

Table S1. Information on 90 AAL Regions used in regional based morphometry analysis

ROI Index	Region	(x)	(y)	(z)	ROI Index	Region	(x)	(y)	(z)
1	Precentral_L	-39	-7	50	46	Cuneus_R	13	-81	27
2	Precentral_R	41	-10	51	47	Lingual_L	-15	-69	-6
3	Frontal_Sup_L	-19	33	41	48	Lingual_R	16	-68	-5
4	Frontal_Sup_R	22	30	43	49	Occipital_Sup_L	-17	-86	27
5	Frontal_Sup_Orb_L	-17	46	-15	50	Occipital_Sup_R	24	-82	29
6	Frontal_Sup_Orb_R	18	47	-15	51	Occipital_Mid_L	-33	-82	15
7	Frontal_Mid_L	-34	31	34	52	Occipital_Mid_R	37	-81	18
8	Frontal_Mid_R	37	32	33	53	Occipital_Inf_L	-36	-80	-9
9	Frontal_Mid_Orb_L	-31	49	-11	54	Occipital_Inf_R	38	-83	-9
10	Frontal_Mid_Orb_R	33	51	-12	55	Fusiform_L	-31	-41	-22
11	Frontal_Inf_Oper_L	-49	11	18	56	Fusiform_R	34	-40	-22
12	Frontal_Inf_Oper_R	50	14	20	57	Postcentral_L	-43	-24	47
13	Frontal_Inf_Tri_L	-46	29	13	58	Postcentral_R	41	-27	51
14	Frontal_Inf_Tri_R	50	29	13	59	Parietal_Sup_L	-24	-61	58
15	Frontal_Inf_Orb_L	-36	29	-13	60	Parietal_Sup_R	26	-60	61
16	Frontal_Inf_Orb_R	41	31	-13	61	Parietal_Inf_L	-43	-47	45
17	Rolandic_Oper_L	-47	-10	13	62	Parietal_Inf_R	46	-48	48
18	Rolandic_Oper_R	52	-8	13	63	SupraMarginal_L	-56	-35	29
19	Supp_Motor_Area_L	-6	4	60	64	SupraMarginal_R	57	-33	33
20	Supp_Motor_Area_R	8	-1	61	65	Angular_L	-44	-62	34
21	Olfactory_L	-8	14	-13	66	Angular_R	45	-61	37
22	Olfactory_R	10	15	-13	67	Precuneus_L	-8	-57	47
23	Frontal_Sup_Medial_L	-5	48	30	68	Precuneus_R	10	-57	42
24	Frontal_Sup_Medial_R	9	50	29	69	Paracentral_Lobule_L	-8	-27	69
25	Frontal_Med_Orb_L	-5	53	-9	70	Paracentral_Lobule_R	7	-33	67
26	Frontal_Med_Orb_R	8	50	-9	71	Caudate_L	-11	11	9
27	Rectus_L	-5	36	-20	72	Caudate_R	15	12	9

28	Rectus_R	8	34	-19	73	Putamen_L	-24	4	2
29	Insula_L	-35	5	2	74	Putamen_R	28	5	2
30	Insula_R	39	5	1	75	Pallidum_L	-18	0	0
31	Cingulum_Ant_L	-4	34	13	76	Pallidum_R	21	0	0
32	Cingulum_Ant_R	8	36	14	77	Thalamus_L	-10	-18	8
33	Cingulum_Mid_L	-6	-16	40	78	Thalamus_R	13	-18	8
34	Cingulum_Mid_R	8	-10	38	79	Heschl_L	-42	-20	9
35	Cingulum_Post_L	-5	-44	23	80	Heschl_R	46	-18	9
36	Cingulum_Post_R	7	-43	20	81	Temporal_Sup_L	-53	-22	6
37	Hippocampus_L	-25	-22	-11	82	Temporal_Sup_R	58	-23	5
38	Hippocampus_R	29	-21	-12	83	Temporal_Pole_Sup_L	-40	14	-21
39	ParaHippocampal_L	-21	-17	-22	84	Temporal_Pole_Sup_R	48	13	-18
40	ParaHippocampal_R	25	-16	-22	85	Temporal_Mid_L	-56	-35	-4
41	Amygdala_L	-24	-2	-18	86	Temporal_Mid_R	57	-39	-3
42	Amygdala_R	27	-1	-19	87	Temporal_Pole_Mid_L	-37	13	-35
43	Calcarine_L	-7	-80	5	88	Temporal_Pole_Mid_R	44	13	-34
44	Calcarine_R	16	-74	8	89	Temporal_Inf_L	-50	-29	-25
45	Cuneus_L	-6	-81	26	90	Temporal_Inf_R	53	-32	-24

