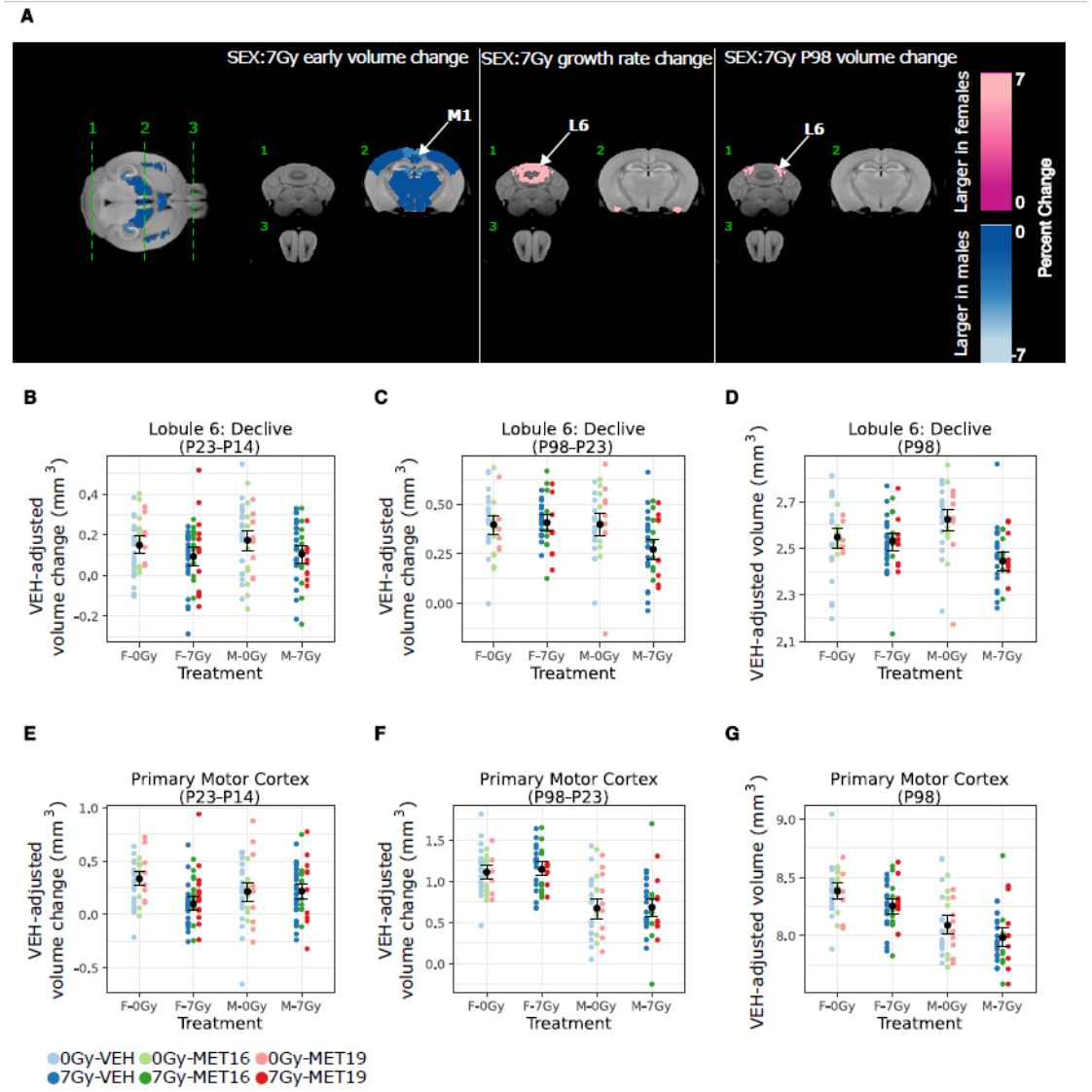
Supplementary Methods

The linear mixed effect model for fitting volume outcomes may be written as:

$$
\begin{aligned}
V_{ID,t_j,s} = & \beta_{t_j}^{P14} + \beta_{t_j}^{P23} + \beta_{t_j}^{P42} + \beta_{t_j}^{P98} + \beta_{sex} s + \\
& \beta_{7Gy}^{P} + \beta_{Met}^{P} + \beta_{7Gy,Met}^{P} + \\
& \beta_{Age:7Gy}^{P}(t_j - 23) + \beta_{Age:Met}^{P}(t_j - 23) + \beta_{Age:7Gy:Met}^{P}(t_j - 23) + \\
& \beta_{sex:7Gy}^{P} s + \beta_{sex:Met}^{P} s + \beta_{sex:7Gy:Met}^{P} s + \\
& \beta_{Age:sex:7Gy}^{P} s(t_j - 23) + \beta_{Age:sex:Met}^{P} s(t_j - 23) + \beta_{Age:sex:7Gy:Met}^{P} s(t_j - 23) + \\
& \gamma_{ID}
\end{aligned}
$$

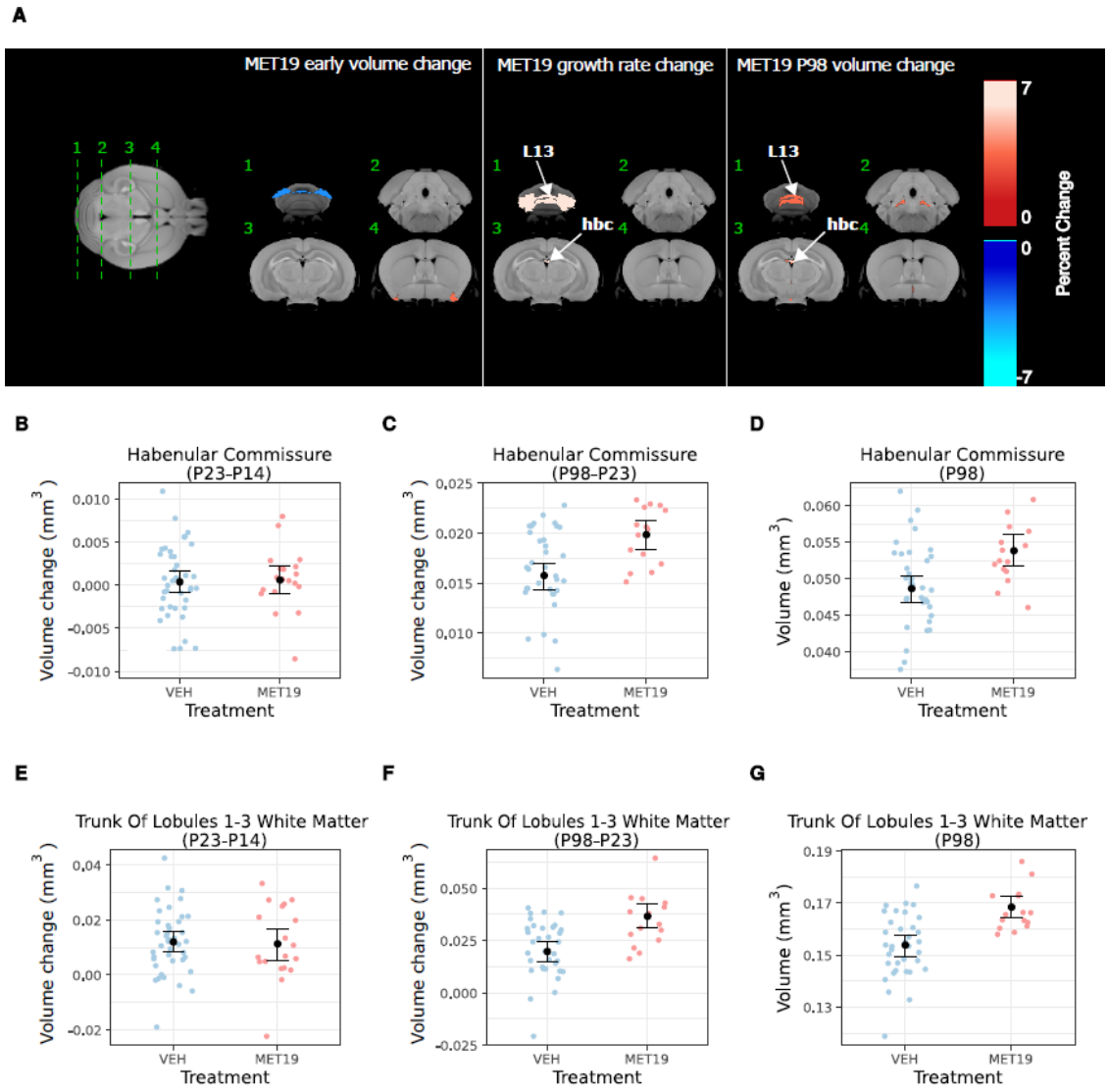
where ID indicates mouse identification, t_j represents time point, and s represents sex (+0.5 for females, -0.5 for males). The β terms all represent fixed effects. Coefficients with superscript $P14$, $P23$, $P42$ and $P98$ apply only at the indicated timepoint. Those with superscript P apply after commencement of treatment (i.e., at P23, P42 and P98). Coefficients with subscript $7Gy$ apply in mice receiving 7Gy only. Similarly, Met indicates coefficients applying only to mice who received metformin, with a distinct coefficient used for the MET16 and MET19 conditions. Terms with subscript Age represent linear growth with age, with origin centered on t_o (adjusted to P23 or P98 so that the "intercept" coefficients represent differences at the respective time point). Terms with subscript sex represent differences between males and females (with positive larger in females and negative larger in males). The γ_{ID} term represents a random effect for each mouse. The ":" indicates interaction coefficients, and were the basis for generation of Figures 4 and 5 in the results.

