gyrus next to the STS, it would probably be involved in face processing. However, the studies that have explored connectivity changes relating age and face processing system have not considered the SLF.

Here, we search for specific age-related differences in fiber tracts connecting the nodes of face processing system across three age groups, children, young adults and elderly adults. We included not only the IFOF and the ILF previously studied, but also included the previously neglected SLF. By Using DTI and by applying deterministic method of Fiber Assignment by Continuous Tracking and regions of interest (ROIs) we were able to reconstruct the inferior fronto-occipital, inferior longitudinal and superior longitudinal fasciculi, the three major white matter tracts involved in the processing of visual stimuli in addition to faces (Tavor et al., 2014; Thomas et al., 2008). In order to characterize the age-dependent variation in brain connectivity, were analyzed in these tracts the fractional anisotropy and number of streamlines.

Methods

Participants

A sample of 32 subjects, aged between 8 and 78 years, with no neurological or psychiatric history, was recruited for this study voluntarily specifically for the purposes of this study. The sample was divided into three age groups: children (n=11, Mean=9.8 years, SD=1.18), young adults (n=12, Mean=28.5 years, SD=3.44) and elderly adults (n=9, Mean=70.2 years, SD=3.92). All participants were native Spanish speakers (30 right handed, ascertained by self-report). All subjects gave written informed consent. The experimental procedures had previously received approval by the ethics committee of the Cuban Center for Neuroscience. The study was carried out in accordance with the principles stated in the declaration of Helsinki (Dale, & Salo, 1996).

Magnetic Resonance Imaging Acquisition Protocol

A Siemens 1.5T Magnetom Symphony system with a standard birdcage head coil for signal transmission/reception (Siemens, Erlangen, Germany) was used to acquire images for all subjects. The scanning protocol included, for each subject, a high resolution T1-weighted anatomical image and a standard diffusion sequence. The T1-weighted structural image (1 x 1 x 1 mm resolution) was acquired for further coregistration with the following parameters: echo time (TE) = 3.93 ms, repetition time (TR) = 3000 ms, flip angle = 8°, and field of view (FOV) = 256x256x176 mm. This yielded 176 contiguous 1 mm thick slices in a sagittal orientation. Axial diffusion weighted images (DWI) was acquired along twelve independent directions, in 52 slices of 2.5 mm, spaced at 2.5 mm, with 2 mm x 2 mm in plane resolution, and a diffusion weighting b value of 1200s/ mm^2. The following parameters were used: acquisition matrix size = 128 x 128, TE=102 ms, TR=9000 ms, flip angle=90°. A reference image (b0 image) with no diffusion weighting was also obtained (b = 0 s/mm^2).

In order to correct the distortions caused by magnetic field inhomogeneities, in the series of DWI detailed phase and magnitude maps were obtained. The parameters used were: acquisition matrix size = 64 x 64, 52 slices of 3 mm, spaced at 3 mm, with 4 mm x 4 mm in plane resolution, TE (phase image) = 10.87 ms, TE (magnitude image) = 6.11, TR = 525 ms, flip angle = 60°. After correction for image distortions due to the diffusion gradients, the diffusion tensor and the fractional anisotropy

(FA) were determined in each voxel (Pierpaoli & Basser, 1996).

» *Correction of magnetic field inhomogeneities*

The DTI images were movement-, eddy-current, and distortion-corrected. Using the magnitude and phase images and the package of Unwarping (Anderson, 2001), the effects of the principal inhomogeneities of magnetic fields were corrected.

» *Fiber Tracking Computation*

Computation of the diffusion tensor and fiber tracking was performed using DTI and Fiber Tools v.3.0 (www.uniklinik-reiburg.de/mr/live/arbeitsgruppen/diffusion_en.html) (Kreher, Hennig, & Il'yasov, 2006), implemented in Matlab v.7.7 (Mathworks). According to the formulation of Basser, Mattiello and LeBihan, (1994), and by diagonalizing the diffusion tensor for each voxel, the toolbox generates as output six components of a diffusion tensor (Dxx, Dyy, Dzz, Dxy, Dxz, and Dyz) and three eigenvectors that characterize the direction of diffusion and three eigenvalues that characterize the magnitude of the diffusion in the corresponding eigenvector calculated (Basser et al., 1994). A tensor-smoothing algorithm (Westin et al., 2002) was employed before fiber tracking as this is known to reduce residual errors and increase group differences (Jones et al., 2006).