ROI index, label and standard space center-of-gravity coordinates for each ROI (mm), defined by Automated Anatomical labeling atlas (AAL). (Tzourio-Mazoyer et al. 2002). (Neurofunctional Imaging Group (GIN-IMN) <http://www.gin.cnrs.fr/en/tools/aal/>).

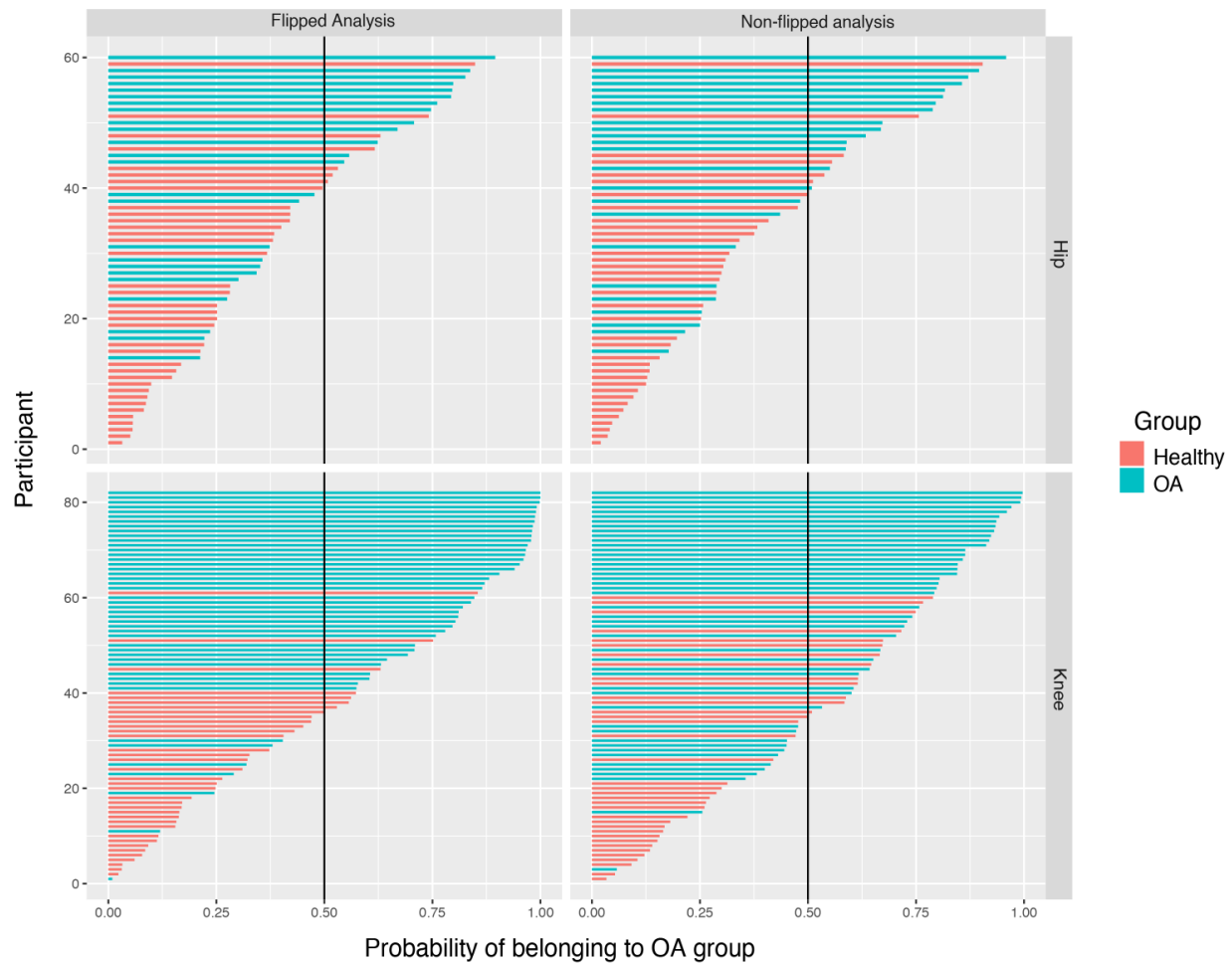


Figure S1. Group prediction performance: probability of classification by subject.