Supplementary Figures



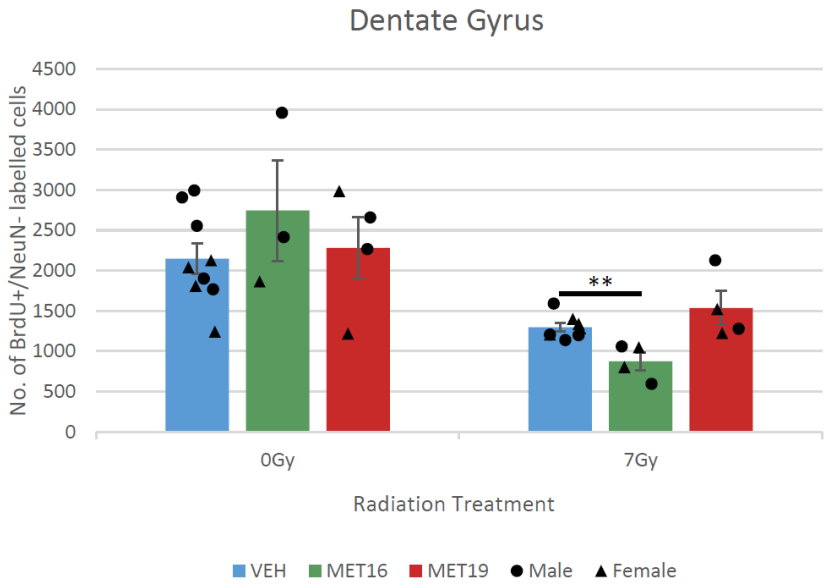
Supplementary Figure S.1 Sex-dependent differences in brain development after irradiation. Comparison of neuroanatomical outcomes in males and females after irradiation were evaluated based on the interaction of sex and radiation (SEX:7Gy). In (A), a colour map shows all structures that had a significant volume difference in radiation-induced volume change between males and females (FDR<10%). In (B-G), individual plots compare structure volumes between sexes, evaluating early (P23-P14) and long-term (P98-P23) volume differences, and the final P98 volumes. To better visualize the contribution of sex on radiation across all groups in

these plots, volumes were plotted after adjustments to subtract the fitted metformin treatment effects. At the early time point (A, E), a larger volume was observed in irradiated males relative to irradiated females in several regions including the primary motor cortex, shown in (E,F,G). On the other hand, an increased long-term growth was observed in females in some structures, predominantly cerebellar regions including lobule 6, which resulted in a significant increase in volume at P98 compared to males. Black points and error bars represent the mean volume and bootstrapped 95% confidence intervals. Small coloured dots represent individual structure volumes after subtraction of metformin treatment effects. Abbreviation: L6 = Lobule 6: Declive, M1 = Primary Motor Cortex, VEH = treated with vehicle, MET16 = treated with metformin at P16, MET19 = treated with metformin at P19, 0Gy = unirradiated, 7Gy = irradiated with a 7 Gy dose.

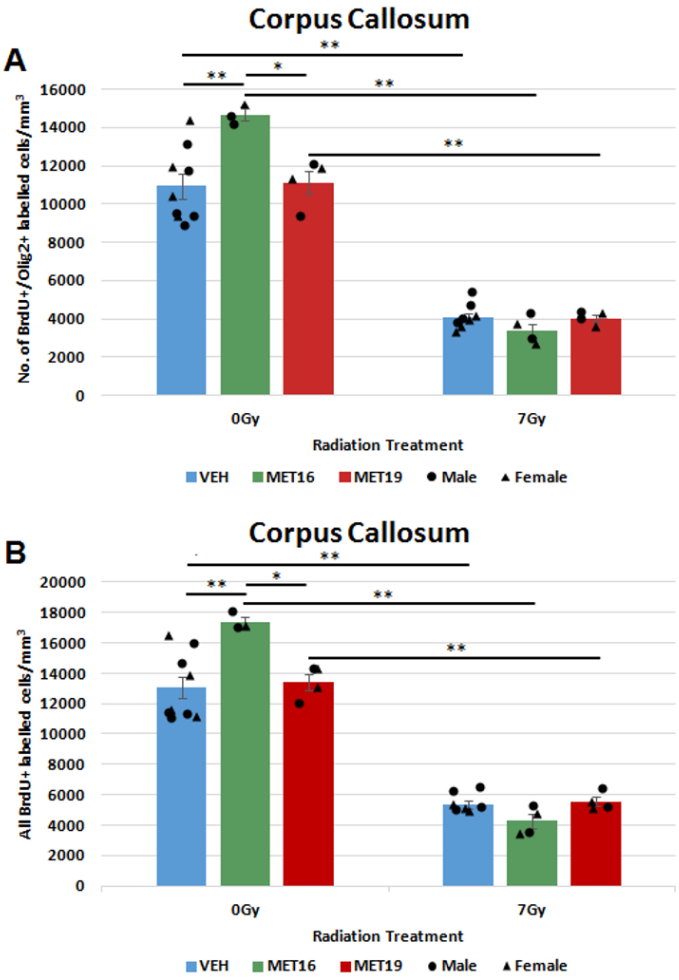


Supplementary Figure S.2 The impact of delayed metformin treatment on brain development. In (A), a colour map overlay shows all structures that had a significant volume difference in MET19-treated mice compared to VEH-treated mice (FDR<10%). Slice position matches Figure 3. There was a subtle effect of MET19 on the brain in 0-Gy mice at P23 (early). Enhanced growth rate was observed in regions of the cerebellum, and habenular commissure, leading to increased volumes by P98. Representative plots of the habenular commissure (B,C,D) and trunk of lobules 1-3 white matter (cerebellum) (E,F,G) show no significant early volume change as visualized by the P23-P14 volume difference in (B,E). Increased growth rate and long-term

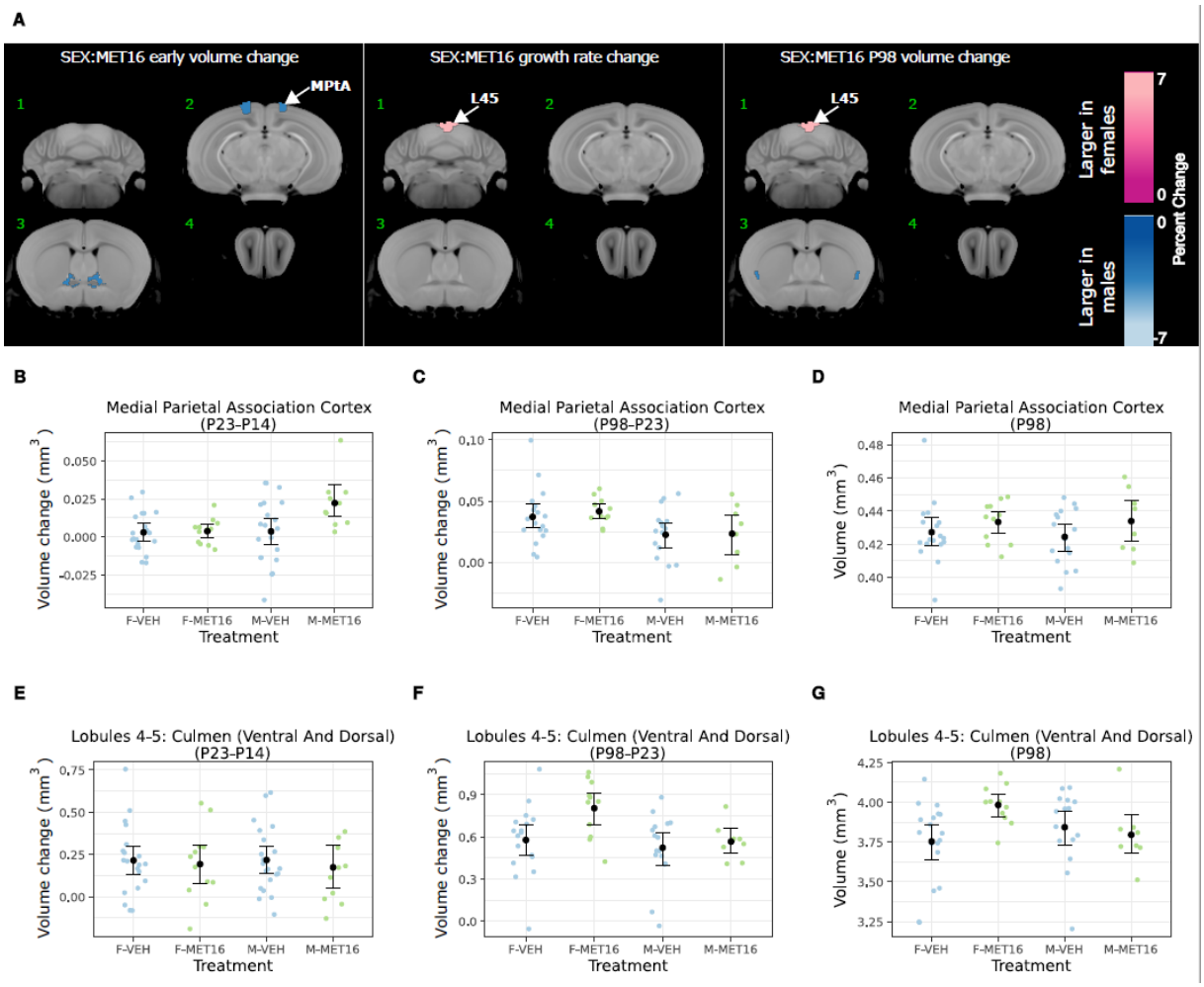
outcome is significantly increased in both structures, as shown by the P98-P23 volume differences (C,F). This results in increased volume by the final P98 time point (D,G). Treatment effects within the fitted model are represented as the average of males and females. Black points and error bars represent the mean volume and bootstrapped 95% confidence intervals. Smaller coloured dots represent individual brain volumes. Abbreviation: hbc = habenular commissure, trunk of lobules 1-3 white matter = L13, VEH = treated with vehicle, MET19 = treated with metformin at P19, for 14 days.



Supplementary Figure S.3 BrdU-positive, NeuN-negative cell counts within the dentate gyrus of the hippocampus for unirradiated (VEH-0Gy, n=9; MET16-0Gy, n=3, MET19-0Gy, n=4) or irradiated (VEH-7Gy, n=8; MET16-7Gy, n=4, MET19-7Gy, n=4) mice. A significant decrease in BrdU-positive, NeuN-negative cells is observed with MET16 treatment in irradiated mice compared to VEH controls (** $p<0.01$, Student's t test). Coloured bars represent means, whereas small black circles and triangles represent individual male or female mice, respectively. Error bars are SEM. Abbreviation: VEH = treated with vehicle, MET16 = treated with metformin at P16, MET19 = treated with metformin at P19, 0Gy = unirradiated, 7Gy = irradiated with a 7 Gy dose.

