Supplementary Data

Radiologic evidence that hypothalamic gliosis is improved after bariatric surgery in obese women with type 2 diabetes

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Supplementary Table 1. Patient anthropometric and laboratorial records at baseline.

	Controls of Healthy Weight (N=13)	Non-Diabetics with Obesity (N=19)	Type 2 Diabetics with Obesity (N=14)	P-value of statistical model
Age, *y*	30.1 (7.0)	35.7 (8.0)	40.7 (5.3)*	0.001†
Weight, *kg*	54.8 (6.2)	105.7 (11.3)*	116.6 (6.7)*§	<0.0001†
BMI, *kg/m²*	21.4 (2.0)	40.3 (5.2)*	45.2 (3.4)*§	<0.0001†
Fasting glucose, *mg/dl*	78.2 (8.5)	83.8 (6.7)	110.8 (26.2)*§	<0.0001†
Fasting insulin, *uU/ml*	4.3 (2.0–5.4)	8.7 (6.5–12.0)*	28.2 (14.6–38.5)*§	0.0001‡
HbA1c, *%*	5.2 (0.3)	5.5 (0.4)	6.7 (1.1)*§	<0.0001†
Triglycerides, *mg/dL*	90.0 (47.9)	110 (64.7)	124 (42.7)	0.26†
CRP, *mg/L*	0.14 (0.1–0.4)	0.97 (0.5–1.9)*	0.80 (0.7–1.1)*	0.0004‡
AST, *U/L*	16 (13–17)	20 (16–27)*	21 (18–22)*	0.02‡
ALT, *U/L*	16 (11–21)	22 (16–26)	20 (17–35)	0.06‡
HOMA-IR	0.8 (0.3)	2.1 (0.9)	8.0 (4.6)*§	<0.0001†
M-value	58.3 (15.1)	27.7 (12.4)*	18.5 (11.4)*	<0.0001†

Data are mean (SD) or median (Interquartile range). Group comparisons are unadjusted and were done by †one-way ANOVA with Bonferroni (normally distributed) or by ‡Kruskal-Wallis with Mann-Whitney (non-normally distribution). For plasma measures, HOMA-IR and M-value Ns were N=10–13 for controls of healthy weight, N=9–17 for non-diabetics with obesity, N=13–14 for type 2 diabetics with obesity. *P=0.02–0.0001 vs. Controls; §P=0.01–0.0001 vs. non-diabetics.

Supplementary Table 2. List of articles that used MRI or fMRI to evaluate hypothalamic structure and function in obesity.