Three-dimensional reconstruction of the tracts was performed using the deterministic tractography method Fiber Assignment by Continuous Tracking algorithm and a brute-force reconstruction approach (Mori, Crain, Chacko, & Van Zijl, 1999). Fiber tracking was initiated by specifying six parameters: the minimum FA threshold for starting tracking, the minimum FA for stopping tracking, the maximum trace (Tr) for starting tracking, the maximum trace for stopping tracking and the critical angle threshold for stopping tracking in case the algorithm encounters a sharp turn in the fiber direction and a minimum fiber length. The start criteria used in the reconstruction of the tracts were FA = 0.1, Tr = 0.0016, and a stop criteria FA = 0.15, Tr = 0.002. A turning angle threshold of 53.1° and minimum fiber length of five voxels were used. DTI and Fiber Tools v.3.0 used these parameters to generate the coordinates of all fibers in the brain from which the tract trajectory are reconstructed after drawing a ROI in a user-defined region of the brain. This software allows quantifying the number of streamlines and the fractional anisotropy in each tract, *the former one as a FA mean of voxels that integrate the tracts.*

» *Definition of ROIs*

A multiple ROIs approach was used for the reconstruction of the tracts of interest because it has been tested that the two-ROI and brute-force approach could effectively reduce the sensitivity to the noise and ROI placement (Huang, Zhang, van Zijl, & Mori, 2004). The fiber tracking was performed on all voxels of the brain, and fibers that penetrated the previously defined ROIs were assigned to the specific tracts associated to each pair of ROIs.

ROIs defined in previous publications (Valdés-Sosa et al., 2011) were used for defining the following tracts: ILF, IFOF and SLF (Mori et al., 2002). The ROIs were drawn using the program MRIcroN (http://www.mricron.com) in an anatomical reference image, in the Montreal Neurological Institute (MNI) stereotactic space (Evans et al., 1993). They were then transformed back to the native brain space of each individual automatically, using custom-made Matlab 7.7. These routines perform rigid registration (Ashburner &

Friston, 1999) of T1-structural images to MNI stereotactic space and to correspondent b0 image (mutual information) (Studholme, Hawkes, & Hill, 1998). This was done via inverse transformations of the mappings used for: 1) Realignment of a high-resolution anatomical T1 image, initially coregistered to DTI (b0 image), to the standard position on the AC-PC plane; 2) Normalization (jointly with segmentation) of the T1 image to MNI space using the procedure from SPM5.

› *Inferior fronto-occipito fasciculus (IFOF)*

The IFOF was defined as those fibers in contact with an occipital ROI, with the sagittal stratum, and with a frontal ROI, while not in contact with central grey nuclei, nor the cerebral midline, nor the temporal ROI used to define ILF. The occipital ROI was traced on the coronal slices -64 < y < -58, from the transverse parieto-occipital sulcus to the ventral border of the occipital lobe. The homonymous region from a white matter parcellation map in MNI space (Mori et al., 2008) was used to create the sagittal stratum ROI, which was then dilated at the surface by 3 voxels. The frontal ROI was traced at the anterior border of the insula and included all the frontal lobe, on the coronal slices -20 < y < 25.

› *Inferior longitudinal fasciculus (ILF)*

The ILF were defined as those fibers in contact with the same occipital ROI as IFOF, with the sagittal stratum, and with a temporal ROI, while not in contact with the frontal ROI used to define IFOF (see above), nor the central grey nuclei, nor the cerebral midline. The temporal ROI included the inferior and middle temporal gyri (and underlying white matter) in coronal slices -3 <y< 3 mm.

