

## Supplementary Material

Testing the connections within face processing circuitry in Capgras delusion with diffusion imaging tractography.

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## 1. Neuropsychological assessment

Supplementary Table S1

Mini-Mental State		Raw Scores	
Total Score (0-30)		23	
Time and place orientation subscore (0-10)		8	
Word registration subscore (0-3)		3	
Attention subscore (0-5)		1	
Word recall subscore (0-3)		2	
Language subscore (naming; repetition; following commands, reading and writing) (0-8)		8	
Pentagon copying subscore (0-1)		1	
WAIS-R Estimated IQ			
WAIS-R Subtest (range scale)	Scaled Score Equivalents of Raw Score	Sum of scaled scores	Full Scale IQ Equivalents
WAIS-R Estimated Verbal IQ (0-19)	11	17	104
WAIS-R Estimated Non-verbal IQ (0-19)	6		
Neuropsychological Test	Raw score	Equivalent score	Cut-off score
Phonetic Verbal Fluency	1	-	$\leq 7.09$
Semantic Verbal Fluency	4	-	$\leq 11.13$
Trial making			
Trial making A	141	114	$\geq 94$
Trial making B *	*	*	$\geq 283$
Trial making B-A *	NA	NA	$\geq 187$
Forward Digit Span WAIS-III	4	-	$\leq 4.69$
Forward Spatial Span (Corsi blocks)	4	4	$\leq 3.50$
Attentional digit matrix task	26	28	$\leq 30$

\* Patient was unable to complete trial making (part B) due to cognitive impairment (reduced in alertness, attentional visual search deficits). The task could not be completed, since the patient had not finished part B of the task after five minutes, therefore part B-A was not applied (NA).

## 2. Tractography analysis.

### ROIs for tract fiber selection in the streamline tractography method

ROIs defined in previous publications were used as the basis for the tract definitions (Wakana et al., 2007).

All ROI were first manually traced on the MNI152 average brain, and then transformed to each subject's DTI native space. 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. Each ROI

mapped to DTI native space was then inspected visually and corrected with deletions or additions of voxels if necessary.

The inferior fronto-occipital fasciculus (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 the temporal ROI used to define ILF (see below), nor the central grey nuclei, nor the cerebral midline. 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 frontal ROI was traced at the anterior border of the insula and included all the frontal 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 inferior longitudinal fasciculi (ILF) were defined as 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 ILF was subdivided into a dorsal and ventral tracts according to the temporal ROI that was used. For the ventral tract (vILF), the temporal ROI included the inferior and middle temporal gyri (and underlying white matter) while excluding the superior temporal gyrus, in coronal slices  $-3 < y < 3$  mm. For the dorsal tract (dILF), the temporal ROI included the superior temporal gyrus (and underlying white matter), while excluding the inferior and middle temporal gyri, also in coronal slices  $-3 < y < 3$  mm.

Other white matter association tracts were reconstructed using the protocol defined previously (Wakana et al., 2007) for the left and right hemispheres: the uncinate fasciculus (UNC), cingulum-cingulate gyrus (CGC); cingulum-hippocampal part (CGH); Cortico-spinal tract (CST); anterior thalamic radiation (ATR). Several measures were obtained from each tract: streamline count, number of intersected voxel (NIV), and the average of FA and the average of the mean diffusivity (MD) and radial diffusivity (RD) for each tract. The mean values for the controls as well as the value obtained for patient J.R. in the first and second study are displayed in the following table. The results of the statistical comparison between the patient and controls was carried out using the tests developed for single case studies (Crawford & Garthwaite, 2002), as described in the article.

#### 4- Tractography additional results

##### Supplementary Table S2

Diffusion tensor measurements values in the controls and J.R. patient. Mean values and standard deviations of streamline counts (SC), number of intersected voxel (NIV), fractional anisotropy (FA), mean diffusivity (MD) and radial diffusivity (RD) are shown. T and p-value resulted from the statistical comparison for single case studies.