Plots of probabilities for OA membership in knee OA validation and hip OA groups using the models generated in the knee OA test sample (flipped and non-flipped models). X-axis represents the probability of being classified as OA patient or control. Y-axis represents subject group (red: healthy; blue: OA patient). A probability threshold of 0.5 (black line), was selected for evaluating the performance of the classification models.

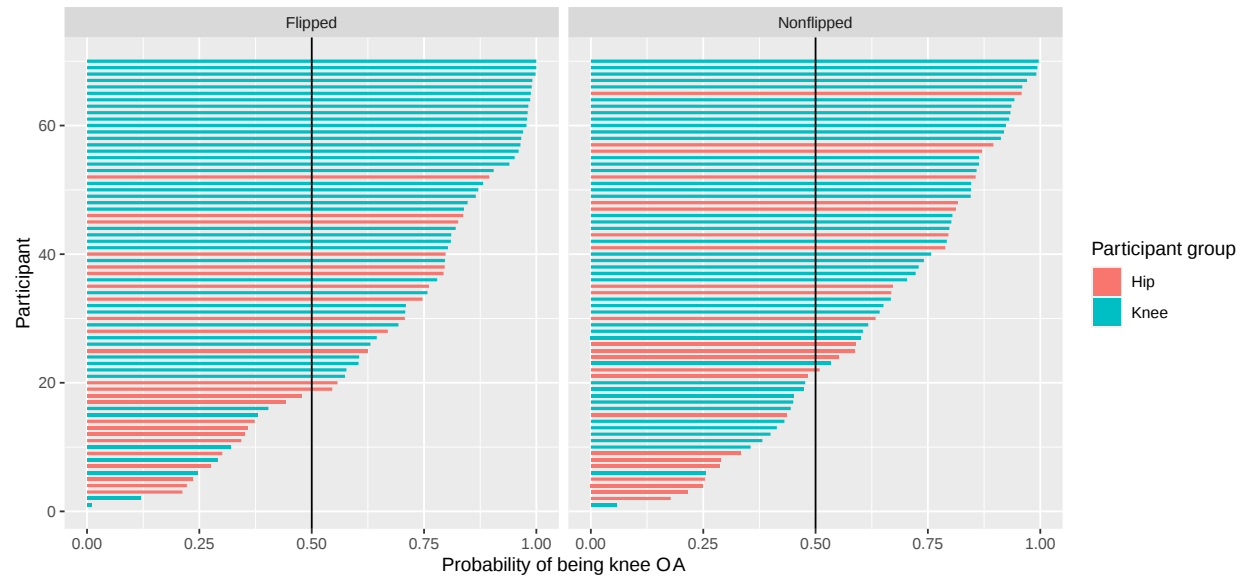


Figure S2. Group prediction performance: probability of classification by subject in OA. Plots of probabilities for Knee OA membership in knee OA validation and hip OA groups using the models generated in the knee OA training sample (flipped and non-flipped models). *X-axis* - probability of being classified as KOA patient. *Y-axis* represents rank-ordered subjects (red: HOA; blue: KOA). Black line represents probability threshold of 0.5.