Reference	Year	Method	Stimulus	N total	Lean	Ob/Ow	T2D	Intervention	Result
Matsuda *Diabetes* 48:1801	1999	fMRI	Oral glucose	20	10	10	0	None	Attenuation and retardation of glucose-induced fMRI signal the hypothalamus in obese
Smeets *Neuroimage* 24:363	2005	fMRI	Oral glucose	15	15	0	0	None	Glucose promoted a prolonged decrease in the fMRI signal in hypothalamus/dose dependent
Vidarsdottir *Diabetes* 56:2547	2007	fMRI	Oral glucose	17	10	0	7	None	Attenuation of glucose-induced fMRI signal in diabetes
Alkan *Magn Reson Imaging* 26:446	2008	MRI	None	110	29	81	0	None	Increased MRI signal for apparent difusion coeficient in the hypothalamus of obese
Page *Diabetes* 58:448	2009	fMRI	Insulin/glucose	9	9	0	0	None	Increased hypothalamic fMRI signal during hypoglycemia
Cornier *PLoS One* 4:e6310	2009	fMRI	Overfeeding	41	22	19	0	None	Reduction of overfeeding-induced fMRI singna in the hypothalamus in obese
Fletcher *J Neurosci* 30:14346	2010	fMRI	Food image cue	24	0	24	0	Sibutramine	Reduction of food image-induced fMRI signal in the hypothalamus after sibutramine
van de Sande-Lee *Diabetes* 60:1699	2011	fMRI	Oral glucose	21	8	13	0	RYGB	Attenuation of glucose-induced fMRI signal in the hypothalamus in obese; partial recovery after RYGB
Teeuwisse Diabetes 61:3255	2012	fMRI	Oral glucose	10	0	0	10	Normal versus low calory diet	Attenuation of fMRI signal in hypothalamus only after low calory diet
Thaler *J Clin Invest* 122:153	2012	MRI	None	34	12	22	0	None	Direct correlation between BMI and MRI signs of hypothalamic gliosis
Hinkle *PLoS One* 8:e59114	2013	fMRI	Leptin	10	0	10	0	Formula for 10% reduction of body mass	Increased connectivity of hypothalamus with regions of interoceptive system after leptin
Frank *Int J Obes* 38:341	2014	fMRI	Food image cue	31	11	20	0	RYGB	Higer hypothalamic fMRI signal after low vs. high calory food image presentation
Wang Int J Obes 38:682	2014	fMRI	Food image cue	40	0	40	0	Naltrexone/Bupropion	Atenuation of food image-induced hypothalamic fMRI signal after Natrexone/Bupropion
Lips *Am J Clin Nutr* 100:524	2014	fMRI	Liquid meal	58	12	19	27	None	Abrogation of food intake-induced attenuation of hypothalamic connectivity with frontal regions
Heni *Diabetes* 63:4083	2014	fMRI	Intranasal insulin	11	8	3	0	None	Direct correlation between hypothalamic fMRI signal and whole body insulin sensitivity
Kilpatrick *Gastroenterology* 146:1212	2014	fMRI	Sucrose	22	11	11	0	None	Higher connectivity of hypothalamus and reward regions after sucrose in obese
Blasco *Diabetes care* 37:3076	2014	MRI	None	43	20	23	0	None	Higher iron load in hypothalamus of obese; positive correlation of hypothalamic iron load and insulin resistance
Kullmann *Human Brain Mapp* 35:6088	2014	fMRI	None	48	25	23	0	None	Heigher baseline connectivity within the medial hypothalamus in obese
Wijngaarden *Behav Brain Res* 287:127	2015	fMRI	Prolonged fasting	24	11	13	0	None	Attenuation of fasting-induced connectivity of the hypothalamus with cingulate cortex in obese
Puig *J Clin Endocrinol Metabol* 100:E276	2015	MRI	None	44	20	24	0	None	Attenuation of lambda1 diffusion tensor imagin in the hypothalmus in obese
Kullman *Diabetes care* 38:1044	2015	fMRI	Insulin	48	25	23	0	None	Inverse correlation between insulin-induced hypothalamic blood-flow and visceral adiposity
Rachid *Int J Obes* 39:1515	2015	fMRI	Cold exposure	24	12	12	0	RYGB	Attenuation of cold-induced change in hypothalamic fMRI signal in obesity; no change after RYGB
Fernadez-Real *J Clin Endocrinol Metabol* 100:4505	2015	MRI	None	39	19	20	0	None	Gut microbiota profile clustered with hypothalamic microstructure
Schur *Obesity* 23:2142	2015	MRI	None	45	22	23	0	None	Direct correlation between BMI/magnitude of insulin resistance and MRI signs of hypothalamic gliosis
Jastreboff *Diabetes* 65:1929	2016	fMRI	Glucose/fructose	38	14	24	0	None	Increased hypothalamic perfusion after glucose in obese
Geha *Hum Brain Mapp* 38:1403	2017	fMRI	Liquid meal	61	33	28	0	None	Reduction in liquid meal-induction of fMRI signal in hypothalamus in obese
Jacobson *Perception* 46:283	2017	fMRI	Sucrose	52	26	26	0	Fasting	Reduced hypothalamic activation after sucrose in obese
Kreutzer *Diabetes* 66:2407	2017	MRI	None	111	54	57	0	None	Increased T2 signal intensity in the left mediobasal hypothalamus in obese
Kreutzer *Diabetes* 66:2407	2017	MRI	None	10	0	10	0	RYGB	No change in hypothalamic T2 signal after RYGB
Zoon *Biol Psycol* 137:34	2018	fMRI	Food image cue	18	0	18	0	RYGB	Attenuation of food image-induced fMRI signal in the hypothalamus afte RYGB

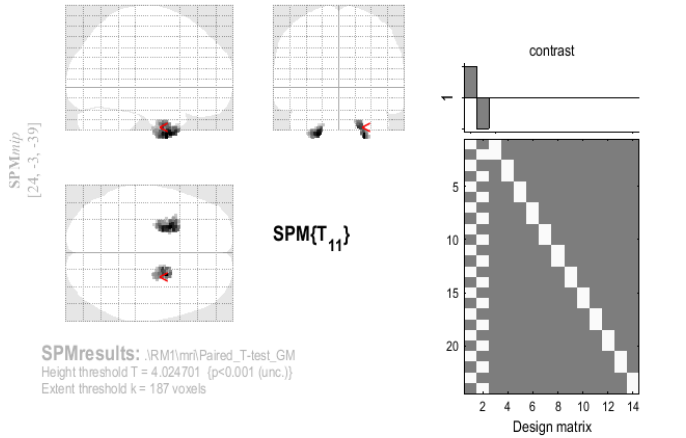
The articles were selected in PubMed, in the first week of January, 2019, using the terms: magnetic resonance, MRI, fMRI, obesity, hypothalamus and neuroimaging. fMRI, functional magnetic resonance imaging; MRI, magnetic resonance imaging; Ob/Ow, obese/overweight; RYGB, Roux-in-Y gastric bypass; T2D, type 2 diabetes.

