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IMPROVEMENT OF OLFACTORY FUNCTION AFTER SINUS SURGERY CORRELATES WITH WHITE MATTER PROPERTIES MEASURED BY DIFFUSION TENSOR IMAGING

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Abstract—Impaired olfaction is associated with a volume decrease in the olfactory bulb as well as in the gray matter of cortical olfactory areas. On the other hand, restitution of an impaired olfaction results in a regain of volume in these regions. Studies investigating similar changes in the cerebral white matter are virtually not existent. The aim of this prospective study therefore was to investigate cerebral white matter using magnetic resonance diffusion tensor imaging (DTI). 31 patients (54 ± 13 years) with olfactory impairment (chronic rhinosinusitis) and planned functional endoscopic sinus surgery (FESS) were included. Magnetic resonance imaging (MRI) data sets were acquired preoperatively and 3 months after surgery. Pre- and postoperative olfactory testing was performed to assess the olfactory threshold, discrimination, and identification (TDI) score. A significant postoperative TDI improvement by 9.06 ± 8.81 points was observed. Two groups were subsequently formed – one with relevant postoperative olfactory gain (ΔTDI $\geq$ 10 points, 12 patients) and one without gain (ΔTDI $<$ 10 points, 19 patients). DTI parameter showed a significant correlation with the TDI score in the left anterior cingulate cortex and the right amygdala. In the group with relevant olfactory improvement higher values of fractional anisotropy and apparent diffusion coefficient were found in the right parahippocampal area and in the white matter below the left inferior temporal sulcus. Tract-specific diffusion property analysis revealed significant group differences in the cingulate cortex in spatial relationship to the perisplenial cortex. Overall, this prospective study indicates structural changes in white matter after postoperative restoration of olfaction.

Key words: olfaction, structural plasticity, magnetic resonance imaging, diffusion tensor imaging, parahippocampal cortex, cingulate cortex.

INTRODUCTION

In the olfactory system a strong correlation between structure and function can be observed. This extraordinary plasticity was first demonstrated in the 19th century in the leporine olfactory bulb (OB) (Gudden, 1870). Here, absence of unilateral olfactory input resulted in volume decreases of the OB of the same side. In more recent human studies, a positive correlation between OB volume and olfactory performance was observed (Yousem et al., 1998; Seubert et al., 2012). Furthermore, OB volume decreases were also described in several olfactory disorders (Duprez and Rombaux, 2010). The reversibility of this volume loss following successful therapy was demonstrated in a prospective study on patients with chronic rhinosinusitis (Gudziol et al., 2009). Cortical areas beyond the olfactory bulb are also involved in these conditions. Voxel-based morphometry (VBM) analysis revealed gray matter volume decreases in several olfactory diseases (Bitter et al., 2010b; Bitter et al., 2011; Peng et al., 2013). Furthermore, correlations between olfactory performance and cortical thickness or cortical volume have been observed in several olfactory areas (Frasnelli et al., 2010; Seubert et al., 2012).

In contrast, there is only little knowledge about the influence of an altered olfactory input on cerebral fiber connections. We hypothesize that the high plasticity of the OB and the cortical olfactory areas is also reflected in changes of the properties of the connecting fibers between olfactory centers in white matter. This hypothesis is supported by fMRI experiments showing modification of functional connectivity between olfactory areas by olfactory training (Kollndorfer et al., 2014). These connectivity alterations could have their origin in underlying structural connectivity changes.

Magnetic resonance-based diffusion tensor imaging (DTI) is a powerful tool to analyze fiber tract properties (Choudhri et al., 2014). DTI incorporates the acquisition of several sets of diffusion-weighted MR imaging volumes of the object, while the diffusion weighting direction is

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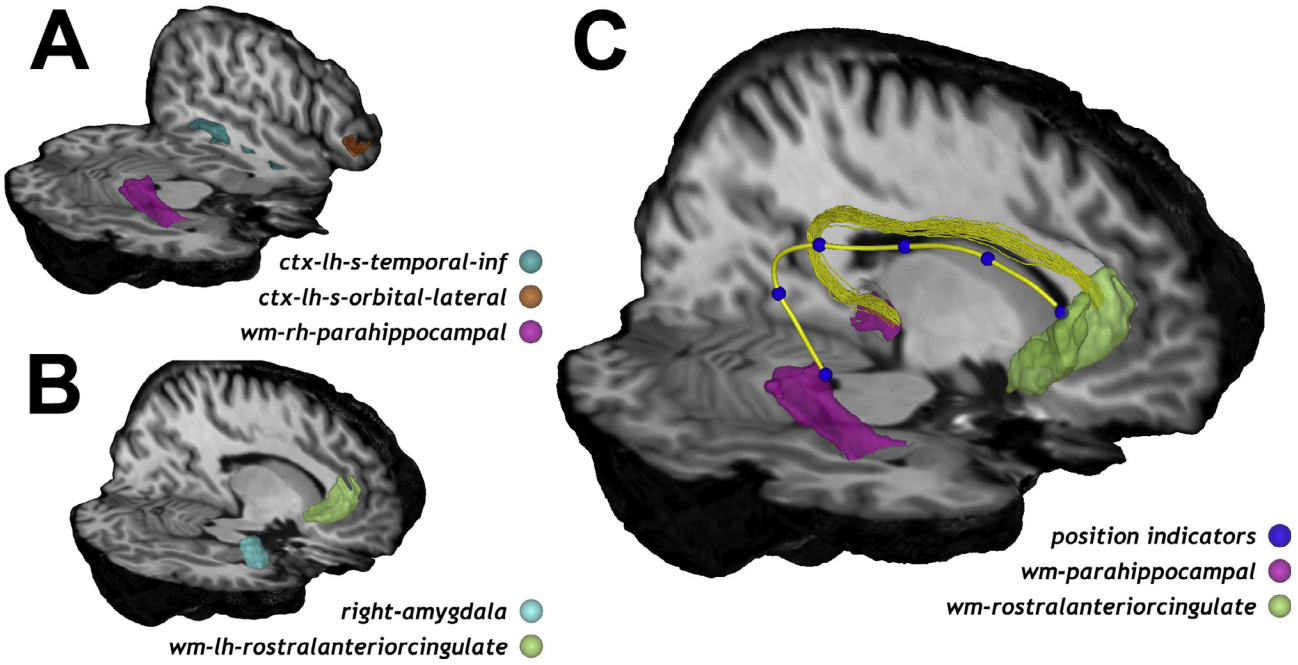