	UNC left	UNC right	ATR left	ATR right	CGC left	CGC right	CGH left	CGH right	CST left	CST right
<b>SC</b>										
mean	80,4000	174,2000	233,6000	191,6000	55,6000	91,9000	98,5000	98,5000	164,3000	52,3000
SD	46,1572	120,3530	135,3097	113,0803	37,7659	54,2923	62,6724	62,6724	104,5254	29,7659
J.R. Study 1	148,0000	288,0000	302,0000	165,0000	4,0000	52,0000	56,0000	56,0000	135,0000	77,0000
T	1,0939	0,8507	0,6070	0,1072	-2,0291	-0,3820	-0,7272	-0,7272	0,1506	0,8021
p	0,1512	0,2085	0,2794	0,4585	0,0365	0,3556	0,2428	0,2428	0,4418	0,2216
J.R. Study 2	43,0000	36,0000	432,0000	336,0000	41,0000	103,0000	242,0000	242,0000	180,0000	11,0000
T	-0,6132	-1,3762	1,0971	0,8953	0,0114	0,3984	1,8251	1,8251	0,3525	-1,9469
p	0,2774	0,1010	0,1505	0,1970	0,4956	0,3498	0,0506	0,0506	0,3663	0,0417
<b>NIV</b>										
mean	321,5000	558,2000	1117,1000	983,0000	333,0000	406,3000	587,4000	449,3000	842,7000	440,1000
SD	171,5454	309,0591	386,4630	375,6597	78,4219	211,6265	192,8293	198,9204	323,7304	150,9845
J.R. Study 1	480,0000	816,0000	1392,0000	1043,0000	61,0000	343,0000	342,0000	250,0000	927,0000	684,0000
T	0,8030	0,7736	0,7100	0,2877	-3,3384	-0,0494	-1,5196	-1,1798	0,3213	1,1609
p	0,2213	0,2295	0,2479	0,3901	0,0043	0,4808	0,0815	0,1342	0,3777	0,1378
J.R. Study 2	580,0000	739,0000	626,0000	276,0000	85,0000	121,0000	240,0000	231,0000	1541,0000	1282,0000
T	1,0720	0,6360	-1,3216	-2,3025	-2,6384	-1,7571	-2,6024	-1,3630	1,0018	2,5952
p	0,1558	0,2703	0,1094	0,0234	0,0135	0,0564	0,0143	0,1030	0,1713	0,0145
<b>AF</b>										
mean	0,28724	0,29314	0,34965	0,34865	0,35642	0,33260	0,32839	0,29066	0,42536	0,43205
SD	0,03546	0,03156	0,03111	0,02513	0,03863	0,03238	0,03105	0,03317	0,03341	0,02350
J.R. Study 1	0,27508	0,28709	0,33159	0,37664	0,31879	0,33132	0,27400	0,27371	0,41104	0,41350
T	-0,32709	-0,18268	-0,55338	1,06199	-0,93734	-0,03771	-1,67000	-0,48730	-0,40867	-0,75291
p	0,37554	0,42955	0,29674	0,15795	0,18653	0,48537	0,06463	0,31885	0,34617	0,23537
J.R. Study 2	0,27828	0,28347	0,31396	0,36028	0,33498	0,28449	0,31241	0,26558	0,39527	0,41344
T	-0,24109	-0,29226	-1,09375	0,44133	-0,53879	-1,41675	-0,49067	-0,72104	-0,85875	-0,75535
p	0,40744	0,38836	0,15124	0,33469	0,30155	0,09511	0,31770	0,24460	0,20638	0,23467
<b>MD</b>										
mean	0,00085	0,00086	0,00082	0,00082	0,00079	0,00077	0,00094	0,00098	0,00079	0,00080
SD	0,00006	0,00007	0,00005	0,00004	0,00006	0,00005	0,00005	0,00006	0,00004	0,00004
J.R. Study 1	0,00083	0,00082	0,00078	0,00078	0,00078	0,00072	0,00096	0,00093	0,00083	0,00079
T	-0,36189	-0,63507	-0,70712	-0,89909	-0,00528	-0,98252	0,42020	-0,87494	0,95214	-0,18191
p	0,36289	0,27060	0,24870	0,19601	0,49795	0,17576	0,34210	0,20218	0,18295	0,42984
J.R. Study 2	0,00083	0,00084	0,00082	0,00081	0,00073	0,00081	0,00094	0,00097	0,00080	0,00082
T	-0,30406	-0,23908	0,04852	-0,28812	-0,86353	0,75111	-0,06560	-0,19631	0,15958	0,48442

p	0,38400	0,40820	0,48118	0,38989	0,20514	0,23588	0,47457	0,42436	0,43837	0,31983
<b>RD</b>										
mean	0,00111	0,00113	0,00113	0,00114	0,00110	0,00106	0,00127	0,00128	0,00118	0,00121
SD	0,00007	0,00008	0,00005	0,00004	0,00008	0,00006	0,00006	0,00007	0,00006	0,00006
J.R. Study 1	0,00108	0,00107	0,00107	0,00112	0,00105	0,00098	0,00123	0,00119	0,00122	0,00117
T	-0,51039	-0,75646	-1,32787	-0,43310	-0,59968	-1,26481	-0,55398	-1,31355	0,61906	-0,58818
p	0,31103	0,23435	0,10846	0,33757	0,22843	0,11885	0,29654	0,11075	0,27561	0,28544
J.R. Study 2	0,00109	0,00110	0,00110	0,00113	0,00100	0,00106	0,00123	0,00123	0,00116	0,00122
T	-0,36430	-0,36181	-0,59860	-0,17308	-1,21634	-0,00359	-0,61584	-0,74546	-0,45663	0,14556
p	0,36202	0,36292	0,28210	0,43321	0,26461	0,49861	0,27663	0,23751	0,32938	0,44374

No p-values survived the Bonferroni criterion of  $p < 0.00125$ .

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