Voxel-Based Morphometry (VBM) Results

1. Longitudinal Analysis (pre *versus* post Roux-n-Y gastric bypass surgery)

1.1. Obese Diabetic Subjects (T2D)

1.1.1. Whole Brain Grey Matter Analysis



Statistics: ***p-values adjusted for search volume***

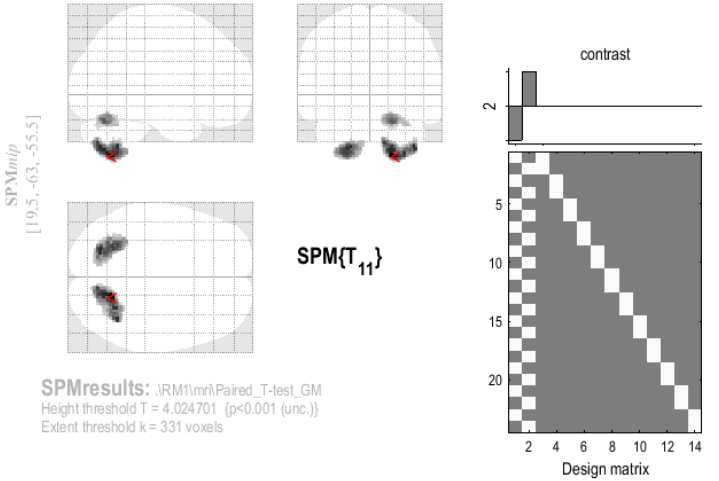
set-level		cluster-level				peak-level					mm mm mm		
p	c	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	T	$(Z_{\equiv})$	p_{uncorr}			
0.004	**2**	**0.018**	**0.014**	**272**	**0.001**	**0.671**	**0.510**	**7.30**	**4.32**	**0.000**	**-24**	**6**	**-48**
						0.774	0.510	6.98	4.23	0.000	-21	-2	-47
						0.979	0.510	5.99	3.92	0.000	-21	12	-44
		0.088	**0.036**	**187**	**0.003**	**0.676**	**0.510**	**7.29**	**4.32**	**0.000**	**24**	**2**	**-48**
						0.920	0.510	6.42	4.06	0.000	18	-2	-41
						1.000	0.590	5.10	3.58	0.000	23	-9	-44

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 4.02, p = 0.001 (1.000)
Extent threshold: k = 187 voxels, p = 0.003 (0.088)
Expected voxels per cluster, <k> = 17.802
Expected number of clusters, <c> = 0.09
FWEp: 11.056, FDRp: Inf, FWEc: 272, FDRc: 187

Degrees of freedom = [1.0, 11.0]
FWHM = 10.3 9.7 10.5 mm mm mm; 6.8 6.4 7.0 {voxels}
Volume: 1256003 = 372149 voxels = 874.2 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 309.20 voxels)

Supplementary Figure 1: Pre- *versus* post-operative grey matter density reduction in T2D subjects. Paired T-test (uncorrected p<0.001. showing only FDR cluster level significant results), showing reduction of grey matter density in the temporal poles.



SPMresults: .\RM1\mri\Paired_T-test_GM
Height threshold T = 4.024701 {p<0.001 (unc.)}
Extent threshold k = 331 voxels

Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm
p	*c*	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	*T*	$(Z_{=})$	p_{uncorr}	
0.000	3	0.000	0.000	887	0.000	**0.249**	**0.333**	**8.91**	**4.72**	**0.000**	**20 -63 -56**
						0.469	0.333	7.94	4.49	0.000	17 -69 -51
						0.528	0.333	7.74	4.44	0.000	39 -56 -48
		0.000	0.000	798	0.000	**0.532**	**0.333**	**7.73**	**4.44**	**0.000**	**-23 -72 -50**
						0.633	0.333	7.42	4.35	0.000	-24 -60 -54
						0.875	0.333	6.63	4.12	0.000	-29 -53 -53
		0.004	0.002	351	0.000	**0.834**	**0.333**	**6.78**	**4.17**	**0.000**	**18 -69 -24**
						0.997	0.474	5.60	3.78	0.000	23 -62 -24
						1.000	0.648	4.89	3.49	0.000	32 -57 -29