› *Superior longitudinal fasciculus (SLF)*

The SLF was defined as those fibers in contact with an occipital ROI and a temporal ROI. Occipital ROI was drowned on coronal slice 53 < y < 55, when in sagittal view the fornix can be identified as a unique structure. Then in sagittal view is selected a coronal plane in the middle of the splenium of corpus callosum, and a temporal ROI was drowned on coronal slice 9 < y < 11.

Statistical Analysis

Streamline count and FA measures for each tract were submitted to a repeated measure analysis of variance (rmANOVA) using Group as categorical factor and Tracts and Hemisphere as within effects. A Greenhouse and Geisser correction was applied (Greenhouse & Geisser, 1959) Then planned comparison between these groups were implemented for each tract.

Results

The reconstruction of the tracts of interest IFOF, ILF and SLF was successfully performed (seeFigure 1).

FA values are shown on Graph 1 ILF and SLF showed a similar FA values for the three age groups. However, the IFOF evince a FA decrease in elderly adults. The rmANOVA for FA revealed a main effect for group (F = 2.76, d.f = 2, p = 0.08), and a significant main effect for tracts (F = 4.77, d.f. = 2, p = 0.012) and hemisphere (F = 15.18, d.f. = 1, p = 0.001). The most important results, however, were a highly significant interactions for Tract x Group x Hemisphere (ε=0.893815; p<0.05) and Tract x Group (ε=0.868127; p<0.01). Planned comparison tests revealed differences in FA measures between some of the three groups in all tracts. Elderly adults showed a decrease in the FA related to children (Left: F (1,29) = 21.43, p < 0.01;

Right: F (1,29) =22.32, $p<0.01$) and young adults (Left: F (1,29) = 14.19, $p < 0.01$; Right: F (1,29) = 11.28, $p < 0.01$) for bilateral IFOF.

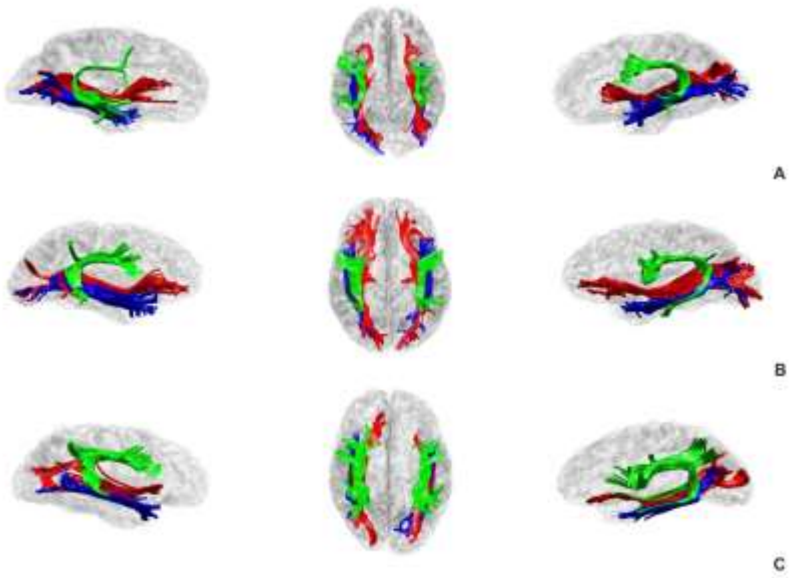
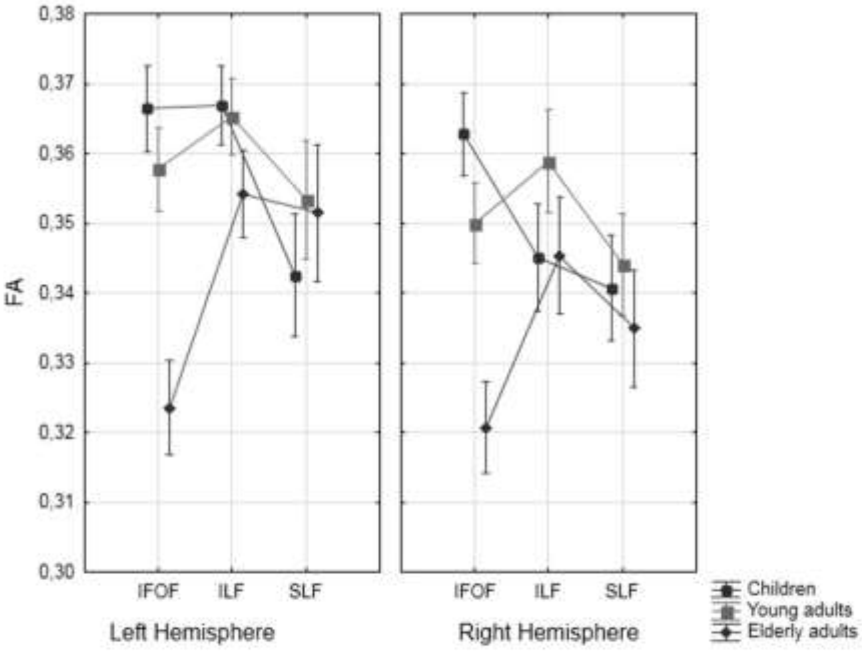


