In Ledig et al. [1], the normalization coefficients for the correction for nuisance factors were calculated on all analyzed healthy control subjects. This allows consistent feature correction across all experiments and simplifies statistical group comparison. We have confirmed that the simpler correction approach we took does not cause any substantial quantitative differences in our experiments. Specifically, we confirmed that quantitative differences in the calculated statistics are negligible when calculating normalization coefficients based on either the healthy control group (c.f. Table 2) or the stable MCI group (c.f. Table 3). Both normalization approaches yield a substantial improvement over uncorrected features (c.f. Table 1).

References

1. Ledig, C., Schuh, A., Guerrero, R., Heckemann, R. A. & Rueckert, D. Structural brain imaging in Alzheimer's disease and mild cognitive impairment: biomarker analysis and shared morphometry database. *Sci. Reports* (2018).

Cross-sectional analysis at baseline (AD vs. HC, uncorrected volumes)

Table 1. Classification results in % (6-fold CV, LDA 100 runs, RF/SVM 20 runs) for distinguishing between AD and HC. Significant group differences indicated by + ($p < 0.05$) and ++ ($p < 0.001$). Bonferroni-corrected significance in parentheses. Sorted by effect size.

AD patients (N = 322, Positives^P) vs. **Healthy Controls** (N = 404, Negatives^N) **(baseline analysis, uncorrected volumes)**								
structure	ACC (bACC)	SENS	SPEC	mean (SD) [mm^3]^P	mean (SD) [mm^3]^N	effect size (d)	p-value	sig. (corr.)
RandomForest (all features)	85 (85)	81	88					
SVM (all features)	90 (90)	86	93					
Gender (female = 0, male = 1)	52 (52)	55	50	0.5 (0.5)	0.5 (0.5)	0.099	0.18349	o (o)
Age	51 (51)	51	51	75.1 (7.7)	74.9 (5.7)	0.027	0.71340	o (o)
(surrogate structures)								
Ventricles	66 (65)	55	75	63295.6 (28189.0)	46227.4 (20971.9)	0.698	<0.00001	++ (++)
CorticalGreyMatter	61 (61)	62	60	491782.0 (56040.1)	519904.6 (50579.3)	0.530	<0.00001	++ (++)
BrainTissue	56 (56)	57	55	1133344.3 (118326.9)	1163549.9 (110731.1)	0.265	0.00042	++ (+)
DeepGreyMatter	55 (55)	57	54	172879.2 (18868.2)	175625.6 (16551.2)	0.156	0.03725	+ (o)
Brain	54 (55)	56	53	1199158.5 (132290.9)	1212115.6 (118623.9)	0.104	0.16526	o (o)
WhiteMatter	48 (47)	47	48	468683.1 (62373.7)	468019.7 (60538.5)	0.011	0.88497	o (o)
(individual structures)								
LeftHippocampus	76 (76)	76	75	2608.0 (479.7)	3221.8 (434.3)	1.349	<0.00001	++ (++)
Amygdala	75 (75)	73	78	1825.9 (388.6)	2296.6 (314.5)	1.348	<0.00001	++ (++)
Hippocampus	75 (75)	75	75	5429.2 (943.8)	6601.4 (825.8)	1.332	<0.00001	++ (++)
RightAmygdala	75 (75)	73	76	925.6 (209.5)	1168.0 (171.6)	1.280	<0.00001	++ (++)
EntA	73 (73)	71	75	3427.5 (675.5)	4245.4 (609.2)	1.279	<0.00001	++ (++)
LeftAmygdala	75 (75)	73	77	900.3 (205.1)	1128.6 (162.7)	1.250	<0.00001	++ (++)
RightHippocampus	73 (73)	71	75	2821.2 (546.5)	3379.6 (427.4)	1.154	<0.00001	++ (++)
InfLatVent	73 (72)	58	85	3432.1 (1556.6)	2107.1 (825.3)	1.099	<0.00001	++ (++)
LeftInfLatVent	75 (74)	63	85	1652.9 (765.4)	1006.8 (420.7)	1.079	<0.00001	++ (++)
RightInfLatVent	70 (68)	55	82	1779.3 (902.2)	1100.3 (447.5)	0.988	<0.00001	++ (++)
ITG	66 (66)	66	65	21776.6 (3325.8)	24529.3 (2916.2)	0.887	<0.00001	++ (++)
PHG	66 (66)	68	65	6447.4 (977.5)	7217.3 (899.2)	0.824	<0.00001	++ (++)