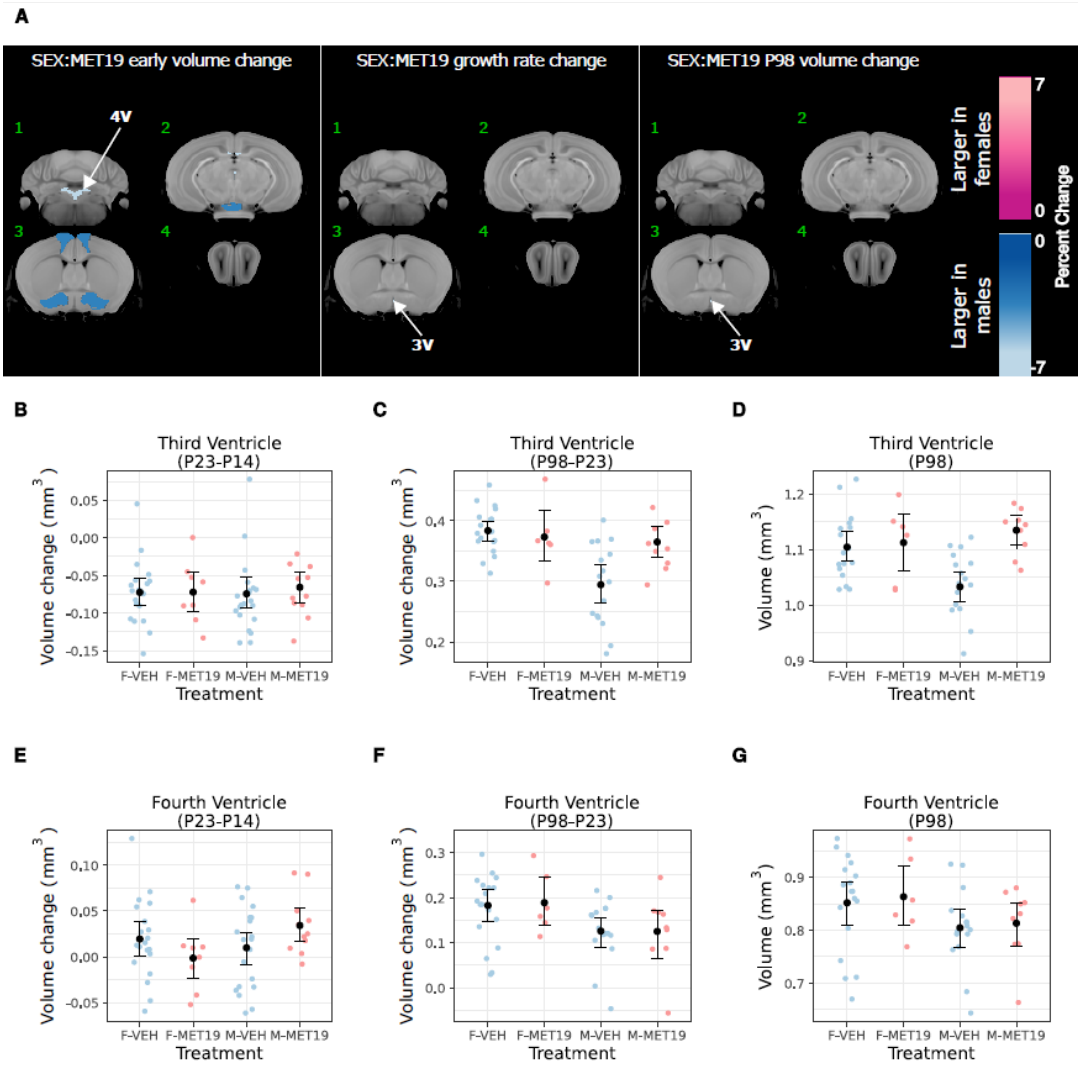


Supplementary Figure S.4 Within the corpus callosum (A, B), there is loss of proliferative (BrdU-positive) cells and new-born/proliferative oligodendrocytes (BrdU/Olig2-positive) at 42 days of age after irradiation. An increase in BrdU-positive and BrdU/Olig2-positive cells is observed with MET16 mice compared with VEH control and MET19 mice. A significant decrease in BrdU-positive and BrdU/Olig2-positive cells is seen in irradiated mice in all 3 groups compared to non-irradiated controls. Coloured bars represent means and black circles and triangles represent individual male and female mice respectively. Error bars are SEM. Abbreviation: VEH = treated with vehicle, MET16 = treated with metformin at P16, MET19 = treated with metformin at P19. (*p <0.01, **p <0.001, two-way ANOVA with Bonferroni post-hoc analysis).



Supplementary Figure S.5 The impact of sex differences in metformin treatment on brain development. In (A), a colour map overlay shows all structures that had a significant volume difference in MET16-treated mice compared to VEH-treated mice (FDR<10%). Slice position matches Figure 3. Comparison of neuroanatomical outcomes in males and females after metformin treatment were evaluated based on the interaction of sex and metformin (SEX:MET16). In (A), a colour map shows all structures that had a significant volume difference in metformin-induced volume change between males and females (FDR<10%). In (B-G), individual plots compare structure volumes between sexes, evaluating early (P23), growth rate (P98-P23), and P98 differences. Presented are representative plots of the medial parietal association cortex (MPtA) (B,C,D) and lobules 4-5:culmen (L45) (E,F,G). At the early time point, a

relatively larger volume was observed in metformin-treated males in the MPtA (B). An increased growth rate is observed in L45 in females (F), resulting in an increased volume by the final P98 time point (G). Treatment effects within the fitted model are represented as the average of males and females. Black points and error bars represent the mean volume and bootstrapped 95% confidence intervals. Smaller coloured dots represent individual brain volumes. Abbreviation: MPtA = medial parietal association cortex, L45 = lobules 4-5:culmen of the cerebellum, VEH = treated with vehicle, MET16 = treated with metformin at P16, for 14 days.



Supplementary Figure S.6 The impact of sex differences in delayed metformin treatment on brain development. In (A), a colour map overlay shows all structures that had a significant volume difference in MET19-treated mice compared to VEH-treated mice (FDR<10%). Slice position matches Figure 3. Comparison of neuroanatomical outcomes in males and females after metformin treatment were evaluated based on the interaction of sex and metformin (SEX:MET19). In (A), a colour map shows all structures that had a significant volume difference in metformin-induced volume change between males and females (FDR<10%). In (B-G), individual plots compare structure volumes between sexes, evaluating early (P23), growth rate

(P98-P23), and P98 differences. Representative plots of the third ventricle (B,C,D) and fourth ventricle (E,F,G). At the early time point, a relatively larger volume was observed in metformin-treated males in the fourth ventricle (E). An increased growth rate is observed in the third ventricle in males (C), resulting in an increased volume by the final P98 time point (D). Treatment effects within the fitted model are represented as the average of males and females. Black points and error bars represent the mean volume and bootstrapped 95% confidence intervals. Smaller coloured dots represent individual brain volumes. Abbreviation: 3V = third ventricle, 4V = fourth ventricle, VEH = treated with vehicle, MET19 = treated with metformin at P19, for 14 days.

