Anatomical connections of the Visual Word Form Area

Florence Bouhali[1], Michel Thiebaut de Schotten[1,2], Philippe Pinel[3], Cyril Poupon[3], Jean-François Mangin[3], Stanislas Dehaene[4], and Laurent Cohen[1]
[1]Brain and Spine Institute, Paris, France, [2]Natbrainlab - Institute of Psychiatry, Paris, France, [3]Neurospin, Paris, France, [4]Collège de France, Paris, France

Purpose. Based upon over a century of studies of patients with pure alexia following brain lesions (1-3), and upon 20 years of functional brain imaging (4-6), a region in the left ventral occipito-temporal cortex, which has been termed the Visual Word Form Area (VWFA) (7), has been identified as instrumental to the identification of written words. The VWFA is located just lateral to the mid segment of the fusiform gyrus, with a remarkable reproducibility across subjects. Its coordinates vary only in the range of a few millimeters, even across a variety of cultures and script types (5, 7-9). Such reproducibility is surprising, given that reading is a very recent cultural function for which the brain did not evolve. Here, we test the hypothesis that the VWFA recycles a region of the ventral visual cortex that shows a high degree of anatomical connectivity to perisylvian language areas and hence, should be overall more connected to language areas than a functionally distinct but anatomically contiguous area devoted to face processing (the Fusiform Face Area, or FFA) in order to produce an efficient circuit for both grapheme-phoneme conversion and lexical access.

Material and methods. Seventy-nine French subjects gave written informed consent to participate. We used a 3-Tesla MRI (Siemens Trio TIM) with a 12-channel head coil, and a gradient-echo planar imaging sequence sensitive to brain oxygen-level dependant (BOLD) contrast (40 contiguous axial slices, acquired using ascending interleaved sequence, 3 mm thickness; TR = 2400 ms; Flip angle = 90°, TE = 30 ms, in-plane resolution = 3 × 3 mm, matrix = 64 × 64).
We delineated the VWFA using fMRI contrasting activations by visual words minus checkerboards. To this end, we used a subpart of a functional localizer experiment whose details can be found in (10). To isolate the FFA, we used a subpart of the experimental conditions included in another short protocol designed to investigate social cognition, contrasting activations by faces minus scrambled images.
In parallel high angular resolution diffusion imaging (HARDI) data were acquired in 60 directions with a b-value of 1500 s/mm2 (voxel size of 1,7 mm3) using a twice refocusing spin echo technique (11) compensating eddy currents to the first order. Geometrical distortions linked to susceptibility artifacts were corrected using a phase map acquisition. T1 and diffusion weighted data of each subject were optimally aligned using a rigid 3D transform estimated by an automatic registration algorithm based on mutual information. Registration was performed between one diffusion-free T2-weighted image and the high-resolution T1-weighted image (1x1x1.1mm resolution). The diffusion orientation distribution function (ODF) was reconstructed in each voxel with an analytical solution of the q-ball model (12). Fiber tracts were reconstructed using the diffusion model estimation and a streamline deterministic tractography algorithm provided in Connectomist software. The tracts were calculated as the trajectories of particles with inertia, leading to regularized curvature (13).
We produced 1-voxel-thick region of interests (ROIs) of white matter just beneath group cortical activation for the VWFA and the FFA (14). We intersected these two region of interest, thus deriving 3 ROIs: a reading-only or VWFA ROI, a more mesial face-only or FFA ROI, and in between the intersection of the ROIs, which was activated during both reading and face perception. Tractography was seeded from these three ROIs for each participant to produce connectivity maps for the VWFA and the FFA that we binarized and registered to an optimal FA template in MNI space drawn from the present dataset using Advance Normalization Tools (ANTs, http://www.picsl.upenn.edu/ANTS/) (15, 16). Normalized connectivity maps were finally smoothed using a Gaussian kernel of 4 mm FWHM.
In order to assess differences between VWFA and FFA connectivity, we statistically compared the connectivity maps of the VWFA ROI and of the FFA ROI across the whole brain. To this end, we used a non-parametric repeated measures ANOVA using the permutation method, as implemented in FSL software (17). This analysis included one within-subject factor (the 3 ROIs), one regressor of no interest (the individual volume of the ROI), and subjects were treated as a random factor. 5000 permutations were run and the threshold-free cluster enhancement (TFCE) method was applied (18). Statistics were corrected for multiple comparisons (TFCE corrected threshold $P<0.05$). Within this model, we contrasted the projections of the VWFA ROI and of the FFA ROI minus the other two ROIs (TFCE corrected threshold $P<0.05$; Figure 2C).

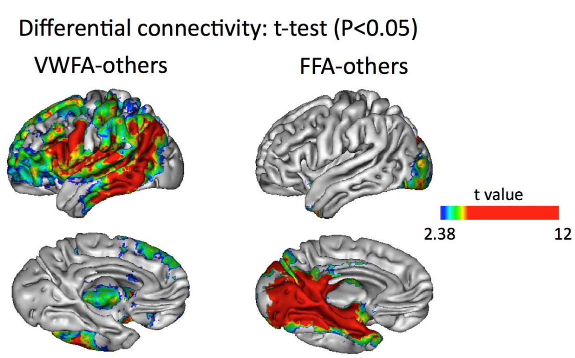

Figure 1. Value of the t-test comparing connectivity from the VWFA minus the FFA and intersection ROIs, and from the FFA minus the VWFA and the intersection ROIs, with a threshold of corrected $P<0.05$. The VWFA was more connected to lateral language-related areas, while the FFA was more connected to inferior and mesial temporal areas.

Results. This showed that the VWFA connected significantly more to most perisylvian language-related areas, including Broca's area, the superior and lateral temporal lobe, the angular gyrus. In contrast, the FFA connected more to the mesial occipital and temporal lobes, including the hippocampus, the lingual and parahippocampal gyri and the amygdala, and to the posterolateral occipital lobe.

Discussion and Conclusion. The present results, based on a large database of high-resolution diffusion data, clarify the anatomical connections of the VWFA area. Paralleling similar work on the face system (19), they reveal a systematic pattern of connectivity to left-hemispheric language areas at the precise left occipito-temporal location which, in expert readers of all cultures, is reproducibly and preferentially activated by written words. These results confirm that the VWFA plays a prominent role in reading by serving as an interface between the ventral visual recognition system and left-hemispheric perisylvian language areas.

References. (1) Cohen *et al. Cereb Cortex* (2003). (2) Dejerine. *Mém Soc Biol* (1892). (3) Pflugshaupt *et al. Brain* (2009). (4) Glezer and Riesenhuber. *J Neurosci* (2013). (5) Jobard et al. *Neuroimage* (2003). (6) Nobre et al. *Nature* (1994). (7) Cohen *et al. Brain* (2000). (8) Bolger et al. *Hum Brain Mapp* (2005). (9) Dehaene et al. *Neuroreport* (2002). (10) Pinel *et al. BMC Neurosci* (2007). (11) Reese et al. *Magn Reson Med* (2003). (12) Descoteaux et al. *Magn Reson Med* (2007). (13) Perrin *et al. Inf Process Med Imaging* (2005). (14) Thiebaut de Schotten et al. *Cortex* (2012). (15) Avants *Med Image Anal* (2008). (16) Klein *et al. NeuroImage* (2009). (17) Nichols and Holmes. *Hum. Brain Mapp* (2002). (18) Smith and Nichols *Neuroimage* (2009). (19) Saygin *et al. Nat Neurosci* (2012).