AnG	67 (67)	67	67	15507.5 (2580.5)	17559.5 (2480.9)	0.812	<0.00001	++ (++)
MTG	64 (64)	66	62	25677.9 (4030.6)	28511.8 (3713.2)	0.735	<0.00001	++ (++)
TMP	64 (63)	61	65	13730.4 (2468.4)	15339.5 (2004.0)	0.724	<0.00001	++ (++)
LateralVentricle	65 (64)	55	73	55184.7 (26190.1)	39883.0 (19481.1)	0.674	<0.00001	++ (++)
LeftLateralVentricle	66 (65)	55	75	29062.5 (14264.5)	20827.4 (10483.3)	0.669	<0.00001	++ (++)
SMG	62 (63)	64	61	13731.4 (2077.6)	15086.0 (2006.8)	0.664	<0.00001	++ (++)
RightLateralVentricle	63 (62)	54	71	26122.3 (12557.2)	19055.6 (9403.3)	0.647	<0.00001	++ (++)
STG	63 (63)	62	63	12671.1 (2031.8)	13889.0 (1933.7)	0.616	<0.00001	++ (++)
OFuG	60 (60)	61	60	7382.1 (1324.3)	8129.7 (1267.7)	0.578	<0.00001	++ (++)
ThalamusProper	61 (61)	63	60	12486.4 (1477.5)	13304.8 (1426.0)	0.565	<0.00001	++ (++)
3rdVentricle	60 (60)	54	65	2319.7 (828.7)	1891.2 (721.5)	0.556	<0.00001	++ (++)
BasalForebrain	62 (62)	64	60	795.6 (215.5)	914.0 (213.2)	0.552	<0.00001	++ (++)
FuG	60 (61)	63	59	15951.4 (2428.3)	17131.2 (2281.3)	0.503	<0.00001	++ (++)
AIns	62 (62)	63	60	8241.7 (1225.1)	8820.0 (1142.4)	0.490	<0.00001	++ (++)
AccumbensArea	60 (60)	57	62	617.0 (184.6)	695.7 (148.3)	0.475	<0.00001	++ (++)
MOG	59 (59)	61	57	10087.5 (1773.4)	10837.5 (1524.1)	0.457	<0.00001	++ (++)
IOG	58 (58)	57	59	11413.2 (2016.2)	12233.2 (1815.4)	0.430	<0.00001	++ (++)
SPL	58 (58)	59	57	16943.2 (2469.3)	17977.7 (2441.6)	0.422	<0.00001	++ (++)
PIns	58 (59)	60	57	4482.8 (701.8)	4771.4 (703.1)	0.411	<0.00001	++ (++)
PP	58 (58)	60	55	3682.5 (589.7)	3912.8 (549.4)	0.406	<0.00001	++ (++)
FO	57 (57)	58	55	3504.1 (549.2)	3718.8 (539.9)	0.395	<0.00001	++ (++)
MFG	59 (59)	60	59	33109.0 (5125.3)	34968.2 (4791.0)	0.376	<0.00001	++ (++)
SFG	56 (57)	58	55	26326.6 (3837.4)	27676.8 (3441.8)	0.373	<0.00001	++ (++)
PT	57 (57)	61	54	3658.7 (712.6)	3926.4 (769.4)	0.359	<0.00001	++ (++)
TrIFG	54 (54)	55	54	6113.5 (1082.3)	6494.0 (1071.5)	0.354	<0.00001	++ (++)
Caudate	58 (56)	43	69	7535.3 (2705.8)	6812.7 (1705.2)	0.328	0.00001	++ (+)
Putamen	56 (56)	57	55	7455.9 (1342.8)	7878.8 (1331.8)	0.316	0.00003	++ (+)
SCA	56 (57)	58	55	2367.0 (496.3)	2510.7 (434.7)	0.310	0.00004	++ (+)
PCu	55 (56)	58	53	21742.5 (3583.1)	22743.6 (3039.0)	0.304	0.00005	++ (+)
PCgG	56 (56)	57	55	8494.1 (1311.2)	8862.3 (1128.5)	0.304	0.00005	++ (+)
CSF	57 (56)	51	61	2419.4 (579.6)	2250.7 (598.6)	0.286	0.00014	++ (+)
POrG	55 (55)	57	54	6068.4 (927.5)	6312.4 (859.2)	0.274	0.00026	++ (+)
MCgG	55 (54)	48	60	10326.7 (1674.5)	9905.0 (1511.3)	0.266	0.00040	++ (+)
MSFG	56 (57)	61	53	12685.2 (2000.5)	13151.5 (1735.4)	0.251	0.00082	++ (o)
SOG	55 (55)	57	54	7063.8 (1242.6)	7354.8 (1136.5)	0.246	0.00106	+ (o)
MFC	54 (54)	54	54	3510.2 (716.9)	3663.4 (603.6)	0.233	0.00185	+ (o)
OCP	53 (53)	57	50	4494.6 (931.2)	4728.0 (1076.0)	0.230	0.00215	+ (o)
CerebellarVermalLobulesI-V	54 (54)	56	52	4464.0 (672.4)	4616.9 (672.9)	0.227	0.00244	+ (o)
OrIFG	55 (55)	60	50	2749.4 (587.8)	2879.5 (568.2)	0.225	0.00263	+ (o)
LOrG	54 (55)	57	52	3713.5 (688.9)	3853.3 (600.1)	0.218	0.00363	+ (o)
OpIFG	52 (53)	57	49	5649.2 (1036.1)	5864.9 (1065.5)	0.205	0.00624	+ (o)
GRe	53 (53)	55	52	3228.0 (549.0)	3335.1 (512.8)	0.202	0.00691	+ (o)
PO	54 (55)	58	52	4251.3 (792.1)	4409.9 (796.3)	0.200	0.00770	+ (o)
CerebellumWhiteMatter	54 (52)	40	65	32795.7 (8328.0)	31344.3 (7506.8)	0.184	0.01393	+ (o)