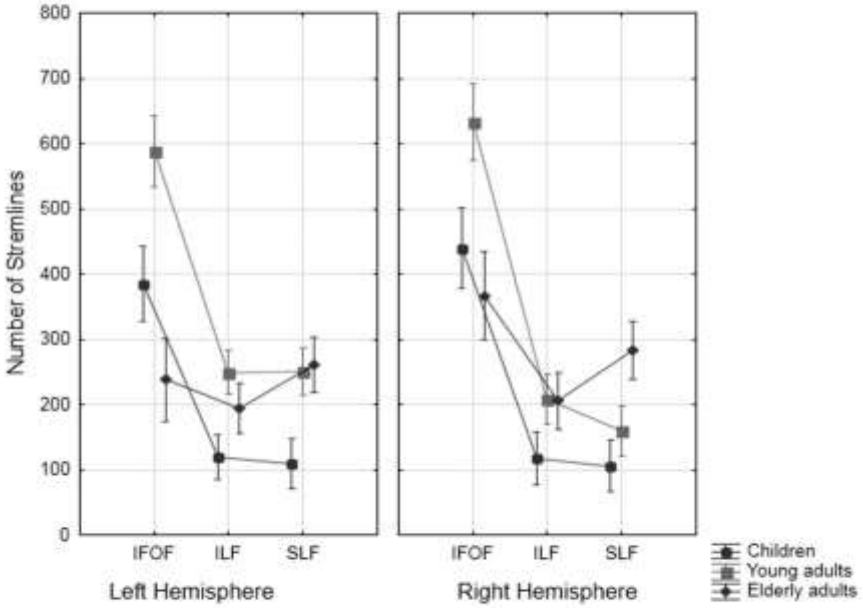
Figure 1. Reconstruction of left inferior fronto-occipital fasciculus (IFOF) in red, left dorsal inferior longitudinal fasciculus (ILF) in blue and left superior longitudinal fasciculus (SLF) in green, in children (A), young adults (B) and elderly adults (C) projected on the individual brain of one subject from each group.



Graph 1. Fractional anisotropy of IFOF, ILF and SLF in both hemispheres for the three study groups (children, young adults and elderly adults). Whiskers represent standard errors.

Streamlines count analysis is showed in Graph 2. Young adults showed significantly higher number of streamlines compared to children and elderly adults. The difference between young adults and children was the biggest, and this difference was of similar magnitude for all the tracts analyzed in both hemispheres. However, elderly adults showed an intermediate pattern between children and young adults, with a more pronounced difference for the IFOF, in which their number of streamlines reached lower values than the other two groups. SLF show greater number of streamlines in elderly adults than in children and young adults (Graph 2).