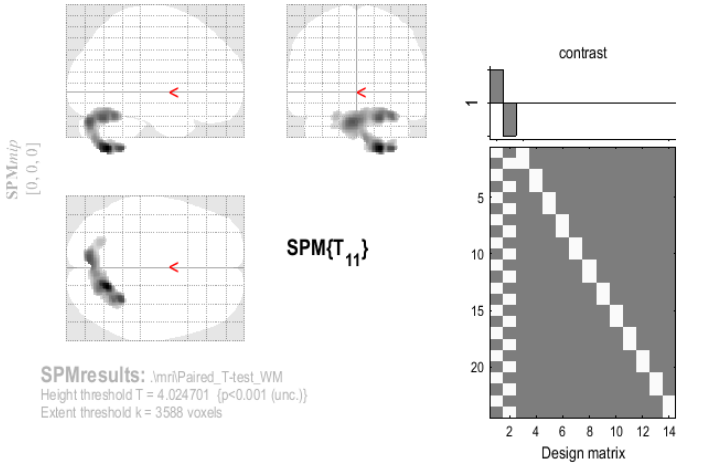
table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 4.02, p = 0.001 (1.000)
Extent threshold: k = 331 voxels, p = 0.000 (0.006)
Expected voxels per cluster, <k> = 17.802
Expected number of clusters, <c> = 0.01
FWEp: 11.056, FDRp: Inf, FWEc: 311, FDRc: 311

Degrees of freedom = [1.0, 11.0]
FWHM = 10.3 9.7 10.5 mm mm mm; 6.8 6.4 7.0 {voxels}
Volume: 1256003 = 372149 voxels = 874.2 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 309.20 voxels)

Supplementary Figure 2: Pre- *versus* post-operative increased grey matter density in T2D subjects. Paired T-test (uncorrected p<0.001. showing only FDR cluster level significant results), showing grey matter density increases in cerebellar areas.

1.1.2. Whole Brain White Matter Analysis



Statistics: ***p-values adjusted for search volume***

cluster-level				peak-level					mm mm mm
$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_{\equiv})$	p_{uncorr}	
0.011	0.044	3588	0.007	0.038	0.170	7.78	4.45	0.000	20 -63 -54
				0.118	0.211	6.48	4.08	0.000	32 -50 -54
				0.135	0.211	6.32	4.03	0.000	-5 -80 -29

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 4.02, p = 0.001 (0.785)
Extent threshold: k = 3588 voxels, p = 0.007 (0.011)
Expected voxels per cluster, <k> = 436.764
Expected number of clusters, <c> = 0.01
FWEp: 7.455, FDRp: Inf, FWEc: 2623, FDRc: 3588

Degrees of freedom = [1.0, 11.0]
FWHM = 28.6 30.1 29.7 mm mm mm; 19.0 20.1 19.8 {voxels}
Volume: 1507511 = 446670 voxels = 55.1 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 7585.94 voxels)

Supplementary Figure 3: Pre- *versus* post-operative white matter density reduction in T2D subjects. Paired T-test (uncorrected p<0.001. showing only FDR cluster level significant results) showing reduced white matter density in cerebellar areas.

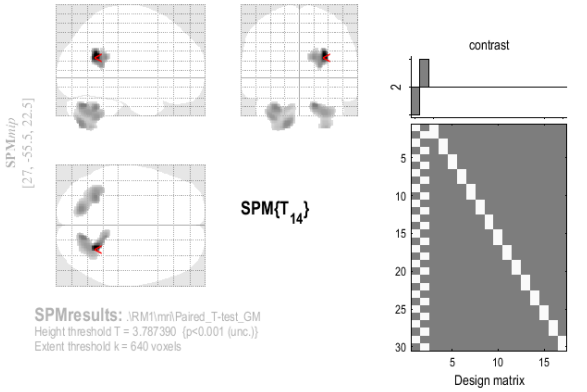
No results observed in the opposite direction (There was no white matter density increase in the post-operative period).

1.1.3. Hypothalamus restricted GM Analysis

There were no differences between pre- and post-operative MRIs.