SMC	53 (53)	57	49	10285.9 (1713.6)	10567.8 (1418.9)	0.181	0.01558	+ (o)
AOrG	51 (51)	52	50	3804.7 (617.0)	3906.9 (598.1)	0.168	0.02448	+ (o)
TTG	56 (57)	62	52	2387.0 (557.6)	2477.1 (532.0)	0.166	0.02684	+ (o)
CerebellarVermalLobulesVI-VII	53 (53)	50	55	2417.3 (432.6)	2355.7 (390.0)	0.150	0.04435	+ (o)
PoG	53 (53)	55	51	18093.5 (2551.3)	18449.6 (2321.8)	0.147	0.04984	+ (o)
MPoG	54 (54)	56	52	1644.7 (394.0)	1699.2 (370.6)	0.143	0.05604	o (o)
PrG	52 (52)	53	51	23676.0 (3462.6)	24096.7 (3052.7)	0.130	0.08268	o (o)
CO	53 (53)	55	51	7785.8 (1114.5)	7923.9 (1090.1)	0.125	0.09374	o (o)
Calc	53 (53)	50	55	7085.9 (1722.2)	6884.2 (1531.2)	0.125	0.09586	o (o)
FRP	51 (52)	53	50	5444.2 (1113.1)	5565.8 (996.7)	0.116	0.12123	o (o)
MPrG	53 (53)	55	51	5428.2 (957.0)	5531.1 (847.0)	0.115	0.12515	o (o)
MOrG	52 (52)	54	51	8243.5 (1150.7)	8361.5 (1010.3)	0.110	0.14236	o (o)
ACg	51 (51)	54	49	8487.7 (1576.8)	8613.8 (1458.5)	0.083	0.26466	o (o)
VentralDC	51 (51)	52	50	8448.8 (965.4)	8523.1 (931.8)	0.079	0.29369	o (o)
BrainStem	50 (50)	52	49	18742.3 (2233.9)	18885.5 (2141.8)	0.066	0.38005	o (o)
Pallidum	51 (51)	49	52	2668.2 (454.5)	2645.4 (394.7)	0.054	0.47061	o (o)
Cun	49 (49)	49	48	10691.9 (2079.7)	10753.0 (1794.8)	0.032	0.67110	o (o)
CerebellarVermalLobulesVIII-X	48 (48)	47	49	2823.6 (474.2)	2814.5 (428.5)	0.020	0.78685	o (o)
4thVentricle	48 (48)	45	51	2359.0 (691.3)	2346.0 (690.8)	0.019	0.80132	o (o)
CerebralWhiteMatter	48 (48)	49	48	435887.4 (58972.0)	436675.4 (56880.4)	0.014	0.85528	o (o)
CerebellumExterior	48 (48)	48	49	97168.8 (12890.5)	97279.6 (11151.4)	0.009	0.90128	o (o)
LiG	48 (48)	47	48	18512.9 (2794.7)	18524.4 (2476.3)	0.004	0.95334	o (o)

Cross-sectional analysis at baseline (AD vs. HC, corrected volumes based on HC group)

Table 2. Classification results in % (6-fold CV, LDA 100 runs, RF/SVM 20 runs) for distinguishing between AD and HC. Significant group differences indicated by + ($p < 0.05$) and ++ ($p < 0.001$). Bonferroni-corrected significance in parentheses. Sorted by effect size. Mean also shown in % with respect to sample-specific reference volume used for feature correction.

AD patients (N = 322, Positives^{P}) vs. **Healthy Controls** (N = 404, Negatives^{N}) **(baseline analysis, †volumes corrected for age/gender/brain size)**								
structure	ACC (bACC)	SENS	SPEC	mean [rel. to HC] (SD) [mm^3]^{P,†}	mean (SD) [mm^3]^{N,†}	effect size (d)	p-value	sig. (corr.)
RandomForest (all features)	87 (86)	83	90					
SVM (all features)	90 (89)	86	92					
Gender (female = 0, male = 1)	52 (52)	55	50	0.5 (0.5)	0.5 (0.5)	0.099	0.18349	o (o)
Age	50 (50)	50	50	75.1 (7.7)	74.9 (5.7)	0.027	0.71340	o (o)
(surrogate structures)								
BrainTissue	72 (71)	63	78	-17942.8 [≙ -1.5%] (22718.7)	0 (17403.6)	0.900	<0.00001	++ (++)
CorticalGreyMatter	68 (67)	63	72	-23635.9 [≙ -4.6%] (28907.3)	0 (24078.1)	0.898	<0.00001	++ (++)
Ventricles	72 (71)	63	79	17757.3 [≙ 46.2%] (22639.6)	0 (17293.9)	0.895	<0.00001	++ (++)
WhiteMatter	57 (56)	51	61	7242.2 [≙ 1.7%] (29309.8)	0 (28686.1)	0.250	0.00086	++ (o)
DeepGreyMatter	52 (52)	50	54	-1549.1 [≙ -0.9%] (13310.2)	0 (11142.2)	0.127	0.08834	o (o)
Brain	54 (55)	56	53	1199158.5 (132290.9)	1212115.6 (118623.9)	0.104	0.16526	o (o)
(individual structures)								
Amygdala	80 (80)	76	84	-452.0 [≙ -20.0%] (332.0)	0 (250.5)	1.561	<0.00001	++ (++)