The rmANOVA for number of streamlines revealed a significant main effect for group (F = 9.62, d.f = 2, p = 0.001) and tracts (F = 42.51, d.f. = 2, p = 0.000) and no significant effects for hemisphere (F = 0.72, d.f. = 1, p = 0.402). The most important results were that there is no significant Tract x Group x Hemisphere interaction (F (4,58) = 0.21, p < 0.93), but there is a Tract x Group interaction (F (4,58) = 6.35, p<0.0026, ε = 0.953277, p < 0.01). Planned comparisons tests revealed significant differences in the number of streamlines between some of the three groups in all tracts. Young adults showed an increase in the number of streamlines related to children for all tracts of interest bilaterally, including IFOF (F (1,29) = 8.79, p<0.01), ILF (F (1,29) = 6.50, p < 0.02) and SLF (F (1,29) = 4.50, p < 0.04). Elderly adults exhibited a decrease in the number of streamlines related to young adults for IFOF (F (1,29) = 18.94, p < 0.01). The only difference detected between children and elderly adults was a significant increase on number of streamlines in older subjects in SLF (F (1,29) = 10.83, p < 0.01). In this tract the number of streamlines in elderly participants was closer to the values of young adults, which was exceeded in right hemisphere by elderly group.



Graph 2. Number of streamlines of IFOF, ILF and SLF in both hemispheres for the three study groups (children, young adults and elderly adults). Whiskers represent standard errors.

Discussion

Tractography is a unique tool to characterize white matter architecture threedimensionally and non-invasively. This technique illustrated quantitatively the trajectories of IFOF, ILF and SLF, which is useful for comparing these tracts between age groups. We reconstructed previously documented tracts using anatomical constraints (multiple ROIs) based on a priori knowledge (Mori et al., 2002; Valdés-Sosa et al., 2011). The semiautomatic procedure of transformation used here minimized the error of each ROI by drawing them in the individual space of each subject's brain. However, it is possible that some parts of the trajectory will contain inaccuracies due to partial volume effects, noise, and crossing fibers. It is also important to understand that the visualized pathways do not necessarily reflect brain connectivity because individual axons could be merging and blanching at any point along the bundle (Wakana et al., 2007).

Fractional anisotropy

Fractional anisotropy is an index that reflects the degree to which diffusion of water molecules is restricted by microstructural elements such as cell bodies, axons, myelin, and other constituents of cytoskeleton (Beaulieu, 2002), thus describing the microstructural properties of the axons within a voxel (Thomas et al., 2008). Thus, using this index the characterization of IFOF, ILF and SLF can explain the changes in white matter integrity that occurs across life spam. Previous reports of DTI studies have shown an increased FA (Beaulieu, 2002) throughout brain white matter during childhood, adolescence, and young adulthood (Eluvathingal, Hasan, Kramer, Fletcher, & Ewing-Cobbs, 2007; Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008; Mukherjee, Nissen, & Topol, 2001; Schmithorst, Wilke, Dardzinski, & Holland, 2002). Our findings confirm these reports and support the idea that white matter maturation may starts from early childhood to adolescence and continues into the midlife after a large *increase from early childhood to adolescence* (Ge et al., 2002), having the largest relative FA increase of 58%, observed in a sample from 8 to 30 years (Tamnes et al., 2010).

Our results support the theory of Lebel and Beaulieu (2011) suggesting that maturation continues during the twenties in association tracts, especially in IFOF and ILF, and also in SLF (Giorgio et al., 2008), with an increase of FA. However, Asato et al. (2010) found that IFOF and SLF attain 90% of their maximum FA value between 13 and 20 years of age (Asato, Terwilliger, Woo, & Luna, 2010; Bashat et al., 2005; Lebel et al., 2008). On the other hand, Lebel et al. (2008) reported nonlinear age-related increases in FA of all tracts studied in the age span 5-29 years, including the tracts analyzed in this work.

In adultness there is a progressive reduction in FA, consistent with white matter damage due to axonal loss, causing age-related cognitive decline (Charlton et al., 2006; Salat et al., 2005; Stadlbauer et al., 2008; Thomas et al., 2008). It has been reported that there is a 10% decrease in myelinated fibers length per decade (Marner, Nyengaard, Tang, & Pakkenberg, 2003). Stadlbauer et al. (2008) suggested that this decrease was related to the significant increase in the perpendicular component of diffusion λ_2 and it may have been due to increased extracellular space (Meier-Ruge, Ulrich, Brühlmann, & Meier, 1992; Nusbaum, Tang, Buchsbaum, Wei, & Atlas, 2001). In our data a decrease of FA values was detected when comparing children and elderly adults, and young and elderly adults, in bilateral IFOF. However, the data of

Voineskos et al. (2012) displayed significant age-related decline for IFOF, ILF and SLF.