1.2. Non-diabetes obesity Group (ND) pre *versus* post Roux-n-Y gastric bypass surgery

1.2.1. Whole Brain Grey Matter Analysis



Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_{=})$	p_{uncorr}	
0.000	3	0.041	0.026	640	0.005	0.011	0.036	9.44	5.21	0.000	27 -56 23
						0.474	0.341	5.82	4.08	0.000	15 -45 21
						0.522	0.341	5.71	4.04	0.000	21 -50 14
		0.001	0.001	1434	0.000	0.312	0.341	6.26	4.25	0.000	17 -71 -33
						0.641	0.343	5.45	3.93	0.000	27 -63 -41
						0.869	0.598	4.92	3.69	0.000	29 -63 -56
		0.000	0.000	2209	0.000	0.416	0.341	5.96	4.14	0.000	-30 -56 -35
						0.466	0.341	5.84	4.09	0.000	-17 -74 -53
						0.599	0.343	5.54	3.97	0.000	-33 -56 -45

table shows 3 local maxima more than 8.0mm apart

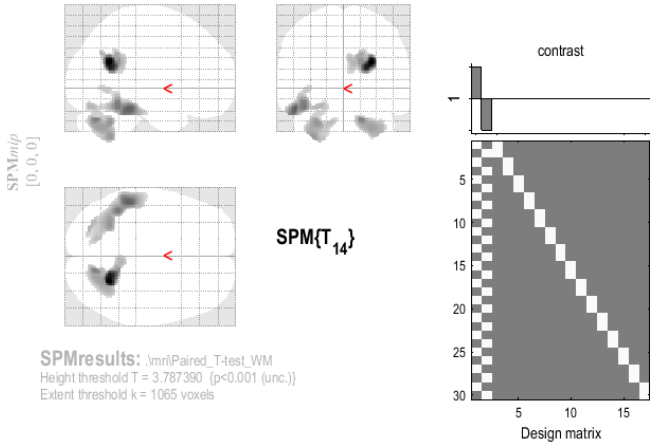
Height threshold: T = 3.79, p = 0.001 (1.000)
Extent threshold: k = 640 voxels, p = 0.005 (0.041)
Expected voxels per cluster, <k> = 68.994
Expected number of clusters, <c> = 0.04
FWEp: 7.960, FDRp: 9.437, FWEc: 640, FDRc: 640

Degrees of freedom = [1.0, 14.0]
FWHM = 14.8 16.2 14.3 mm mm mm; 9.9 10.8 9.5 (voxels)
Volume: 1622471 = 4807.32 voxels = 441.4 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 1014.34 voxels)

Supplementary Figure 4: Pre- *versus* post-operative increased grey matter density in the non-diabetes obese group (ND). Paired T-test (uncorrected p<0.001. showing only FDR cluster level significant results) showing increased grey matter density in the right precuneus and bilateral cerebellum.

There was no grey matter density reduction comparing pre- and post-operative MRIs

1.2.2. Whole Brain White Matter Analysis



Statistics: ***p-values adjusted for search volume***

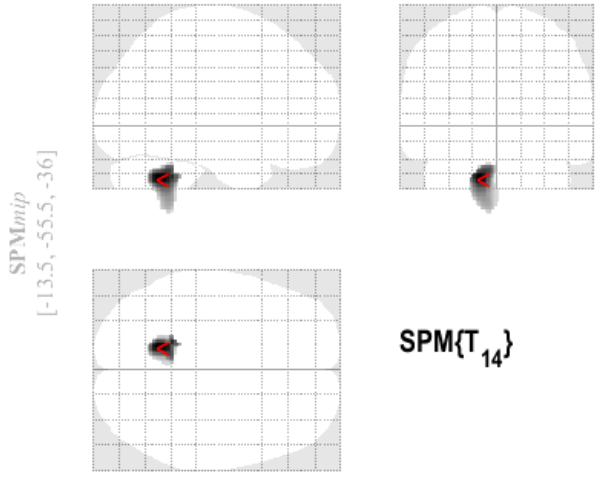
set-level		cluster-level				peak-level					mm mm mm		
p	c	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	T	$(Z_{\equiv})$	p_{uncorr}			
0.000	**3**	**0.003**	**0.006**	**1206**	**0.001**	**0.004**	**0.040**	**9.96**	**5.33**	**0.000**	**27**	**-57**	**24**
						0.336	0.396	5.87	4.10	0.000	15	-48	24
						0.731	0.531	4.96	3.71	0.000	8	-45	23
		0.000	**0.000**	**3071**	**0.000**	**0.074**	**0.234**	**7.25**	**4.60**	**0.000**	**-51**	**-38**	**-21**
						0.169	0.336	6.51	4.35	0.000	-42	-48	-20
						0.378	0.396	5.75	4.06	0.000	-29	-56	-35
		0.006	**0.008**	**1065**	**0.001**	**0.201**	**0.338**	**6.36**	**4.29**	**0.000**	**17**	**-71**	**-33**
						0.497	0.396	5.46	3.93	0.000	27	-65	-41