Supplementary Tables

Structure	β_{7Gy}	p_{7Gy}	q_{7Gy}	$\beta_{7Gy:Growth}$	$p_{7Gy:Growth}$	$q_{7Gy:Growth}$	$\beta_{SEX:7Gy}$	$p_{SEX:7Gy}$	$q_{SEX:7Gy}$	$\beta_{SEX:7Gy:Growth}$	$p_{SEX:7Gy:Growth}$	$q_{SEX:7Gy:Growth}$
Amygdala	−0.15	0.0046	0.023	−0.0015	0.11	0.28	−0.12	0.11	0.26	0.0033	0.056	0.17
Anterior Commissure: Pars Anterior	−0.046	2.7e-09	2e-08	−1e-04	0.46	0.65	0.0016	0.88	0.95	−0.00035	0.18	0.36
Anterior Commissure: Pars Posterior	−0.015	5.1e-09	3.8e-08	3.6e-05	0.44	0.63	−5e-04	0.89	0.95	−6.1e-05	0.47	0.65
Basal Forebrain	−0.091	0.0015	0.0085	0.00022	0.68	0.82	−0.068	0.1	0.25	0.00083	0.38	0.57
Bed Nucleus Of Stria Terminalis	−0.043	1.5e-07	1.1e-06	7.9e-05	0.6	0.76	−0.026	0.028	0.1	5.8e-05	0.83	0.91
Cerebellar Peduncle: Inferior	−0.018	0.0035	0.018	0.00021	0.087	0.23	−0.0083	0.35	0.56	0.00046	0.032	0.12
Cerebellar Peduncle: Middle	−0.055	7.2e-08	5.2e-07	9.2e-06	0.96	0.98	−0.015	0.32	0.52	0.00041	0.23	0.43
Cerebellar Peduncle: Superior	−0.038	1.4e-08	1e-07	−3.8e-05	0.76	0.87	−0.011	0.25	0.46	4e-04	0.072	0.2
Cerebral Aqueduct	−0.033	4.2e-09	3.2e-08	0.00011	0.34	0.54	−0.009	0.27	0.48	−2e-04	0.3	0.51
Cerebral Peduncle	−0.13	1.7e-21	1.6e-20	−0.00011	0.64	0.79	−0.024	0.2	0.39	1e-04	0.81	0.9
Colliculus: Inferior	−0.15	1.7e-06	1.2e-05	−0.00039	0.54	0.71	−0.06	0.2	0.39	0.0019	0.093	0.24
Colliculus: Superior	−0.36	5.1e-06	3.5e-05	0.00033	0.83	0.91	−0.2	0.083	0.22	0.0036	0.19	0.38
Corpus Callosum	−0.43	1.7e-10	1.3e-09	−0.00089	0.45	0.63	−0.12	0.22	0.41	0.00076	0.72	0.85
Corticospinal Tract/Pyramids	−0.043	4.7e-06	3.2e-05	1.1e-05	0.95	0.98	−0.024	0.08	0.22	5e-04	0.11	0.27
Cuneate Nucleus	−0.0027	0.11	0.27	7.2e-07	0.98	0.99	−0.0027	0.29	0.5	0.00013	0.041	0.14
Dentate Gyrus Of Hippocampus	−0.12	6.2e-11	4.9e-10	−0.00058	0.09	0.23	−0.066	0.016	0.067	0.00095	0.13	0.3
Facial Nerve (Cranial Nerve 7)	−0.0051	0.0028	0.015	9.8e-06	0.78	0.88	−0.0027	0.28	0.49	9.3e-05	0.13	0.3
Fasciculus Retroflexus	−0.0072	2.1e-06	1.5e-05	−2.9e-05	0.3	0.51	−0.0042	0.053	0.17	2.7e-05	0.58	0.75
Fimbria	−0.2	4.3e-18	3.7e-17	−0.00058	0.16	0.35	−0.046	0.16	0.35	0.00036	0.63	0.79
Fornix	−0.025	8.4e-13	6.8e-12	−6.2e-05	0.31	0.51	−0.012	0.011	0.048	1.2e-05	0.92	0.96
Fourth Ventricle	−0.026	0.0018	0.0099	0.00031	0.068	0.19	−0.02	0.11	0.26	4e-04	0.18	0.37
Fundus Of Striatum	−0.0025	0.0016	0.0088	2.1e-06	0.89	0.95	0.00048	0.67	0.81	−1.7e-05	0.52	0.7
Globus Pallidus	−0.17	9.7e-22	8.9e-21	0.00039	0.2	0.4	−0.025	0.31	0.52	0.00041	0.45	0.64
Habenular Commissure	−0.0037	1.3e-06	9e-06	3.6e-06	0.8	0.9	−0.00031	0.78	0.89	−1e-05	0.69	0.83
Hippocampus	−0.53	3.4e-08	2.5e-07	−0.0034	0.043	0.14	−0.24	0.082	0.22	0.0036	0.24	0.44
Hypothalamus	−0.3	1.7e-08	1.2e-07	−0.00097	0.3	0.51	−0.22	0.0049	0.024	0.00033	0.85	0.92
Inferior Olivary Complex	−0.0056	5.3e-06	3.6e-05	4.4e-05	0.069	0.2	−0.001	0.56	0.74	7.3e-05	0.088	0.23
Internal Capsule	−0.21	1.6e-27	1.5e-26	0.00035	0.28	0.49	−0.02	0.44	0.63	0.00022	0.71	0.84
Interpedunclar Nucleus	−0.007	0.00091	0.0054	−3.6e-05	0.37	0.57	−0.0011	0.72	0.85	4.4e-05	0.54	0.72
Lateral Olfactory Tract	−0.025	1.1e-09	8.8e-09	−0.00025	0.00077	0.0046	−0.003	0.62	0.78	5.5e-05	0.69	0.82
Lateral Septum	−0.076	3.1e-06	2.2e-05	−0.00045	0.11	0.28	−0.054	0.021	0.082	0.00047	0.36	0.56
Lateral Ventricle	−0.18	1.7e-07	1.3e-06	−0.0018	0.0043	0.022	−0.064	0.18	0.38	0.0016	0.17	0.35
Mammillary Bodies	−0.011	0.00075	0.0045	−0.00024	0.00014	0.00088	−0.0033	0.49	0.68	−0.00017	0.12	0.29
Mammilothalamic Tract	−0.0042	0.0031	0.017	5.2e-07	0.98	0.99	−0.0042	0.04	0.13	−2.5e-05	0.59	0.76
Medial Lemniscus/Medial Longitudinal Fasciculus	−0.11	2.4e-10	1.9e-09	−0.00016	0.61	0.77	−0.035	0.15	0.33	7e-04	0.2	0.4
Medial Septum	−0.02	0.0018	0.01	7e-05	0.54	0.71	−0.012	0.2	0.4	4.7e-05	0.82	0.91
Medulla	−0.58	0.0011	0.0065	0.00031	0.93	0.97	−0.34	0.19	0.39	0.012	0.045	0.15
Midbrain	−0.56	5.4e-14	4.4e-13	−0.0021	0.1	0.26	−0.19	0.064	0.19	0.0019	0.41	0.61
Nucleus Accumbens	−0.073	0.0035	0.018	−3.4e-05	0.94	0.98	−0.0053	0.88	0.95	−0.00014	0.87	0.94
Olfactory Bulbs	−1	5.8e-13	4.7e-12	−0.016	1.4e-09	1.1e-08	−0.021	0.92	0.96	0.0015	0.76	0.87
Olfactory Tubercle	−0.03	0.19	0.38	−0.00028	0.52	0.7	0.0051	0.88	0.94	9.3e-05	0.9	0.96
Optic Tract	−0.085	2.4e-22	2.2e-21	1e-04	0.51	0.69	−0.023	0.06	0.18	0.00032	0.25	0.45
Periaqueductal Grey	−0.15	5.1e-08	3.7e-07	9.9e-06	0.99	0.99	−0.072	0.08	0.22	0.00028	0.77	0.88
Pons	−0.56	1.8e-06	1.3e-05	0.0017	0.44	0.63	−0.31	0.072	0.2	0.0092	0.022	0.084
Pontine Nucleus	−0.026	1.1e-05	7.3e-05	3e-05	0.79	0.89	−0.016	0.058	0.18	0.00041	0.041	0.14
Posterior Commissure	−0.0054	2e-05	0.00013	−2.4e-05	0.31	0.52	−0.0038	0.038	0.13	2.5e-05	0.56	0.73
Pre-Para Subiculum	−0.025	0.12	0.28	−4e-04	0.18	0.37	−0.036	0.12	0.29	0.00058	0.28	0.48
Stratum Granulosum Of Hippocampus	−0.036	4.1e-12	3.3e-11	−8.6e-05	0.36	0.56	−0.018	0.016	0.065	0.00028	0.1	0.25
Stria Medullaris	−0.029	1.6e-07	1.2e-06	5.7e-05	0.58	0.75	−0.011	0.18	0.37	5.1e-05	0.78	0.89
Stria Terminalis	−0.068	5.5e-31	5.3e-30	0.00012	0.23	0.43	−0.011	0.18	0.37	−2.8e-05	0.88	0.94
Striatum	−0.63	6.4e-08	4.7e-07	0.00027	0.9	0.95	−0.21	0.2	0.4	0.0023	0.53	0.71
Subependymale Zone / Rhinocele	−0.00026	0.59	0.75	−2.7e-05	0.0038	0.019	0.0012	0.089	0.23	−3.2e-05	0.057	0.18
Superior Olivary Complex	−0.017	0.00038	0.0024	0.00012	0.2	0.4	−0.014	0.051	0.16	2e-04	0.23	0.44