Table S2. Partial correlations between clinical variables and volumetric changes in whole-brain VBM analysis

Peak MNI coordinate region (Harvard-Oxford Cortical structural atlas)	Pain Duration (years)	Pain Intensity (NRS)	KOOS/ HOOS (S)	KOOS/ HOOS (P)	KOOS/ HOOS (ADL)	KOOS/ HOOS (SR)	KOOS/ HOOS (QoL)	Group
Non-flipped brain analysis (Fig.1(C))								
Paracingulate gyrus (20%), Cingulate Gyrus, anterior division (14%), Juxtapositional lobule cortex (7%)	0.2	-0.16	-0.12	-0.23	-0.11	-0.21	-0.04	Hip OA
Flipped brain analysis (Fig.2(A))								
Cingulate Gyrus, anterior division (9%), posterior division (4%)	-0.16	-0.27	0.23	0.03	0.22	0.04	-0.27	Hip OA
Precentral Gyrus (54%)	0.03	0.1	0.01	-0.04	0.02	-0.05	-0.19	Knee/Hip OA
Temporal Pole (34%)	0.08	0.03	0.04	-0.11	0.07	-0.01	-0.04	Knee/Hip OA
Precuneus Cortex (49%), Intracalcarine Cortex (27%)	-0.06	0.04	0.15	0.32	0.04	-0.05	0.04	Knee OA
Middle Frontal Gyrus (23%), Superior Frontal Gyrus (2%)	0.12	0.01	0.16	0.14	0.02	-0.05	-0.04	Knee OA

(Cont.)

Peak MNI coordinate region (Harvard-Oxford Cortical structural atlas)	HADS Anxiety	HADS Depression	PCS	DN4	TUG	6MWT	Group
Non-flipped brain analysis (Fig.1(C))							
Paracingulate gyrus (20%), Cingulate Gyrus, anterior division (14%), Juxtapositional lobule cortex (7%)	-0.05	0.07	-0.28	0.19	-0.01	0.21	Hip OA
Flipped brain analysis (Fig.2(A))							
Cingulate Gyrus, anterior division (9%), posterior division (4%)	-0.37	0.1	-0.28	-0.01	0.09	-0.16	Hip OA
Precentral Gyrus (54%)	-0.23	-0.17	-0.2	-0.07	-0.12	0.03	Knee/Hip OA
Temporal Pole (34%)	-0.14	-0.02	-0.01	0.14	-0.08	0.16	Knee/Hip OA
Precuneus Cortex (49%), Intracalcarine Cortex (27%)	0.03	0.09	-0.02	-0.12	-0.26	-0.06	Knee OA
Middle Frontal Gyrus (23%), Superior Frontal Gyrus (2%)	-0.02	0.03	-0.08	-0.05	-0.02	0.12	Knee OA

Partial correlations between identified clusters (mean volume) and clinical variables, while controlling for age, gender and total ICV, for original space and flipped brain analysis. Correlations did not yield significant results when controlling for multiple comparisons using an FDR correction at $p < 0.05$.

Table S3. Multiple regression analysis for clinical features association with OA brain morphological classification models for the OA testing group.

Dependent Variable	RMSE	R ²	Adj. R ²	F-value (45,29)	p-value
Pain Duration	4.78	0.28	-0.086	0.76	0.7
NRS	1.49	0.28	-0.084	0.77	0.69
DN4	2.17	0.53	0.29	2.19	0.03*
HADS_A	4.22	0.44	0.15	1.54	0.15
HADS_D	3.88	0.26	-0.11	0.7	0.75
KOOS_Pain	2.32	0.29	-0.073	0.79	0.67
KOOS_Symptoms	18.8	0.23	-0.16	0.59	0.86
KOOS_ADL	12.9	0.44	0.158	1.55	0.15
KOOS_SR	14.5	0.48	0.22	1.85	0.07
PCS	13.8	0.396	0.083	1.27	0.28
KLS	0.81	0.23	-0.164	0.58	0.86

TUG	3.5	0.47	0.207	1.76	0.09
6MWT	68.9	0.336	-0.006	0.98	0.49

Independent variables entered were the 15 features obtained in the L_1 regularized logistic model for OA classification using the 90 ROIs (for x-axis mirrored brain, regarding lateralization of OA). 6MWT (6 Minute Walking Test); DN4 (*Doleur Neuropathique en 4 questions*); HADS_A (Hospitalar Anxiety and Depression Scale, Anxiety); HADS_D (Hospitalar Anxiety and Depression Scale, depression); KLS (Kellgren Lawrence Scale); KOOS (Knee injury and Osteoarthritis Outcome Score) – ADL (activities if daily living); NRS (numeric rating scale); SR (sports and recreational); PCS (Pain Catastrophizing Scale); TUG (Stand up and go test); RMSE (root mean squared error). None of these models were considered informative.