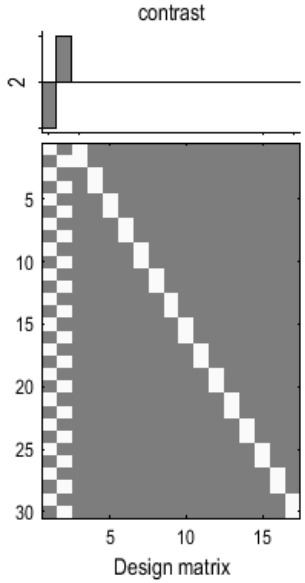
table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 3.79, p = 0.001 (0.997)
Extent threshold: k = 1065 voxels, p = 0.001 (0.006)
Expected voxels per cluster, <k> = 77.786
Expected number of clusters, <c> = 0.01
FWEp: 7.608, FDRp: 9.133, FWEc: 1065, FDRc: 1065

Degrees of freedom = [1.0, 14.0]
FWHM = 15.8 16.9 14.4 mm mm mm; 10.5 11.3 9.6 {voxels}
Volume: 1221065 = 361797 voxels = 293.1 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 1143.61 voxels)

Supplementary Figure 5: Pre- *versus* post-operative white matter density reduction in ND group. Paired T-test (uncorrected p<0.001. showing only FDR cluster level significant results) showing reduced white matter density in the right precuneus, inferior temporal gyrus and right cerebellum.





SPMresults: .\mri\Paired_T-test_WM
Height threshold T = 3.787390 {p<0.001 (unc.)}
Extent threshold k = 1065 voxels

Statistics: ***p-values adjusted for search volume***

cluster-level				peak-level					mm mm mm
$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	T	$(Z_{\equiv})$	p_{uncorr}	
0.002	0.012	1292	0.000	0.375	0.396	5.76	4.06	0.000	-14 -56 -36
				0.541	0.408	5.36	3.89	0.000	-17 -47 -36

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 3.79, p = 0.001 (0.997)
Extent threshold: k = 1065 voxels, p = 0.001 (0.006)
Expected voxels per cluster, <k> = 77.786
Expected number of clusters, <c> = 0.01
FWEp: 7.608, FDRp: Inf, FWEc: 1040, FDRc: 1040

Degrees of freedom = [1.0, 14.0]
FWHM = 15.8 16.9 14.4 mm mm mm; 10.5 11.3 9.6 {voxels}
Volume: 1221065 = 361797 voxels = 293.1 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 1143.61 voxels)

Supplementary Figure 6: Pre- *versus* post-operative white matter density increase in ND group. Paired T-test (uncorrected p<0.001. showing only FDR cluster level significant results) showing increase white matter density in the left cerebellum.

1.2.3. VBM ROI analyses including only the hypothalamic area, comparing GM density between pre and post Roux-n-Y gastric bypass surgery

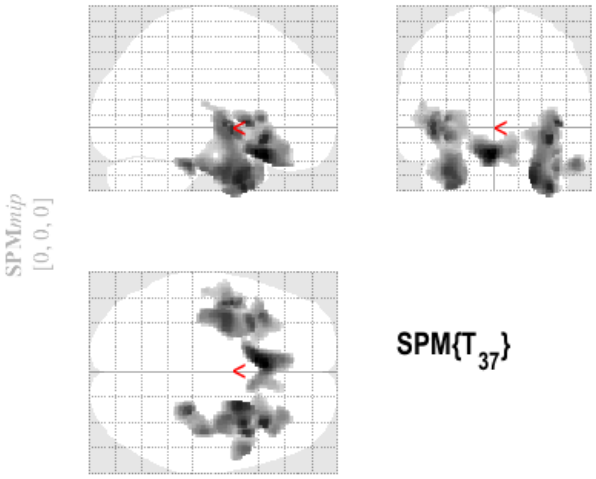
There were no differences between pre- and post-operative MRIs.

2. Transversal Analysis of pre-operative MRIs (pairwise comparisons between all groups)

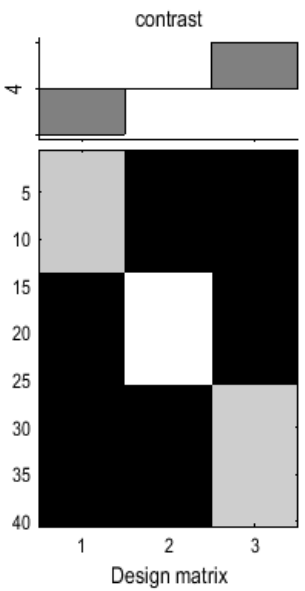
2.1. Whole Brain Grey Matter Analysis

There were no differences in these analyses.