Hippocampus	78 (78)	75	80	-1115.4 [≙ -17.0%] (817.7)	0 (660.7)	1.519	<0.00001	++ (++)
EntA	78 (78)	76	80	-801.3 [≙ -19.0%] (583.3)	0 (485.3)	1.509	<0.00001	++ (++)
LeftHippocampus	79 (78)	76	81	-588.1 [≙ -18.4%] (423.1)	0 (364.6)	1.502	<0.00001	++ (++)
RightAmygdala	80 (80)	77	83	-232.2 [≙ -20.2%] (182.6)	0 (139.4)	1.452	<0.00001	++ (++)
LeftAmygdala	78 (78)	75	81	-219.8 [≙ -19.7%] (179.7)	0 (135.5)	1.403	<0.00001	++ (++)
RightHippocampus	76 (75)	71	79	-527.3 [≙ -15.7%] (488.0)	0 (339.1)	1.280	<0.00001	++ (++)
InfLatVent	78 (77)	65	89	1330.8 [≙ 65.8%] (1367.4)	0 (702.2)	1.267	<0.00001	++ (++)
LeftInfLatVent	77 (76)	66	86	649.5 [≙ 68.2%] (677.1)	0 (360.6)	1.237	<0.00001	++ (++)
ITG	71 (71)	69	73	-2588.0 [≙ -10.7%] (2506.9)	0 (1954.5)	1.168	<0.00001	++ (++)
RightInfLatVent	75 (73)	59	87	681.3 [≙ 63.6%] (814.9)	0 (391.3)	1.106	<0.00001	++ (++)
PHG	68 (68)	64	72	-739.8 [≙ -10.3%] (832.6)	0 (702.4)	0.970	<0.00001	++ (++)
MTG	69 (69)	69	70	-2534.0 [≙ -9.0%] (2853.0)	0 (2411.3)	0.969	<0.00001	++ (++)
AnG	68 (67)	65	70	-1880.5 [≙ -10.6%] (2345.6)	0 (1973.2)	0.876	<0.00001	++ (++)
TMP	66 (65)	64	67	-1521.7 [≙ -10.1%] (1967.2)	0 (1539.3)	0.873	<0.00001	++ (++)
LateralVentricle	71 (70)	62	78	15972.2 [≙ 50.5%] (21196.2)	0 (16214.4)	0.859	<0.00001	++ (++)
LeftLateralVentricle	70 (69)	61	76	8584.7 [≙ 51.4%] (11586.9)	0 (8816.1)	0.847	<0.00001	++ (++)
RightLateralVentricle	70 (69)	59	78	7387.5 [≙ 49.6%] (10387.1)	0 (7883.2)	0.814	<0.00001	++ (++)
STG	65 (65)	64	66	-1100.3 [≙ -7.9%] (1610.7)	0 (1478.6)	0.715	<0.00001	++ (++)
3rdVentricle	67 (66)	63	70	434.3 [≙ 27.9%] (699.9)	0 (591.1)	0.677	<0.00001	++ (++)
SMG	64 (64)	63	65	-1196.5 [≙ -7.8%] (2003.1)	0 (1697.8)	0.650	<0.00001	++ (++)
ThalamusProper	63 (63)	61	65	-680.6 [≙ -5.0%] (1214.1)	0 (1005.2)	0.617	<0.00001	++ (++)
FuG	62 (62)	62	61	-1072.1 [≙ -6.4%] (1750.6)	0 (1769.3)	0.609	<0.00001	++ (++)
OFuG	60 (60)	58	62	-690.7 [≙ -8.4%] (1225.8)	0 (1061.2)	0.607	<0.00001	++ (++)
BasalForebrain	63 (63)	66	61	-109.6 [≙ -12.0%] (195.4)	0 (189.3)	0.571	<0.00001	++ (++)
AIns	59 (60)	62	58	-509.3 [≙ -5.8%] (995.9)	0 (915.4)	0.535	<0.00001	++ (++)
MOG	60 (60)	61	59	-643.3 [≙ -6.1%] (1375.1)	0 (1195.7)	0.503	<0.00001	++ (++)
IOG	59 (59)	60	59	-697.2 [≙ -5.8%] (1571.8)	0 (1386.2)	0.474	<0.00001	++ (++)
AccumbensArea	60 (60)	59	61	-71.7 [≙ -10.3%] (177.2)	0 (138.5)	0.457	<0.00001	++ (++)
PP	58 (58)	61	56	-200.0 [≙ -5.2%] (464.5)	0 (433.4)	0.447	<0.00001	++ (++)
MCgG	58 (57)	54	60	544.3 [≙ 5.6%] (1270.6)	0 (1190.1)	0.444	<0.00001	++ (++)
PIns	58 (58)	58	58	-231.1 [≙ -4.9%] (524.6)	0 (547.9)	0.430	<0.00001	++ (++)
MFG	58 (58)	56	60	-1467.9 [≙ -4.2%] (3689.2)	0 (3194.1)	0.429	<0.00001	++ (++)
SPL	56 (56)	57	56	-867.5 [≙ -4.7%] (2175.8)	0 (1972.5)	0.420	<0.00001	++ (++)
SFG	59 (59)	60	58	-1124.3 [≙ -4.1%] (3032.2)	0 (2632.7)	0.399	<0.00001	++ (++)
Caudate	58 (57)	46	68	799.5 [≙ 11.2%] (2447.8)	0 (1597.5)	0.396	<0.00001	++ (++)
FO	60 (60)	59	60	-187.3 [≙ -4.9%] (506.5)	0 (458.7)	0.390	<0.00001	++ (++)
PT	56 (56)	58	55	-232.4 [≙ -5.8%] (590.0)	0 (636.4)	0.377	<0.00001	++ (++)
TrIFG	57 (57)	56	58	-331.8 [≙ -5.0%] (985.1)	0 (933.4)	0.347	<0.00001	++ (++)
PCu	56 (56)	57	54	-788.1 [≙ -3.6%] (2502.1)	0 (2124.3)	0.343	<0.00001	++ (++)
PCgG	57 (57)	59	56	-306.1 [≙ -3.7%] (960.5)	0 (898.4)	0.330	0.00001	++ (++)