Fig. 1. A-C: A) location of ROIs, which showed significant differences in diffusion parameters between good and bad responders (see also Table 2). The ROIs are visualized as semi-transparent colored surface volumes with sagittal and axial sectional slices. B) location of the ROIs, which showed correlation between changes in diffusion parameters and changes in olfactory performance before and after surgery (see also Table 3). C) Schematic illustration of the analysis steps performed for data evaluation along the cingulum bundle. Selected tracts of the cingulum bundle between rostral anterior cingulate (position 0) and parahippocampal region (position 100) are shown for the left hemisphere. These tracts were obtained by tracking from the parahippocampal WM to the rostral anterior cingulate. These tracts were reduced to a center tract for each cingulum (left and right) by averaging the spatial positions along all tracts within the bundle. This center tract is show for the right hemisphere. Equidistant position indicators are presented along the center tract to facilitate spatial assignment for the data presented in Fig. 2.

Table 1. Group properties. Two groups were formed based on the Threshold, discrimination, identification (TDI) score difference (ΔTDI: TDIpost – TDIpre). Group 1 was defined by ΔTDI ≥ 10 points and group 2 by ΔTDI < 10 points. TDI_{pre} – pre-operative TDI score, TDI_{post} – post-operative TDI score

	Group 1 good responders (ΔTDI ≥ 10 points)	Group 2 bad responders (ΔTDI < 10 points)
N	12	19
Sex (male in %)	58.3	68.4
Age (years)	53 ± 9.9	52 ± 13.7
TDI_{pre} (points)	9.31 ± 8.09	26.21 ± 6.44
TDI_{post} (points)	27.75 ± 5.17	29.34 ± 6.94
ΔTDI (points)	18.44 ± 6.42	3.13 ± 2.92
p value $TDI_{pre\ vs\ post}$	< 0.00001	0.0002

changed from volume to volume. Based on these diffusion-weighted volume sets (at least six) in combination with an unweighted data volume, one is able to derive a diffusion tensor in each voxel of the data set. This diffusion tensor is represented by a 3 × 3 symmetric matrix and allows the voxel-wise computation of diffusion tensor properties like apparent diffusion coefficient (ADC), fractional anisotropy (FA), radial diffusion (RD) and parallel diffusion (PD) reflecting diffusion properties of water molecules within biological tissue. This technique has been applied to investigate white matter properties in different neurological conditions e.g. Parkinson's disease (Zhang et al., 2015), Alzheimer's disease (Acosta-Cabronero and Nestor, 2014) or multiple sclerosis (Erb et al., 2012). Additionally, the diffusion tensor data allow the virtual reconstruction of white matter pathways (Mori and van Zijl, 2002) and thus in turn facilitates fiber-specific data analysis in the white matter of the brain (Corouge et al., 2006).

Patients with olfactory impairment due to chronic rhinosinusitis provide an ideal neurobiological model to investigate the plasticity of the olfactory system. Their olfactory input can often be restored by a standardized surgical procedure called functional endoscopic sinus surgery (FESS). This intervention improves olfactory function by restoring nasal ventilation and access to the olfactory cleft (Rudmik and Smith, 2012). Aim of our prospective study was to use this neurobiological model in combination with DTI analysis to evaluate possible changes along major fiber tracts in patients with olfactory improvement.

EXPERIMENTAL PROCEDURE

Subjects

31 patients (64.5% male) with chronic rhinosinusitis as defined by the European position paper on rhinosinusitis and nasal polyps (Fokkens et al., 2012) diagnosed by an expert physician were included. The average age was 54 ± 12.5 years. Neurological, psychiatric or malignant diseases were excluded by anamnesis. In addition, mini-mental state examination (MMSE) and