2.2. Whole Brain White Matter Analysis



SPM{T_{37}}



SPMresults: .\mri\smwp2\ANOVA_WholeBrain
Height threshold T = 3.325631 {p<0.001 (unc.)}
Extent threshold k = 5964 voxels

Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm		
p	*c*	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	*T*	($Z_{\equiv}$)	p_{uncorr}			
0.000	**2**	**0.000**	**0.000**	**5969**	**0.000**	**0.037**	**0.438**	**5.21**	**4.48**	**0.000**	**-3**	**20**	**-20**
						0.118	0.438	4.73	4.15	0.000	-44	-3	-5
						0.138	0.438	4.66	4.11	0.000	-33	-8	-32
		0.000	**0.000**	**5964**	**0.000**	**0.075**	**0.438**	**4.92**	**4.29**	**0.000**	**24**	**2**	**-38**
						0.083	0.438	4.88	4.26	0.000	36	5	-42
						0.083	0.438	4.87	4.26	0.000	36	18	-11

table shows 3 local maxima more than 8.0mm apart

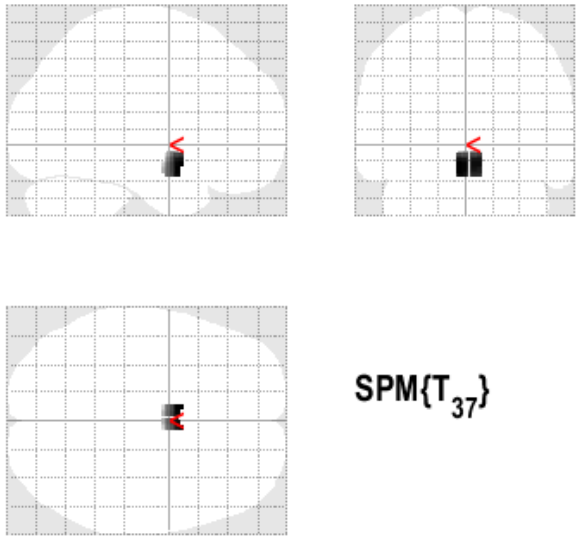
Height threshold: T = 3.33, p = 0.001 (0.949)
Extent threshold: k = 5964 voxels, p = 0.000 (0.000)
Expected voxels per cluster, <k> = 200.407
Expected number of clusters, <c> = 0.00
FWEp: 5.084, FDRp: Inf, FWEc: 5964, FDRc: 5964

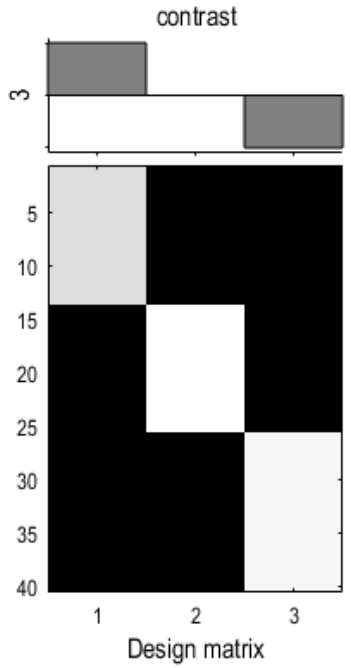
Degrees of freedom = [1.0, 37.0]
FWHM = 19.7 18.8 18.8 mm mm mm; 13.2 12.5 12.5 {voxels}
Volume: 1438094 = 426102 voxels = 191.5 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 2065.02 voxels)

Supplementary Figure 7: White matter density increases in ND group compared to controls. ANOVA test (uncorrected $p<0.001$. showing only FDR cluster level significant results).

There was no reduction of white matter densities comparing controls and T2D.