Structure	β_{7Gy}	p_{7Gy}	q_{7Gy}	$\beta_{7Gy:Growth}$	$p_{7Gy:Growth}$	$q_{7Gy:Growth}$	$\beta_{SEX:7Gy}$	$p_{SEX:7Gy}$	$q_{SEX:7Gy}$	$\beta_{SEX:7Gy:Growth}$	$p_{SEX:7Gy:Growth}$	$q_{SEX:7Gy:Growth}$
Thalamus	−0.59	2.9e-08	2.2e-07	−0.00068	0.72	0.85	−0.36	0.019	0.076	0.0018	0.59	0.76
Third Ventricle	−0.035	0.00056	0.0034	−0.00033	0.091	0.24	−0.014	0.35	0.55	−3.7e-05	0.92	0.96
Ventral Tegmental Decussation	−0.0059	6.1e-07	4.4e-06	−2.6e-05	0.25	0.45	−0.001	0.55	0.72	2.3e-05	0.57	0.74
Lobules 1-2: Lingula And Central Lobule (Ventral)	−0.084	4.3e-06	3e-05	0.00032	0.35	0.55	−0.023	0.39	0.59	−0.00099	0.11	0.27
Lobule 3: Central Lobule (Dorsal)	−0.054	0.004	0.021	−0.00039	0.32	0.52	−0.018	0.53	0.71	7.6e-05	0.91	0.96
Lobules 4-5: Culmen (Ventral And Dorsal)	−0.059	0.075	0.21	−7e-04	0.3	0.5	−0.07	0.16	0.34	0.0034	0.0046	0.023
Lobule 6: Declive	−0.052	0.018	0.074	−0.00051	0.25	0.46	−0.018	0.58	0.75	0.0019	0.016	0.065
Lobule 7: Tuber (Or Folium)	−0.015	0.073	0.2	−0.00013	0.46	0.65	−0.00016	0.99	1	0.00021	0.51	0.7
Lobule 8: Pyramis	−0.015	0.33	0.53	−0.00058	0.066	0.19	−0.017	0.45	0.64	−0.00028	0.62	0.78
Lobule 9: Uvula	−0.028	0.21	0.41	−0.00076	0.11	0.26	−0.049	0.15	0.33	0.00074	0.38	0.58
Lobule 10: Nodulus	−0.012	0.39	0.59	0.00025	0.39	0.59	−0.028	0.18	0.37	0.00082	0.12	0.28
Anterior Lobule (Lobules 4-5)	−0.041	0.00016	0.001	−0.00025	0.26	0.47	−0.024	0.13	0.3	0.00022	0.57	0.74
Simple Lobule (Lobule 6)	−0.073	0.0068	0.032	−0.00016	0.77	0.88	−0.018	0.64	0.8	0.0013	0.17	0.36
Crus 1: Ansiform Lobule (Lobule 6)	−0.091	0.0014	0.0081	2.2e-05	0.97	0.99	−0.022	0.61	0.77	0.0019	0.067	0.19
Crus 2: Ansiform Lobule (Lobule 7)	−0.069	0.0077	0.036	−0.00049	0.35	0.55	−0.014	0.71	0.84	0.0018	0.05	0.16
Paramedian Lobule (Lobule 7)	−0.092	0.012	0.051	−0.00047	0.52	0.7	−0.028	0.6	0.77	0.0014	0.3	0.5
Copula: Pyramis (Lobule 8)	−0.057	0.0035	0.018	3.7e-05	0.92	0.97	−0.018	0.54	0.72	0.00089	0.21	0.4
Flocculus(Fl)	−0.013	0.071	0.2	5.9e-05	0.67	0.81	−0.01	0.34	0.54	0.00044	0.083	0.22
Paraflocculus(Pfl)	0.011	0.78	0.89	0.00014	0.85	0.93	−0.14	0.012	0.054	0.0019	0.16	0.34
Trunk Of Arbor Vita	−0.12	0.00051	0.0031	8e-04	0.24	0.44	−0.073	0.14	0.32	0.0022	0.075	0.21
Lobule 1-2 White Matter	−0.0041	0.0021	0.012	1.5e-05	0.53	0.71	−0.00082	0.67	0.81	−7e-05	0.11	0.28
Lobule 3 White Matter	−0.0078	0.0035	0.018	−3.6e-05	0.52	0.7	−0.00061	0.88	0.94	−3.7e-05	0.71	0.84
Trunk Of Lobules 1-3 White Matter	−0.0057	0.0016	0.0093	3.2e-06	0.93	0.97	−0.0023	0.4	0.6	−2.2e-05	0.73	0.85
Lobules 4-5 White Matter	−0.013	0.059	0.18	−0.00019	0.18	0.37	−0.012	0.23	0.43	0.00037	0.14	0.32
Lobules 6-7 White Matter	−0.013	0.054	0.17	−0.00021	0.13	0.3	−0.0088	0.38	0.58	4e-04	0.11	0.26
Lobule 8 White Matter	−0.00089	0.42	0.62	−4e-05	0.078	0.21	−0.0016	0.32	0.53	−2.5e-06	0.95	0.98
Trunk Of Lobules 6-8 White Matter	−0.0011	0.3	0.51	−2.7e-05	0.23	0.43	−0.0024	0.13	0.3	1.6e-05	0.69	0.83
Lobule 9 White Matter	−0.0022	0.35	0.55	−9.4e-05	0.058	0.18	−0.0055	0.12	0.29	7.5e-05	0.39	0.59
Lobule 10 White Matter	9.9e-06	0.99	1	8.7e-06	0.71	0.84	−0.0015	0.38	0.58	5.1e-05	0.22	0.42
Anterior Lobule White Matter	−0.0026	0.0049	0.024	−3e-05	0.1	0.25	−0.0025	0.07	0.2	1.6e-05	0.63	0.79
Simple Lobule White Matter	−0.0089	0.0057	0.028	−1.7e-05	0.79	0.89	−0.0022	0.65	0.8	9e-05	0.44	0.63
Crus 1 White Matter	−0.012	0.00084	0.005	2.5e-05	0.73	0.85	−0.0058	0.29	0.49	0.00023	0.082	0.22
Trunk Of Simple And Crus 1 White Matter	−0.0056	0.00058	0.0035	−8.5e-06	0.8	0.89	−0.0023	0.34	0.54	6e-05	0.31	0.51
Crus 2 White Matter	−0.0049	0.052	0.16	−4.3e-05	0.4	0.6	−0.0016	0.68	0.81	0.00015	0.11	0.26
Paramedian Lobule	−0.0034	0.021	0.082	−1.3e-05	0.67	0.81	−6e-04	0.78	0.88	6.8e-05	0.19	0.38
Trunk Of Crus 2 And Paramedian White Matter	−0.0085	0.0051	0.025	3.8e-05	0.54	0.72	−0.0014	0.75	0.86	0.00016	0.14	0.32
Copula White Matter	−0.0018	0.031	0.11	−9.3e-06	0.58	0.75	−0.0013	0.29	0.5	2.8e-05	0.35	0.56
Paraflocculus White Matter	0.00062	0.84	0.92	2.2e-05	0.71	0.84	−0.0066	0.15	0.33	0.00018	0.096	0.24
Flocculus White Matter	−0.0012	0.033	0.12	1.1e-05	0.32	0.52	−0.00038	0.65	0.8	2.6e-05	0.18	0.37
Dentate Nucleus	−0.0096	0.00061	0.0037	0.00011	0.055	0.17	−0.0054	0.2	0.4	0.00027	0.0098	0.044
Nucleus Interpositus	−0.013	0.005	0.025	0.00016	0.087	0.23	−0.0082	0.23	0.44	0.00039	0.022	0.087
Fastigial Nucleus	−0.0094	0.025	0.094	9.8e-05	0.26	0.46	−0.0098	0.12	0.28	0.00028	0.063	0.19
Cingulate Cortex: Area 24A	−0.021	0.095	0.24	−0.00055	0.016	0.067	−0.023	0.21	0.41	2.1e-05	0.96	0.98
Cingulate Cortex: Area 24A'	0.0026	0.6	0.77	−9.8e-05	0.3	0.5	−0.017	0.017	0.071	−4.8e-05	0.77	0.88
Cingulate Cortex: Area 24B	−0.009	0.38	0.58	−0.00015	0.44	0.63	−0.032	0.035	0.12	7e-05	0.84	0.92
Cingulate Cortex: Area 24B'	−0.0033	0.44	0.63	−2.2e-06	0.98	0.99	−0.017	0.0061	0.029	0.00015	0.31	0.51
Cingulate Cortex: Area 25	−0.0065	0.045	0.15	−4.8e-05	0.41	0.61	0.00045	0.92	0.97	1.2e-05	0.91	0.96
Cingulate Cortex: Area 29A	−0.0055	0.5	0.68	−0.00014	0.39	0.59	−0.026	0.031	0.11	0.00052	0.067	0.19
Cingulate Cortex: Area 29B	−0.0048	0.19	0.38	−1.1e-05	0.87	0.94	−0.0084	0.11	0.27	0.00024	0.05	0.16
Cingulate Cortex: Area 29C	0.016	0.17	0.35	−0.00041	0.071	0.2	−0.035	0.042	0.14	0.00055	0.17	0.36
Cingulate Cortex: Area 30	−0.0076	0.7	0.83	−3e-04	0.41	0.61	−0.038	0.18	0.37	0.0014	0.032	0.11
Cingulate Cortex: Area 32	0.015	0.43	0.63	0.00029	0.41	0.61	−0.027	0.33	0.53	0.00036	0.57	0.74
Amygdalopiriform Transition Area	−0.021	0.00014	0.00091	−0.00015	0.18	0.37	−0.0033	0.69	0.82	0.00031	0.11	0.27