SCA	58 (58)	58	59	-124.5 [≙ -5.1%] (441.7)	0 (388.6)	0.301	0.00006	++ (+)
POrG	57 (57)	54	59	-211.0 [≙ -3.4%] (738.1)	0 (685.9)	0.297	0.00008	++ (+)
CSF	58 (58)	53	62	172.5 [≙ 9.3%] (621.2)	0 (545.8)	0.297	0.00008	++ (+)
Putamen	57 (57)	58	56	-367.5 [≙ -4.6%] (1300.2)	0 (1243.1)	0.290	0.00012	++ (+)
MSFG	54 (54)	55	53	-349.9 [≙ -2.8%] (1447.4)	0 (1334.5)	0.253	0.00076	++ (o)
MFC	53 (53)	54	53	-123.9 [≙ -3.6%] (577.8)	0 (493.6)	0.233	0.00192	+ (o)
CerebellumWhiteMatter	55 (54)	44	64	1677.9 [≙ 5.8%] (7982.2)	0 (6947.8)	0.226	0.00257	+ (o)
OCP	53 (54)	57	50	-207.2 [≙ -4.5%] (815.9)	0 (999.5)	0.225	0.00274	+ (o)
SOG	55 (56)	58	53	-220.0 [≙ -3.1%] (1044.7)	0 (974.8)	0.219	0.00354	+ (o)
CerebralWhiteMatter	56 (55)	52	58	5564.3 [≙ 1.4%] (26392.1)	0 (25736.3)	0.214	0.00434	+ (o)
OrIFG	55 (56)	59	52	-109.5 [≙ -3.9%] (518.0)	0 (510.3)	0.213	0.00446	+ (o)
LOrG	52 (52)	53	51	-111.8 [≙ -3.0%] (565.6)	0 (492.2)	0.213	0.00456	+ (o)
CerebellarVermalLobulesI-V	56 (56)	57	55	-128.8 [≙ -2.8%] (620.1)	0 (632.2)	0.205	0.00610	+ (o)
Calc	53 (53)	51	55	275.0 [≙ 3.8%] (1536.7)	0 (1432.9)	0.186	0.01309	+ (o)
CerebellarVermalLobulesVI-VII	54 (54)	52	55	71.0 [≙ 3.0%] (401.3)	0 (370.4)	0.185	0.01368	+ (o)
OpIFG	51 (51)	53	50	-153.5 [≙ -2.5%] (890.2)	0 (909.9)	0.170	0.02290	+ (o)
GRe	52 (52)	54	51	-77.1 [≙ -2.5%] (463.7)	0 (463.0)	0.166	0.02614	+ (o)
SMC	52 (52)	54	51	-192.1 [≙ -2.0%] (1309.9)	0 (1108.0)	0.160	0.03273	+ (o)
PO	53 (53)	54	52	-105.0 [≙ -2.1%] (682.3)	0 (637.7)	0.160	0.03303	+ (o)
AOrG	52 (52)	52	52	-71.6 [≙ -1.8%] (483.0)	0 (464.7)	0.151	0.04301	+ (o)
TTG	54 (54)	56	53	-70.4 [≙ -2.7%] (481.9)	0 (455.3)	0.151	0.04398	+ (o)
MPoG	53 (53)	53	53	-44.8 [≙ -2.5%] (377.8)	0 (348.2)	0.124	0.09769	o (o)
PrG	52 (53)	55	50	-262.1 [≙ -1.1%] (2723.4)	0 (2472.1)	0.101	0.17534	o (o)
Pallidum	54 (54)	55	53	38.0 [≙ 1.4%] (418.7)	0 (362.0)	0.098	0.19090	o (o)
PoG	52 (52)	52	52	-189.2 [≙ -1.0%] (2124.4)	0 (1913.6)	0.094	0.20803	o (o)
FRP	50 (50)	53	47	-76.0 [≙ -1.5%] (962.3)	0 (901.5)	0.082	0.27406	o (o)
MPrG	51 (51)	53	50	-58.2 [≙ -1.1%] (819.9)	0 (747.4)	0.075	0.31847	o (o)
CO	50 (50)	51	49	-58.3 [≙ -0.7%] (783.8)	0 (796.8)	0.074	0.32384	o (o)
MOrG	51 (51)	53	49	-61.3 [≙ -0.7%] (943.0)	0 (819.7)	0.070	0.34945	o (o)
CerebellarVermalLobulesVIII-X	51 (51)	51	51	22.1 [≙ 0.8%] (423.1)	0 (375.1)	0.056	0.45705	o (o)
LiG	51 (51)	51	51	106.4 [≙ 0.5%] (2022.0)	0 (1846.7)	0.055	0.46010	o (o)
CerebellumExterior	52 (52)	52	51	442.1 [≙ 0.4%] (10408.6)	0 (8931.0)	0.046	0.53842	o (o)
4thVentricle	50 (50)	46	54	19.9 [≙ 1.1%] (646.4)	0 (643.3)	0.031	0.67923	o (o)
Cun	48 (48)	46	49	33.2 [≙ 0.2%] (1619.0)	0 (1403.3)	0.022	0.76765	o (o)
VentralDC	47 (47)	46	47	-13.7 [≙ -0.0%] (709.3)	0 (597.0)	0.021	0.77728	o (o)
BrainStem	48 (48)	47	48	17.8 [≙ 0.2%] (1574.8)	0 (1484.5)	0.012	0.87624	o (o)
ACg	47 (47)	47	48	-5.9 [≙ -0.0%] (1178.5)	0 (1101.8)	0.005	0.94417	o (o)

Cross-sectional analysis at baseline (AD vs. HC, corrected volumes based on sMCI group)

Table 3. Classification results in % (6-fold CV, LDA 100 runs, RF/SVM 20 runs) for distinguishing between AD and HC. Significant group differences indicated by + ($p < 0.05$) and ++ ($p < 0.001$). Bonferroni-corrected significance in parentheses. Sorted by effect size. Mean also shown in % with respect to sample-specific reference volume used for feature correction.