2.3. ROI analyses of Hypothalamus (GM Analysis)





SPMresults: .\mri\smwp1\ANOVA_BilHippotha
Height threshold T = 3.325631 {p<0.001 (unc.)}
Extent threshold k = 0 voxels

Statistics: ***p-values adjusted for search volume***

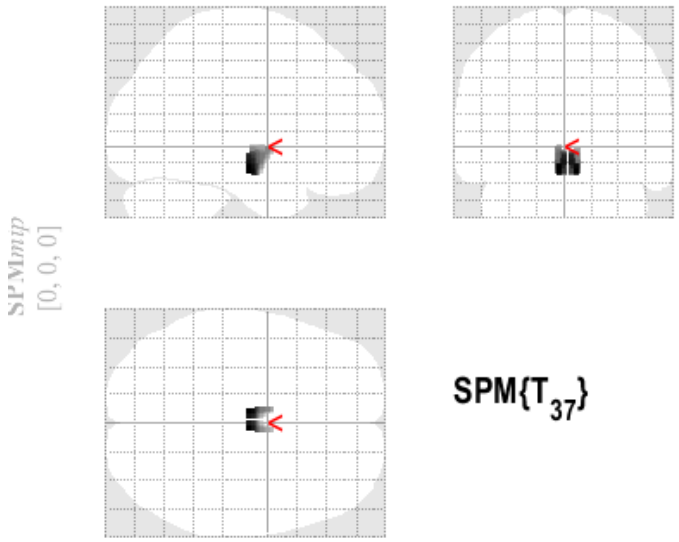
set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_{\equiv})$	p_{uncorr}	
0.000	2	0.010	0.378	149	0.378	0.000	0.000	21.01	Inf	0.000	-6 3 -18
		0.009	0.378	157	0.366	0.000	0.000	19.73	Inf	0.000	6 5 -14

table shows 3 local maxima more than 8.0mm apart

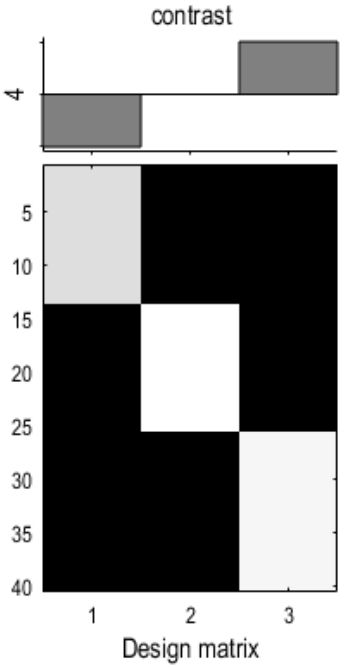
Height threshold: T = 3.33, p = 0.001 (0.025)
Extent threshold: k = 0 voxels
Expected voxels per cluster, <k> = 206.827
Expected number of clusters, <c> = 0.03
FWEp: 3.013, FDRp: 20.818, FWEc: 149, FDRc: Inf

Degrees of freedom = [1.0, 37.0]
FWHM = 21.2 15.9 21.4 mm mm mm; 14.1 10.6 14.3 {voxels}
Volume: 2464 = 730 voxels = 0.2 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 2131.17 voxels)

Supplementary Figure 8: Grey matter density reduction in the ND group compared to controls. ANOVA test (uncorrected $p<0.001$). We found areas of decrease grey matter in the dorsal-superior hypothalamic areas.



$SPM\{T_{37}\}$



SPMresults: \mri\smwp1\ANOVA_BilHippotha
Height threshold T = 3.325631 {p<0.001 (unc.)}
Extent threshold k = 0 voxels

Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm
p	*c*	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	*T*	$(Z_{=})$	p_{uncorr}	
0.000	2	0.009	0.366	173	0.342	0.000	0.000	37.05	Inf	0.000	-5 -14 -17
						0.000	0.000	20.69	Inf	0.000	-5 -8 -8
		0.009	0.366	157	0.366	0.000	0.000	35.97	Inf	0.000	5 -14 -17
						0.000	0.000	14.22	Inf	0.000	6 -5 -8
						0.000	0.000	10.80	7.21	0.000	5 -12 -3

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 3.33, p = 0.001 (0.025)
Extent threshold: k = 0 voxels
Expected voxels per cluster, <k> = 206.827
Expected number of clusters, <c> = 0.03
FWEp: 3.013, FDRp: 10.796, FWEc: 157, FDRc: Inf

Degrees of freedom = [1.0, 37.0]
FWHM = 21.2 15.9 21.4 mm mm mm; 14.1 10.6 14.3 {voxels}
Volume: 2464 = 730 voxels = 0.2 resels
Voxel size: 1.5 1.5 1.5 mm mm mm; (resel = 2131.17 voxels)

Supplementary Figure 9: Grey matter density increase in the ND group compared to controls. ANOVA test (uncorrected $p<0.001$). We found areas of increased grey matter in the ventral hypothalamus.

There were no differences in the comparisons between controls and T2D nor between ND and T2D groups.