Structure	β_{7Gy}	p_{7Gy}	q_{7Gy}	$\beta_{7Gy:Growth}$	$p_{7Gy:Growth}$	$q_{7Gy:Growth}$	$\beta_{SEX:7Gy}$	$p_{SEX:7Gy}$	$q_{SEX:7Gy}$	$\beta_{SEX:7Gy:Growth}$	$p_{SEX:7Gy:Growth}$	$q_{SEX:7Gy:Growth}$
Primary Auditory Cortex	−0.022	0.012	0.053	−9.6e-05	0.56	0.73	−0.012	0.33	0.53	0.00029	0.33	0.53
Secondary Auditory Cortex: Dorsal Area	−0.025	0.0098	0.044	3.2e-05	0.86	0.93	−0.022	0.12	0.28	4e-04	0.21	0.41
Secondary Auditory Cortex: Ventral Area	−0.03	0.014	0.058	−0.00028	0.22	0.42	−0.01	0.56	0.73	0.00039	0.34	0.55
Caudomedial Entorhinal Cortex	−0.11	0.0089	0.041	−0.0016	0.038	0.13	−0.044	0.47	0.65	0.00039	0.78	0.88
Cingulum	−0.024	2.1e-06	1.5e-05	−0.00012	0.19	0.38	−0.012	0.1	0.26	0.00012	0.44	0.63
Claustrum	−0.0074	0.01	0.046	8.4e-05	0.13	0.31	−0.0014	0.74	0.86	2.6e-06	0.98	0.99
Cortex-Amygdala Transition Zones	−8e-04	0.9	0.95	7.2e-06	0.95	0.98	−0.003	0.74	0.86	0.00013	0.55	0.73
Claustrum: Dorsal Part	−0.0049	0.0032	0.017	−1.1e-06	0.97	0.99	−0.0034	0.16	0.34	1.4e-05	0.8	0.89
Dorsal Nucleus Of The Endopiriform	−0.021	0.0023	0.013	−0.00012	0.34	0.54	−0.0028	0.78	0.88	−0.00011	0.62	0.78
Dorsal Intermediate Entorhinal Cortex	−0.038	0.0016	0.0089	−5e-04	0.027	0.098	−0.0078	0.65	0.8	0.00082	0.044	0.15
Dorsolateral Entorhinal Cortex	−0.035	0.023	0.087	−0.00066	0.019	0.076	−0.0083	0.71	0.84	0.00095	0.062	0.18
Dorsolateral Orbital Cortex	−0.02	0.014	0.061	0.00026	0.12	0.29	−0.0074	0.54	0.72	0.00029	0.33	0.53
Dorsal Tenia Tecta	−0.0089	0.046	0.15	−0.00017	0.033	0.12	−0.00014	0.98	0.99	3.9e-05	0.79	0.89
Ectorhinal Cortex	−0.042	0.0048	0.024	−0.00042	0.12	0.29	0.0037	0.86	0.94	0.00045	0.36	0.56
Frontal Cortex: Area 3	−0.016	0.0011	0.0062	7.3e-05	0.42	0.61	−0.01	0.13	0.3	0.00014	0.38	0.58
Frontal Association Cortex	−0.14	0.027	0.1	0.002	0.11	0.28	−0.13	0.17	0.35	0.0035	0.12	0.28
Intermediate Nucleus Of The Endopiriform Claustrum	−0.0062	0.061	0.18	−3.3e-05	0.62	0.78	0.0019	0.7	0.83	−0.00015	0.2	0.4
Insular Region: Not Subdivided	−0.11	0.0088	0.04	3.8e-05	0.96	0.98	−0.1	0.095	0.24	0.00044	0.75	0.87
Lateral Orbital Cortex	−0.005	0.88	0.94	0.0011	0.085	0.23	−0.049	0.3	0.51	0.0019	0.093	0.24
Lateral Parietal Association Cortex	−0.0029	0.057	0.17	1.7e-05	0.57	0.74	−0.0046	0.036	0.13	0.00013	0.01	0.046
Primary Motor Cortex	−0.13	0.0041	0.021	7.9e-05	0.92	0.97	−0.17	0.0073	0.034	0.0013	0.39	0.58
Secondary Motor Cortex	−0.084	0.034	0.12	−0.00045	0.54	0.72	−0.16	0.0067	0.032	0.0012	0.36	0.56
Medial Entorhinal Cortex	−0.022	0.00072	0.0043	−9.9e-05	0.43	0.62	−0.007	0.46	0.65	0.00018	0.41	0.61
Medial Orbital Cortex	0.042	0.0075	0.035	0.00031	0.31	0.51	0.0031	0.89	0.95	0.00085	0.12	0.29
Medial Parietal Association Cortex	−0.0037	0.21	0.41	3.6e-05	0.53	0.71	−0.0085	0.051	0.16	0.00027	0.0095	0.043
Piriform Cortex	−0.14	0.007	0.033	−0.0012	0.24	0.45	−0.027	0.73	0.85	−0.00027	0.88	0.94
Posterolateral Cortical Amygdaloid Area	−0.014	0.091	0.24	−0.00022	0.19	0.38	−0.015	0.22	0.42	0.00076	0.01	0.046
Posteromedial Cortical Amygdaloid Area	−0.03	0.00048	0.0029	−0.00023	0.14	0.32	−0.017	0.17	0.36	0.00059	0.04	0.14
Perirhinal Cortex	−0.035	0.012	0.053	−0.00052	0.047	0.15	−0.0029	0.89	0.95	0.00055	0.24	0.44
Parietal Cortex: Posterior Area: Rostral Part	−0.001	0.12	0.28	8.5e-06	0.49	0.68	−0.0019	0.045	0.15	4.3e-05	0.055	0.17
Rostral Amygdalopiriform Area	−0.0068	0.08	0.22	−8e-05	0.31	0.51	−0.0024	0.67	0.81	0.00028	0.042	0.14
Primary Somatosensory Cortex	−0.086	0.00073	0.0044	0.00022	0.65	0.8	−0.075	0.042	0.14	0.00098	0.25	0.45
Primary Somatosensory Cortex: Barrel Field	−0.15	0.0038	0.019	−0.00079	0.41	0.61	−0.17	0.022	0.084	0.0022	0.2	0.39
Primary Somatosensory Cortex: Dysgranular Zone	−0.0058	0.0047	0.024	1e-05	0.79	0.89	−0.0074	0.013	0.056	7.9e-05	0.25	0.45
Primary Somatosensory Cortex: Forelimb Region	−0.082	0.0017	0.0095	−0.00019	0.7	0.83	−0.093	0.014	0.06	0.00089	0.31	0.51
Primary Somatosensory Cortex: Hindlimb Region	−0.045	0.013	0.055	−0.00014	0.68	0.81	−0.061	0.019	0.077	7e-04	0.25	0.45
Primary Somatosensory Cortex: Jaw Region	−0.016	0.00043	0.0027	4e-05	0.63	0.79	−0.015	0.018	0.071	0.00017	0.26	0.47
Primary Somatosensory Cortex: Shoulder Region	−0.0029	0.077	0.21	−2.8e-05	0.36	0.56	−0.004	0.095	0.24	6.7e-05	0.22	0.42
Primary Somatosensory Cortex: Trunk Region	−0.0057	0.11	0.26	1.9e-05	0.78	0.88	−0.011	0.037	0.13	0.00022	0.068	0.2
Primary Somatosensory Cortex: Upper Lip Region	−0.091	0.0019	0.011	−0.00025	0.64	0.79	−0.11	0.013	0.056	0.0021	0.031	0.11
Secondary Somatosensory Cortex	−0.11	8e-04	0.0048	−0.00038	0.53	0.71	−0.088	0.067	0.19	0.0018	0.089	0.23
Temporal Association Area	−0.036	0.04	0.13	−0.00052	0.11	0.27	0.008	0.76	0.87	0.00041	0.48	0.67
Primary Visual Cortex	−0.017	0.34	0.54	−0.00033	0.33	0.53	−0.024	0.36	0.56	0.00083	0.17	0.35
Primary Visual Cortex: Binocular Area	−0.02	0.13	0.29	0.00012	0.61	0.77	−0.03	0.12	0.28	0.00069	0.12	0.28
Primary Visual Cortex: Monocular Area	−0.024	0.093	0.24	0.00022	0.4	0.6	−0.039	0.058	0.18	0.0011	0.017	0.071
Secondary Visual Cortex: Lateral Area	−0.018	0.3	0.51	−0.00025	0.44	0.63	−0.022	0.39	0.59	0.00053	0.37	0.57
Secondary Visual Cortex: Mediolateral Area	−0.011	0.14	0.32	6.7e-05	0.64	0.79	−0.02	0.064	0.19	0.00061	0.017	0.069
Secondary Visual Cortex: Mediomedial Area	−0.015	0.36	0.56	−0.00014	0.65	0.8	−0.024	0.32	0.52	0.001	0.065	0.19
Claustrum: Ventral Part	−0.01	0.0098	0.044	−9.4e-06	0.89	0.95	−0.0095	0.086	0.23	−2.9e-05	0.81	0.9
Ventral Nucleus Of The Endopiriform Claustrum	−0.0075	0.0063	0.03	−5.3e-05	0.29	0.5	−0.001	0.79	0.89	4.6e-05	0.61	0.77
Ventral Intermediate Entorhinal Cortex	−0.031	0.00012	0.00081	−0.00024	0.12	0.29	−0.0091	0.44	0.63	0.00052	0.059	0.18
Ventral Orbital Cortex	0.013	0.24	0.45	0.00022	0.28	0.48	−0.01	0.51	0.69	0.00047	0.2	0.4
Ventral Tenia Tecta	−0.0023	0.0035	0.018	−1.3e-05	0.41	0.61	−0.00053	0.65	0.8	4.1e-05	0.14	0.31

Supplementary Table S.1 Table of 159 segmented atlas structures affected by irradiation. Columns of the table contain information for the coefficient estimates for age, radiation, sex, interaction terms and corresponding test statistics: p value (p) and FDR adjusted p values (q).

Structure	β_{MET16}	p_{MET16}	q_{MET16}	$\beta_{MET16:Growth}$	$p_{MET16:Growth}$	$q_{MET16:Growth}$	$\beta_{MET16:7Gy}$	$p_{MET16:7Gy}$	$q_{MET16:7Gy}$
Amygdala	−0.121	0.0599	0.18	0.0014	0.221	0.419	−0.0799	0.374	0.573
Anterior Commissure: Pars Anterior	−0.00391	0.68	0.818	0.000362	0.0379	0.13	−0.0232	0.0804	0.218
Anterior Commissure: Pars Posterior	1.83e-05	0.995	0.997	0.000167	0.00358	0.0185	−0.00355	0.402	0.598
Basal Forebrain	−0.0308	0.382	0.58	0.0018	0.00478	0.0237	−0.085	0.0845	0.226
Bed Nucleus Of Stria Terminalis	−0.00204	0.837	0.919	9.39e-05	0.604	0.768	−0.0239	0.0852	0.228
Cerebellar Peduncle: Inferior	0.00875	0.244	0.45	0.000242	0.0996	0.251	−0.0168	0.109	0.267
Cerebellar Peduncle: Middle	0.0106	0.389	0.587	0.000187	0.425	0.618	−0.0363	0.0364	0.126
Cerebellar Peduncle: Superior	−0.0108	0.182	0.372	7.01e-05	0.644	0.796	−0.0169	0.135	0.307
Cerebral Aqueduct	0.0103	0.128	0.296	0.000142	0.291	0.497	−0.0117	0.217	0.414
Cerebral Peduncle	0.00372	0.813	0.903	9.27e-05	0.742	0.859	−0.0373	0.0903	0.235
Colliculus: Inferior	−0.0411	0.29	0.497	0.000507	0.503	0.686	−0.0927	0.0889	0.233
Colliculus: Superior	−0.0233	0.807	0.9	0.000878	0.633	0.79	−0.171	0.2	0.396
Corpus Callosum	−0.0178	0.825	0.91	0.00062	0.664	0.807	−0.321	0.00461	0.0231
Corticospinal Tract/Pyramids	−0.00107	0.926	0.967	0.000332	0.12	0.285	−0.0351	0.0287	0.105
Cuneate Nucleus	0.00162	0.445	0.634	6.09e-05	0.158	0.343	−0.00541	0.0692	0.198
Dentate Gyrus Of Hippocampus	0.0215	0.352	0.554	1.63e-05	0.969	0.988	−0.089	0.00601	0.0289
Facial Nerve (Cranial Nerve 7)	0.00142	0.5	0.684	5.41e-05	0.196	0.392	−0.00416	0.157	0.342
Fasciculus Retroflexus	−0.00195	0.292	0.497	2.98e-05	0.379	0.578	−0.00488	0.0592	0.178
Fimbria	−0.00881	0.749	0.864	−9.53e-05	0.851	0.927	−0.0919	0.0176	0.0712
Fornix	−0.00275	0.507	0.69	7.33e-05	0.328	0.53	−0.0137	0.0183	0.0733
Fourth Ventricle	0.0093	0.359	0.56	0.000644	0.00192	0.0107	−0.0139	0.326	0.529
Fundus Of Striatum	0.000222	0.817	0.905	6.09e-05	0.000814	0.00489	−0.000422	0.753	0.867
Globus Pallidus	−0.0193	0.362	0.562	6.92e-05	0.853	0.928	−0.0231	0.434	0.626
Habenular Commissure	−0.000833	0.374	0.573	1.54e-05	0.375	0.574	−0.00211	0.108	0.264
Hippocampus	0.0222	0.848	0.926	0.000492	0.809	0.901	−0.344	0.0349	0.122
Hypothalamus	−0.0729	0.263	0.468	0.00127	0.266	0.47	−0.152	0.0963	0.245
Inferior Olivary Complex	−0.00173	0.251	0.456	5.16e-05	0.0783	0.215	−0.00189	0.37	0.569
Internal Capsule	0.00575	0.795	0.892	−3.6e-05	0.927	0.968	−0.0558	0.0721	0.202
Interpeduncular Nucleus	0.00162	0.53	0.71	6.17e-05	0.206	0.403	−0.00825	0.0229	0.0875
Lateral Olfactory Tract	0.00387	0.442	0.633	3.31e-05	0.718	0.845	−0.012	0.0898	0.234
Lateral Septum	−0.017	0.392	0.589	0.000155	0.656	0.803	−0.0526	0.0592	0.178
Lateral Ventricle	−0.0356	0.383	0.581	7.38e-05	0.923	0.967	−0.0707	0.215	0.413
Mammillary Bodies	−0.00234	0.558	0.73	−8.88e-05	0.233	0.436	−0.00619	0.267	0.472
Mammillothalamic Tract	9.08e-05	0.959	0.982	6.66e-05	0.0347	0.121	−0.00543	0.0269	0.0995
Medial Lemniscus/Medial Longitudinal Fasciculus	−0.00799	0.697	0.829	0.000386	0.302	0.507	−0.055	0.0557	0.172
Medial Septum	−0.006	0.437	0.629	0.000185	0.178	0.368	−0.0177	0.102	0.255
Medulla	0.0732	0.737	0.858	0.00823	0.0499	0.16	−0.514	0.0923	0.238
Midbrain	−0.145	0.107	0.262	0.00101	0.525	0.707	−0.219	0.0809	0.219
Nucleus Accumbens	−0.0121	0.692	0.828	0.00143	0.0114	0.0502	−0.0434	0.31	0.512
Olfactory Bulbs	0.184	0.285	0.492	0.00411	0.202	0.398	−0.791	0.00106	0.00626
Olfactory Tubercle	0.0285	0.303	0.507	0.0016	0.00273	0.0147	−0.0794	0.0407	0.137
Optic Tract	0.000139	0.989	0.995	3e-04	0.101	0.253	−0.0286	0.0478	0.154
Periaqueductal Grey	−0.066	0.056	0.172	0.000738	0.26	0.467	−0.0352	0.466	0.653
Pons	0.0372	0.795	0.892	0.0059	0.0302	0.109	−0.405	0.0438	0.145
Pontine Nucleus	0.00119	0.868	0.938	0.000172	0.21	0.407	−0.0123	0.22	0.418
Posterior Commissure	−4.71e-05	0.976	0.991	3.81e-05	0.183	0.373	−0.0045	0.0374	0.129
Pre-Para Subiculum	−0.0226	0.249	0.454	3.49e-05	0.923	0.967	−0.0521	0.0578	0.176
Stratum Granulosum Of Hippocampus	0.00514	0.406	0.602	5.86e-05	0.608	0.772	−0.02	0.021	0.0818
Stria Medullaris	0.00706	0.302	0.506	9.86e-05	0.436	0.628	−0.0297	0.002	0.0111
Stria Terminalis	−0.000144	0.983	0.993	−1.42e-05	0.907	0.957	−0.0218	0.0239	0.0907
Striatum	−0.00209	0.988	0.995	0.00456	0.0685	0.196	−0.42	0.0338	0.119
Subependymale Zone / Rhinocele	−0.000376	0.518	0.701	1.2e-05	0.289	0.496	−0.00192	0.0185	0.0742
Superior Olivary Complex	0.00225	0.696	0.829	0.000317	0.00544	0.0265	−0.0156	0.0529	0.166