AD patients (N = 322, Positives^{P}) vs. **Healthy Controls** (N = 404, Negatives^{N}) **(baseline analysis, †volumes corrected for age/gender/brain size)**								
structure	ACC (bACC)	SENS	SPEC	mean [rel. to HC] (SD) [mm^3]^{P,†}	mean (SD) [mm^3]^{N,†}	effect size (d)	p-value	sig. (corr.)
RandomForest (all features)	87 (86)	83	89					
SVM (all features)	89 (89)	86	92					
Gender (female = 0, male = 1)	52 (52)	55	50	0.5 [≙0.5%] (0.5)	0.5 [≙0.5%] (0.5)	0.099	0.18349	o (o)
Age	51 (51)	51	51	75.1 [≙75.1%] (7.7)	74.9 [≙74.9%] (5.7)	0.027	0.71340	o (o)
(surrogate structures)								
BrainTissue	72 (71)	63	78	-13725.4 [≙-1.2%] (22678.2)	4317.4 [≙0.4%] (17492.6)	0.904	<0.00001	++ (++)
CorticalGreyMatter	67 (67)	62	71	-17169.5 [≙-3.4%] (29114.1)	6737.0 [≙1.3%] (24174.3)	0.903	<0.00001	++ (++)
Ventricles	72 (71)	63	78	13491.8 [≙37.4%] (22582.4)	-4374.9 [≙-7.8%] (17395.7)	0.899	<0.00001	++ (++)
WhiteMatter	57 (56)	51	61	3080.0 [≙0.8%] (29406.5)	-4290.7 [≙-0.9%] (28715.8)	0.254	0.00071	++ (o)
DeepGreyMatter	52 (52)	50	54	364.2 [≙0.2%] (13320.9)	1871.2 [≙1.1%] (11183.0)	0.124	0.09805	o (o)
Brain	54 (55)	56	53	1199158.5 [≙1199158.5%] (132290.9)	1212115.6 [≙1212115.6%] (118623.9)	0.104	0.16526	o (o)
(individual structures)								
Amygdala	80 (80)	76	83	-313.0 [≙-14.7%] (335.6)	149.5 [≙7.0%] (256.6)	1.572	<0.00001	++ (++)
Hippocampus	77 (77)	76	78	-562.6 [≙-9.4%] (830.8)	596.4 [≙10.0%] (694.7)	1.529	<0.00001	++ (++)
EntA	79 (79)	76	82	-536.9 [≙-13.6%] (585.5)	285.6 [≙7.2%] (497.5)	1.528	<0.00001	++ (++)
LeftHippocampus	77 (77)	75	79	-294.5 [≙-10.1%] (430.7)	312.2 [≙10.8%] (376.9)	1.510	<0.00001	++ (++)
RightAmygdala	79 (79)	76	82	-157.3 [≙-14.5%] (184.5)	81.7 [≙7.7%] (143.5)	1.466	<0.00001	++ (++)
LeftAmygdala	79 (78)	74	82	-155.7 [≙-14.9%] (181.8)	67.8 [≙6.4%] (138.1)	1.406	<0.00001	++ (++)
RightHippocampus	75 (74)	70	79	-268.1 [≙-8.7%] (491.8)	284.2 [≙9.2%] (359.7)	1.305	<0.00001	++ (++)
InfLatVent	79 (78)	68	88	1019.9 [≙47.8%] (1360.9)	-343.9 [≙-12.9%] (726.2)	1.292	<0.00001	++ (++)
LeftInfLatVent	78 (77)	69	85	507.6 [≙51.1%] (674.5)	-154.9 [≙-12.3%] (368.9)	1.258	<0.00001	++ (++)
ITG	72 (72)	70	74	-1914.4 [≙-8.1%] (2520.3)	714.2 [≙3.0%] (1977.7)	1.176	<0.00001	++ (++)
RightInfLatVent	75 (74)	62	86	512.3 [≙45.1%] (813.3)	-188.9 [≙-13.3%] (406.6)	1.130	<0.00001	++ (++)
PHG	70 (69)	67	71	-375.8 [≙-5.6%] (818.5)	391.3 [≙5.7%] (725.6)	0.999	<0.00001	++ (++)
MTG	69 (69)	69	69	-1814.7 [≙-6.8%] (2906.6)	834.9 [≙2.9%] (2492.7)	0.987	<0.00001	++ (++)
AnG	69 (68)	67	70	-1541.3 [≙-9.1%] (2255.3)	398.2 [≙2.2%] (2012.6)	0.913	<0.00001	++ (++)
TMP	67 (67)	66	68	-1304.7 [≙-8.8%] (2024.3)	286.2 [≙1.9%] (1571.3)	0.891	<0.00001	++ (++)
LateralVentricle	71 (70)	62	78	12099.2 [≙43.0%] (21157.2)	-3927.7 [≙-8.0%] (16307.6)	0.861	<0.00001	++ (++)