In particular, the IFOF is positioned to mediate long-range interactions between the ventral visual stream, subserving object and face recognition, and emotional processing regions (i.e., orbitofrontal cortex). A reduction of integrity in right IFOF seems significantly associated with impaired emotion recognition from facial expressions (Philippi et al., 2009). In our data a dramatic decrease with age in the right IFOF was found (see Lebel & Beaulieu, 2011; Lebel et al., 2008; Scherf et al., 2014). However, we also found a decrease in left IFOF. Thomas et al. 2008, have reported that left hemisphere exhibit a tends towards reduction in microstructural integrity, as revealed in fractional anisotropy values, in spite of the IFOF in the right hemisphere showing a particular age related vulnerability. Also they have documented a robust association between the reduction of IFOF integrity related to age and face processing, suggesting that the alteration in structural connectivity between the ventral temporal and frontal cortices may account for the age-related difficulties in face processing. The age-related FA decline restricted to frontal regions, leaving posterior and inferior brain regions relatively intact, suggests that there is a selective decline of anterior anisotropy across aging, which provides evidence supporting a role of a microstructural white matter mechanism for the commonly observed decline in frontally-based functions (Pfefferbaum & Sullivan, 2003).

Number of streamlines

Only a few studies have focused in the number of streamlines of the whole brain (Thomas et al., 2008) or specific tracts (Stadlbauer et al., 2008; Tavor et al., 2014; Thomas et al., 2008; Valdés-Sosa et al., 2011) for analyzing the relation between aging and fractional anisotropy. Volume is a measure mostly related with number of streamlines. It has been calculated as the size of the image voxel multiplied by the number of voxels conforming a given tract (Scherf et al., 2014). However, as a volume increase has not been directly associated with elevated fractional anisotropy (Lebel & Beaulieu, 2011) this last parameter is not suitable for characterizing the number of streamlines.

Our data shows that young adults exhibit significantly more fibers than both children and elderly adults (except in SLF), although they show the same relative pattern of fiber number in all tracts compared to children. However, elderly adults show a decrease in the number of streamlines compared to young adults in the IFOF, as well as children to young adults in both hemispheres. In addition, elderly adults evince an increased number of streamlines in SLF, predominantly in the right hemisphere. This is in contradiction with reports showing a decrease in the number of fiber projections (4.7%) (Stadlbauer et al., 2008).

It has been reported that white matter volume increases significantly with age between the age range of 5-32 years (Lebel & Beaulieu, 2011), especially during adolescence, when the white matter volume increases it is about 74% (Courchesne et al., 2000). This fact explains the statistically significant increase detected between childhood and youth for all tracts. However, it has been reported that after youth a decline of the number of streamlines of the whole brain takes place as a function of age, meaning a decreased white matter volume (Thomas et al., 2008), especially after the age of 40 (Ge et al., 2002).

The similar pattern of increase/decrease number of streamlines of all tracts comparing children and young adults can be due to developmental processes across all major white matter tracts during childhood, which continues during the twenties in several association tracts, especially the ILF and IFOF (Courchesne et al., 2000; Pfefferbaum & Sullivan, 2003). These reports support the significant increase of white matter volume between children and young adults in all tracts founded here (IFOF, ILF and SLF). It can be due to an earlier maturation in tracts pertaining to intrahemispheric connections, which continues to adulthood. However, Scherft et al. (2014) found a significant increment in ILF but not in IFOF. *On the other hand, analysis directed to obtaining more accurate estimates of the number of streamlines would be perform the data normalization, eliminating the intrinsic differences between brains of children and adults.*

The fact that young adults exhibit more fibers than children (IFOF, ILF, SLF) and elderly adults (IFOF) has been previously described (Ge et al., 2002), with a white matter volume maximum around middle adulthood, suggesting that maturation may continue into the midlife after the aforementioned large increase from early childhood to adolescence (Courchesne et al., 2000; Pfefferbaum et al., 1994). This phenomenon is likely associated with continued myelination and axonal growth (Webb et al., 2001). These facts can support the same pattern in number of streamlines between children and young adults based on adolescent and post-adolescent maturation. A possible explanation is that increase myelination and advancing axons are causing that tissue previously classified as gray matter to be newly classified as white matter, which accounts for the tissue volume changes during adolescent maturation despite the constant total brain volume (Lebel et al., 2008).