Structure	β_{MET16}	p_{MET16}	q_{MET16}	$\beta_{MET16:Growth}$	$p_{MET16:Growth}$	$q_{MET16:Growth}$	$\beta_{MET16:7Gy}$	$p_{MET16:7Gy}$	$q_{MET16:7Gy}$
Thalamus	−0.0123	0.924	0.967	0.00285	0.219	0.418	−0.485	0.00752	0.035
Third Ventricle	0.00191	0.877	0.944	0.000237	0.324	0.527	−0.0379	0.0285	0.104
Ventral Tegmental Decussation	−0.00188	0.196	0.391	4.27e-05	0.118	0.281	−0.00268	0.188	0.38
Lobules 1-2: Lingula And Central Lobule (Ventral)	−0.0431	0.0535	0.167	0.000472	0.264	0.469	−0.00682	0.827	0.911
Lobule 3: Central Lobule (Dorsal)	−0.011	0.635	0.79	−0.000141	0.769	0.879	−0.0516	0.113	0.273
Lobules 4-5: Culmen (Ventral And Dorsal)	−0.0464	0.259	0.465	0.00168	0.0401	0.136	−0.0439	0.445	0.634
Lobule 6: Declive	−0.0255	0.342	0.543	0.00118	0.0307	0.111	−0.0205	0.585	0.752
Lobule 7: Tuber (Or Folium)	−0.00234	0.824	0.91	0.000352	0.103	0.256	−0.0133	0.368	0.567
Lobule 8: Pyramis	0.00291	0.879	0.944	−0.000276	0.474	0.662	−0.0628	0.0192	0.0762
Lobule 9: Uvula	−0.00298	0.916	0.963	0.000295	0.61	0.772	−0.0849	0.0314	0.112
Lobule 10: Nodulus	0.0158	0.369	0.568	0.000815	0.0247	0.0931	−0.0341	0.167	0.353
Anterior Lobule (Lobules 4-5)	−0.0187	0.161	0.346	0.000127	0.635	0.79	−0.032	0.0876	0.231
Simple Lobule (Lobule 6)	−0.0029	0.93	0.97	0.00126	0.0567	0.174	−0.0845	0.0691	0.198
Crus 1: Ansiform Lobule (Lobule 6)	0.00539	0.878	0.944	0.00137	0.0471	0.153	−0.0569	0.246	0.451
Crus 2: Ansiform Lobule (Lobule 7)	−0.00901	0.776	0.882	0.00128	0.0443	0.146	−0.047	0.289	0.496
Paramedian Lobule (Lobule 7)	−0.00677	0.88	0.945	0.000286	0.748	0.863	−0.103	0.103	0.256
Copula: Pyramis (Lobule 8)	−0.00625	0.794	0.892	0.000272	0.571	0.742	−0.0345	0.303	0.507
Flocculus (Fl)	−0.00311	0.735	0.856	0.000242	0.158	0.342	−0.00721	0.574	0.744
Paraflocculus (Pfl)	−0.00319	0.947	0.979	0.00211	0.0191	0.0762	−0.0755	0.263	0.468
Trunk Of Arbor Vita	−0.00233	0.955	0.98	0.00154	0.0639	0.188	−0.103	0.073	0.204
Lobule 1-2 White Matter	−0.00386	0.0173	0.0706	1.58e-05	0.599	0.765	0.000309	0.891	0.95
Lobule 3 White Matter	−0.0025	0.444	0.634	−5.43e-05	0.424	0.618	−0.00492	0.281	0.487
Trunk Of Lobules 1-3 White Matter	−0.00364	0.102	0.254	1.43e-06	0.975	0.991	−0.0023	0.46	0.648
Lobules 4-5 White Matter	−0.00757	0.36	0.561	0.000123	0.481	0.669	−0.013	0.262	0.467
Lobules 6-7 White Matter	−0.00986	0.232	0.435	0.000243	0.151	0.332	−0.0144	0.213	0.411
Lobule 8 White Matter	0.000411	0.762	0.873	−1.08e-05	0.695	0.829	−0.00373	0.0504	0.161
Trunk Of Lobules 6-8 White Matter	−0.000644	0.614	0.775	4.4e-06	0.871	0.94	−0.0028	0.118	0.281
Lobule 9 White Matter	−0.00129	0.659	0.805	2.54e-05	0.673	0.814	−0.00566	0.167	0.353
Lobule 10 White Matter	0.0014	0.317	0.519	6.46e-05	0.0257	0.0958	−0.00251	0.201	0.397
Anterior Lobule White Matter	−0.00137	0.225	0.423	−7.31e-06	0.746	0.861	−0.00263	0.0946	0.242
Simple Lobule White Matter	0.000469	0.906	0.956	0.000103	0.192	0.386	−0.0108	0.0507	0.162
Crus 1 White Matter	0.00124	0.782	0.886	0.000129	0.148	0.327	−0.0136	0.0311	0.112
Trunk Of Simple And Crus 1 White Matter	−0.00221	0.268	0.472	4.36e-05	0.28	0.486	−0.00516	0.0647	0.189
Crus 2 White Matter	−0.00162	0.601	0.767	8.29e-05	0.19	0.384	−0.00674	0.121	0.286
Paramedian Lobule	−0.000944	0.597	0.764	2.93e-05	0.408	0.603	−0.00281	0.261	0.467
Trunk Of Crus 2 And Paramedian White Matter	−0.00161	0.665	0.808	0.000108	0.154	0.336	−0.00751	0.149	0.329
Copula White Matter	−8.44e-05	0.934	0.972	1.72e-05	0.404	0.6	−0.00182	0.202	0.398
Paraflocculus White Matter	−0.000279	0.942	0.975	0.000123	0.0888	0.233	−0.00291	0.585	0.752
Flocculus White Matter	−0.000303	0.665	0.808	1.65e-05	0.205	0.401	−4.35e-05	0.965	0.985
Dentate Nucleus	0.00051	0.882	0.946	0.000164	0.0217	0.0842	−0.00474	0.326	0.528
Nucleus Interpositus	0.000342	0.951	0.979	0.000268	0.0221	0.0854	−0.0116	0.139	0.313
Fastigial Nucleus	−0.000651	0.899	0.954	0.000253	0.0156	0.0654	−0.00977	0.175	0.364
Cingulate Cortex: Area 24A	0.0136	0.382	0.58	−1.62e-05	0.953	0.979	−0.0524	0.0161	0.0668
Cingulate Cortex: Area 24A'	−0.00136	0.825	0.91	0.000157	0.172	0.359	−0.0209	0.0157	0.0657
Cingulate Cortex: Area 24B	0.0154	0.222	0.421	−2.25e-05	0.923	0.967	−0.0463	0.0088	0.0403
Cingulate Cortex: Area 24B'	0.00287	0.59	0.757	9.63e-05	0.34	0.541	−0.015	0.0444	0.146
Cingulate Cortex: Area 25	0.00247	0.537	0.715	7.99e-05	0.261	0.467	−0.0111	0.0468	0.152
Cingulate Cortex: Area 29A	0.000181	0.985	0.994	9.39e-05	0.629	0.788	−0.017	0.219	0.418
Cingulate Cortex: Area 29B	0.000878	0.843	0.922	2.8e-05	0.738	0.858	−0.0112	0.0718	0.202
Cingulate Cortex: Area 29C	−0.00677	0.634	0.79	0.000326	0.233	0.436	−0.0224	0.26	0.467
Cingulate Cortex: Area 30	0.0109	0.647	0.797	0.000155	0.73	0.853	−0.0784	0.0189	0.0757
Cingulate Cortex: Area 32	0.00745	0.748	0.863	0.000277	0.521	0.702	−0.0496	0.127	0.294
Amygdalopiriform Transition Area	−0.00954	0.161	0.345	0.000148	0.268	0.472	−0.00201	0.832	0.915