LeftLateralVentricle	71 (70)	63	77	6354.7 [≙50.3%] (11531.4)	-2266.2 [≙-8.5%] (8897.1)	0.849	<0.00001	++ (++)
RightLateralVentricle	69 (68)	59	78	5744.5 [≙39.5%] (10397.3)	-1661.5 [≙-7.4%] (7902.5)	0.814	<0.00001	++ (++)
STG	65 (65)	65	64	-696.5 [≙-5.4%] (1556.7)	406.0 [≙2.9%] (1525.8)	0.716	<0.00001	++ (++)
3rdVentricle	66 (66)	64	68	334.0 [≙26.4%] (727.5)	-120.7 [≙-5.1%] (602.4)	0.688	<0.00001	++ (++)
SMG	64 (64)	63	65	-842.5 [≙-5.6%] (2007.7)	382.4 [≙2.6%] (1703.2)	0.664	<0.00001	++ (++)
ThalamusProper	64 (64)	63	65	-374.4 [≙-2.8%] (1213.4)	326.0 [≙2.5%] (1012.3)	0.633	<0.00001	++ (++)
FuG	63 (63)	64	62	-852.2 [≙-5.2%] (1762.3)	252.3 [≙1.5%] (1775.8)	0.624	<0.00001	++ (++)
OFuG	60 (59)	58	61	-656.1 [≙-8.0%] (1222.5)	46.9 [≙0.5%] (1074.6)	0.615	<0.00001	++ (++)
BasalForebrain	63 (63)	65	61	-71.2 [≙-8.1%] (194.1)	44.4 [≙5.1%] (191.4)	0.601	<0.00001	++ (++)
AIns	60 (60)	63	57	-379.8 [≙-4.5%] (1005.1)	175.5 [≙2.0%] (942.9)	0.572	<0.00001	++ (++)
MOG	59 (59)	60	58	-596.0 [≙-5.6%] (1367.4)	27.7 [≙0.3%] (1200.4)	0.488	<0.00001	++ (++)
AccumbensArea	60 (60)	59	61	-48.0 [≙-7.0%] (177.5)	27.9 [≙4.4%] (140.8)	0.480	<0.00001	++ (++)
PP	57 (58)	61	54	-67.6 [≙-1.9%] (467.7)	137.7 [≙3.5%] (440.2)	0.454	<0.00001	++ (++)
SPL	57 (57)	58	56	-853.9 [≙-4.7%] (2153.6)	67.5 [≙0.3%] (1987.6)	0.447	<0.00001	++ (++)
IOG	59 (59)	59	60	-615.1 [≙-4.9%] (1610.8)	42.1 [≙0.6%] (1408.8)	0.438	<0.00001	++ (++)
PIns	58 (58)	59	58	-162.8 [≙-3.6%] (525.7)	71.3 [≙1.5%] (549.4)	0.434	<0.00001	++ (++)
MFG	58 (58)	56	60	-891.1 [≙-2.5%] (3695.3)	589.1 [≙1.7%] (3195.0)	0.432	<0.00001	++ (++)
MCgG	58 (58)	55	61	470.6 [≙4.9%] (1280.9)	-55.3 [≙-0.5%] (1198.5)	0.426	<0.00001	++ (++)
PO	59 (59)	59	59	-132.0 [≙-3.5%] (516.2)	73.8 [≙2.0%] (467.7)	0.420	<0.00001	++ (++)
Caudate	59 (58)	47	69	689.0 [≙9.8%] (2404.7)	-133.8 [≙-1.5%] (1618.1)	0.410	<0.00001	++ (++)
SFG	59 (59)	60	58	-933.3 [≙-3.5%] (3028.4)	214.7 [≙0.7%] (2641.4)	0.407	<0.00001	++ (++)
PT	55 (55)	57	53	-43.4 [≙-1.2%] (581.1)	178.7 [≙4.6%] (647.9)	0.359	<0.00001	++ (++)
TrIFG	56 (56)	55	57	-125.4 [≙-1.7%] (1000.8)	199.1 [≙3.2%] (937.8)	0.336	<0.00001	++ (++)
PCu	56 (56)	57	55	-641.8 [≙-2.9%] (2565.9)	112.6 [≙0.5%] (2136.2)	0.323	0.00002	++ (+)
PCgG	57 (57)	58	56	-284.5 [≙-3.3%] (965.4)	0.2 [≙0.1%] (909.4)	0.305	0.00005	++ (+)
SCA	58 (58)	57	59	-69.5 [≙-2.7%] (446.7)	54.8 [≙2.4%] (392.1)	0.298	0.00007	++ (+)
Putamen	57 (58)	58	57	-320.8 [≙-3.9%] (1317.3)	61.1 [≙0.9%] (1253.7)	0.298	0.00007	++ (+)
POrG	56 (56)	54	58	-112.3 [≙-1.8%] (731.8)	96.6 [≙1.6%] (688.8)	0.295	0.00009	++ (+)
CSF	57 (57)	52	62	225.1 [≙10.6%] (581.5)	61.9 [≙2.6%] (557.8)	0.287	0.00013	++ (+)
MSFG	54 (54)	56	53	-241.5 [≙-1.9%] (436.6)	115.4 [≙1.0%] (1344.2)	0.257	0.00060	++ (o)
CerebellumWhiteMatter	55 (54)	46	62	738.8 [≙3.3%] (8174.5)	-1056.6 [≙-2.9%] (7032.0)	0.237	0.00154	+ (o)