The phenomenon of decreased white matter volume in the healthy aging process is still not well characterized (Ge et al., 2002). This decrease of white matter may result from structural changes which include myelin and axonal destruction (Salat, Kaye, & Janowsky, 1999; Van Swieten et al., 1991), dilatation of perivascular spaces (Awad, Spetzler, Hodak, Awad, & Carey, 1986; Fazekas et al., 1993), and gliosis (Fazekas et al., 1991). However, findings from postmortem studies in adult life (Haug, 1985; Peters, Morrison, Rosene, & Hyman, 1998; Terry, DeTeresa, & Hansen, 1987) have suggested that the white matter loss might be correlated with a decrease in the size of large neurons rather than a notable decrease in the number of neurons.

The general decrease in the number of streamlines for most tracts in elderly adults is consistent with previous reports that show a negative correlation of white matter with age (Ge et al., 2002); especially in the association tracts studied in this paper (Stadlbauer et al., 2008). However, Ge et al. (2002), pointed out that such decrease in white matter is not linear but quadratic, decaying by 13% in the oldest subjects (Courchesne et al., 2000). Specifically, our data showed a reduction in the number of streamlines between young and elderly adults in IFOF, which has been associated with visuospatial construction ability (Voineskos et al., 2012). These results are in accordance to data reported by Thomas et al. 2008, which revealed a statistically significant decline of IFOF in the number of streamlines and the number of voxels through which these fibers pass in the whole brain as a function of age. On the other hand, Voineskos et al. (2012), have reported that age-related disruption of the ILF predicted performance in tasks that require visuomotor dexterity and fast visual processing.

The absence of inter-hemispherical asymmetry in our results differs from previous reports, which have revealed larger sizes of tracts in the right hemisphere, perhaps consistent with a more prominent role in face processing (Kanwisher et al., 1997; Meadows, 1974; Sergent, Ohta, & MacDonald, 1992). However, at this point reports are contradictory. It has been reported left-biased (Thomas et al., 2008) and right-biased asymmetries in the IFOF, with no significant differences (Wakana et al., 2007). Our results are in line with these findings.

Several limitations should be noted in the present study. First, cross-sectional studies are limited because they cannot provide information about change within individuals. It is important to consider that tract volume or fiber number as measured by DTI does not represent the true volume of the tract, since the edges of tractography bundles are defined artificially by FA values (Lebel & Beaulieu, 2011). It is important to note that the fiber tracking algorithm used here (Fiber Assignment by Continuous Tracking) is highly susceptible to errors in the orientation of the principal eigenvector, due both to noise and to instances where the direction of the underlying tract anatomy is ambiguous (Valdés-Sosa et al., 2011), which is not ideal for assessment of voxels where fiber bundles cross, diverge, or converge. Also it would be supportive if a coincidence analysis was made between the coordinates of STS reported in literature and the core of SLF, to gain in accuracy about the connection between this face processing node and the wire associated.

Conclusions

In summary, our study compiled evidence about the aging-related changes in three major white matter tracts associated with the face processing system. According to FA values, both ILF and SLF remain unaltered across life. However, the IFOF experiences a decrease in integrity that could partially subserve the increasing difficulty for processing faces in elderly individuals. In addition, all tracts exhibit an increased number of streamlines from childhood to early adulthood, consistent with previously described white matter developmental processes. Interesting, again only the IFOF shows a decrease in this measure in elderly individuals. Thus, both measures point to an overall decrease in the fronto-occipital connectivity through the IFOF at older age. Further additional studies would be required to link such decrease with appropriate scales and tasks characterizing face processing in young and elderly individuals.

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