SOG	56 (56)	58	54	-253.0 [≙-3.4%] (1035.0)	-32.1 [≙-0.3%] (982.0)	0.220	0.00338	+ (o)
CerebralWhiteMatter	55 (55)	52	58	2341.2 [≙0.6%] (26362.0)	-3234.1 [≙-0.8%] (25774.9)	0.214	0.00427	+ (o)
MFC	54 (54)	55	54	20.1 [≙0.5%] (580.2)	132.2 [≙3.8%] (502.0)	0.208	0.00544	+ (o)
Calc	54 (54)	54	54	316.3 [≙5.1%] (1523.0)	9.4 [≙0.7%] (1471.7)	0.205	0.00614	+ (o)
CerebellarVermalLobulesI-V	55 (55)	57	53	-56.5 [≙-1.2%] (620.2)	71.9 [≙1.6%] (634.4)	0.204	0.00637	+ (o)
OCP	53 (53)	57	49	-292.2 [≙-5.9%] (818.1)	-102.2 [≙-1.8%] (1009.3)	0.204	0.00638	+ (o)
CerebellarVermalLobulesVI-VII	55 (54)	52	57	60.7 [≙2.5%] (402.7)	-15.9 [≙-0.7%] (372.9)	0.198	0.00815	+ (o)
OrIFG	55 (55)	59	52	-122.8 [≙-4.3%] (523.6)	-24.6 [≙-0.9%] (514.5)	0.189	0.01150	+ (o)
LOrG	53 (53)	56	50	-80.7 [≙-2.3%] (576.7)	21.3 [≙0.4%] (510.5)	0.189	0.01179	+ (o)
GRe	53 (53)	55	51	-92.7 [≙-2.8%] (463.3)	-10.2 [≙-0.2%] (479.8)	0.175	0.01973	+ (o)
OpIFG	51 (52)	55	48	-153.9 [≙-2.8%] (901.6)	3.2 [≙-0.1%] (943.2)	0.170	0.02326	+ (o)
SMC	52 (52)	54	50	60.6 [≙0.4%] (1314.2)	251.2 [≙2.4%] (1109.5)	0.158	0.03459	+ (o)
AOrG	52 (52)	52	51	8.6 [≙0.2%] (483.6)	71.8 [≙1.8%] (469.0)	0.133	0.07602	o (o)
PO	52 (52)	52	51	-98.1 [≙-2.1%] (672.1)	-12.4 [≙-0.3%] (650.8)	0.130	0.08282	o (o)
MPoG	53 (53)	52	53	19.5 [≙1.2%] (377.8)	65.7 [≙3.9%] (350.7)	0.127	0.08866	o (o)
Pallidum	54 (54)	55	54	49.5 [≙2.0%] (421.2)	4.7 [≙0.3%] (363.8)	0.115	0.12479	o (o)
TTG	52 (52)	53	52	-20.6 [≙-0.6%] (473.0)	27.2 [≙1.3%] (469.5)	0.102	0.17431	o (o)
PrG	52 (52)	55	50	-16.0 [≙-0.1%] (2725.2)	232.1 [≙1.0%] (2480.6)	0.096	0.20045	o (o)
PoG	51 (51)	51	52	-256.6 [≙-1.3%] (2130.7)	-70.4 [≙-0.3%] (1916.2)	0.092	0.21647	o (o)
FRP	50 (50)	54	47	-98.3 [≙-1.9%] (956.4)	-39.5 [≙-0.6%] (906.6)	0.063	0.39674	o (o)
CerebellumExterior	52 (52)	52	52	974.0 [≙1.0%] (10484.0)	441.4 [≙0.4%] (9005.0)	0.055	0.46205	o (o)
MPrG	49 (49)	50	48	-43.3 [≙-0.6%] (823.0)	-0.1 [≙0.2%] (758.0)	0.055	0.46222	o (o)
LiG	52 (52)	52	51	131.7 [≙0.6%] (2042.2)	35.4 [≙0.1%] (1860.5)	0.050	0.50734	o (o)
CO	48 (48)	48	48	48.4 [≙0.6%] (793.3)	85.8 [≙1.1%] (808.2)	0.047	0.53253	o (o)
CerebellarVermalLobulesVIII-X	51 (51)	50	51	-4.3 [≙-0.2%] (423.2)	-22.1 [≙-0.8%] (376.0)	0.045	0.54714	o (o)
4thVentricle	51 (50)	46	55	38.6 [≙1.5%] (648.7)	17.3 [≙0.5%] (649.6)	0.033	0.66059	o (o)
VentralDC	46 (46)	46	47	109.7 [≙1.4%] (706.0)	127.5 [≙1.5%] (597.5)	0.027	0.71330	o (o)
ACg	48 (48)	48	48	28.6 [≙0.2%] (1173.1)	58.9 [≙0.6%] (1127.3)	0.026	0.72327	o (o)
BrainStem	49 (49)	48	50	232.2 [≙1.3%] (1581.1)	192.3 [≙1.0%] (1488.8)	0.026	0.72698	o (o)
MOrG	48 (48)	49	47	8.6 [≙0.1%] (913.1)	30.2 [≙0.4%] (855.7)	0.025	0.74230	o (o)
Cun	48 (48)	47	49	-69.4 [≙-0.8%] (1628.4)	-95.3 [≙-0.9%] (1410.5)	0.017	0.81877	o (o)