Structure	β_{MET16}	p_{MET16}	q_{MET16}	$\beta_{MET16:Growth}$	$p_{MET16:Growth}$	$q_{MET16:Growth}$	$\beta_{MET16:7Gy}$	$p_{MET16:7Gy}$	$q_{MET16:7Gy}$
Primary Auditory Cortex	0.00364	0.736	0.857	9.27e-05	0.647	0.797	−0.0335	0.0269	0.0995
Secondary Auditory Cortex: Dorsal Area	0.00655	0.577	0.746	0.000172	0.427	0.62	−0.0442	0.00716	0.0337
Secondary Auditory Cortex: Ventral Area	0.0035	0.812	0.903	−9.3e-05	0.739	0.858	−0.0385	0.0616	0.183
Caudomedial Entorhinal Cortex	−0.0414	0.411	0.606	−0.000385	0.68	0.818	−0.132	0.0623	0.184
Cingulum	−0.00233	0.7	0.832	6.54e-05	0.55	0.724	−0.0203	0.0167	0.0687
Claustrum	−0.00057	0.872	0.94	0.000208	0.0026	0.0141	−0.00516	0.297	0.502
Cortex-Amygdala Transition Zones	0.00215	0.779	0.883	0.000343	0.0198	0.0779	−0.0206	0.0547	0.17
Claustrum: Dorsal Part	0.00117	0.569	0.739	5.5e-05	0.132	0.302	−0.00686	0.0169	0.0693
Dorsal Nucleus Of The Endopiriform	0.000838	0.922	0.967	0.000476	0.0018	0.0101	−0.0171	0.151	0.332
Dorsal Intermediate Entorhinal Cortex	−0.017	0.245	0.451	0.00013	0.638	0.792	−0.00449	0.826	0.91
Dorsolateral Entorhinal Cortex	−0.0106	0.569	0.739	−9.7e-05	0.779	0.883	−0.018	0.489	0.675
Dorsolateral Orbital Cortex	0.0012	0.904	0.956	0.000284	0.164	0.349	−0.0106	0.447	0.636
Dorsal Tenia Tecta	0.00498	0.366	0.565	6.4e-05	0.516	0.699	−0.0169	0.0285	0.104
Ectorhinal Cortex	0.000646	0.972	0.989	−0.000152	0.646	0.796	−0.0414	0.104	0.258
Frontal Cortex: Area 3	−0.000366	0.95	0.979	0.000149	0.173	0.362	−0.0101	0.213	0.411
Frontal Association Cortex	0.0324	0.677	0.816	0.00152	0.327	0.529	−0.132	0.225	0.423
Intermediate Nucleus Of The Endopiriform Claustrum	0.00173	0.672	0.813	0.000303	0.000166	0.00106	−0.00706	0.217	0.414
Insular Region: Not Subdivided	0.0355	0.503	0.686	0.00188	0.0476	0.154	−0.155	0.0373	0.129
Lateral Orbital Cortex	−0.000839	0.983	0.993	0.00124	0.116	0.278	−0.0562	0.309	0.511
Lateral Parietal Association Cortex	0.00195	0.289	0.496	1.43e-05	0.685	0.823	−0.00637	0.0138	0.0588
Primary Motor Cortex	0.026	0.635	0.79	0.000601	0.553	0.726	−0.172	0.0249	0.0934
Secondary Motor Cortex	0.0611	0.211	0.409	−0.000165	0.853	0.928	−0.19	0.00556	0.027
Medial Entorhinal Cortex	−0.00902	0.264	0.468	−1.56e-05	0.918	0.965	−0.0103	0.363	0.562
Medial Orbital Cortex	−0.00283	0.883	0.946	0.000378	0.31	0.512	−0.0286	0.289	0.496
Medial Parietal Association Cortex	0.00418	0.246	0.451	4.84e-05	0.492	0.677	−0.012	0.0179	0.072
Piriform Cortex	0.0407	0.537	0.715	0.0029	0.0161	0.0668	−0.149	0.106	0.261
Posterolateral Cortical Amygdaloid Area	−0.00715	0.494	0.678	0.000173	0.388	0.587	−0.0143	0.327	0.53
Posteromedial Cortical Amygdaloid Area	−0.0198	0.0604	0.181	−1.6e-05	0.934	0.972	−0.00718	0.626	0.786
Perirhinal Cortex	0.00307	0.86	0.933	−0.000215	0.499	0.683	−0.0385	0.114	0.274
Parietal Cortex: Posterior Area: Rostral Part	0.000896	0.261	0.467	1.67e-05	0.269	0.474	−0.00315	0.00481	0.0238
Rostral Amygdalopiriform Area	−0.00207	0.666	0.808	2.07e-05	0.828	0.911	−0.00325	0.628	0.788
Primary Somatosensory Cortex	0.00496	0.874	0.942	0.000821	0.153	0.334	−0.0831	0.0571	0.175
Primary Somatosensory Cortex: Barrel Field	0.0374	0.561	0.732	0.00106	0.364	0.563	−0.271	0.00267	0.0144
Primary Somatosensory Cortex: Dysgranular Zone	−8.37e-05	0.973	0.99	8.51e-05	0.0639	0.188	−0.00789	0.0248	0.0932
Primary Somatosensory Cortex: Forelimb Region	0.00755	0.813	0.903	0.000661	0.266	0.47	−0.119	0.00801	0.0371
Primary Somatosensory Cortex: Hindlimb Region	0.0147	0.504	0.687	0.000171	0.679	0.818	−0.0824	0.00751	0.035
Primary Somatosensory Cortex: Jaw Region	−0.00227	0.676	0.815	0.000192	0.0611	0.182	−0.0116	0.128	0.297
Primary Somatosensory Cortex: Shoulder Region	0.00115	0.567	0.737	2.94e-05	0.433	0.625	−0.0069	0.0146	0.0618
Primary Somatosensory Cortex: Trunk Region	0.00449	0.305	0.508	4.84e-05	0.559	0.731	−0.0169	0.00589	0.0284
Primary Somatosensory Cortex: Upper Lip Region	0.00613	0.865	0.936	0.000518	0.426	0.619	−0.125	0.0132	0.0564
Secondary Somatosensory Cortex	0.0119	0.772	0.88	0.000365	0.616	0.777	−0.13	0.023	0.0878
Temporal Association Area	−0.00148	0.945	0.977	−0.000105	0.791	0.891	−0.044	0.145	0.324
Primary Visual Cortex	0.016	0.468	0.655	−0.000128	0.753	0.867	−0.0895	0.00379	0.0194
Primary Visual Cortex: Binocular Area	0.00613	0.706	0.837	0.000239	0.425	0.618	−0.0556	0.0147	0.0623
Primary Visual Cortex: Monocular Area	0.00909	0.604	0.768	0.000169	0.603	0.768	−0.056	0.0228	0.0875
Secondary Visual Cortex: Lateral Area	0.0119	0.583	0.751	0.000184	0.643	0.795	−0.0819	0.00682	0.0323
Secondary Visual Cortex: Mediolateral Area	0.00575	0.532	0.712	8.33e-05	0.632	0.79	−0.0291	0.0239	0.0907
Secondary Visual Cortex: Mediomedial Area	0.0154	0.441	0.632	−0.000216	0.567	0.738	−0.0644	0.0219	0.0849
Claustrum: Ventral Part	0.00278	0.557	0.73	0.000187	0.0242	0.0915	−0.0122	0.0665	0.193
Ventral Nucleus Of The Endopiriform Claustrum	−0.000336	0.921	0.966	0.000127	0.0391	0.133	−0.0028	0.554	0.727
Ventral Intermediate Entorhinal Cortex	−0.0129	0.187	0.379	9.61e-05	0.608	0.772	−0.00326	0.811	0.902
Ventral Orbital Cortex	0.0053	0.687	0.824	0.000251	0.316	0.517	−0.028	0.129	0.297
Ventral Tenia Tecta	0.00022	0.82	0.907	2.97e-05	0.112	0.271	−0.00228	0.0922	0.238

Supplementary Table S.2 Table of 159 segmented atlas structures affected by metformin treatment (MET16). Columns of the table contain information for the coefficient estimates for metformin treatment, interactions with age or radiation and corresponding test statistics: p value (p) and FDR adjusted p values (q).

Structure	β_{MET19}	p_{MET19}	q_{MET19}	$\beta_{MET19:Growth}$	$p_{MET19:Growth}$	$q_{MET19:Growth}$	$\beta_{MET19:7Gy}$	$p_{MET19:7Gy}$	$q_{MET19:7Gy}$
Amygdala	−0.0079	0.905	0.956	−6.19e-05	0.96	0.982	−0.0188	0.836	0.918
Anterior Commissure: Pars Anterior	−0.0075	0.445	0.634	6.29e-05	0.739	0.858	0.00752	0.575	0.744
Anterior Commissure: Pars Posterior	−1.84e-05	0.995	0.997	6.03e-05	0.328	0.53	0.00252	0.557	0.73
Basal Forebrain	0.0507	0.164	0.349	−0.000193	0.778	0.883	−0.0445	0.371	0.57
Bed Nucleus Of Stria Terminalis	0.000963	0.925	0.967	0.000197	0.313	0.514	0.0194	0.166	0.352
Cerebellar Peduncle: Inferior	−0.013	0.096	0.245	0.000135	0.397	0.593	0.00463	0.663	0.807
Cerebellar Peduncle: Middle	−0.00934	0.466	0.653	0.00023	0.363	0.563	0.0236	0.178	0.367
Cerebellar Peduncle: Superior	−0.000178	0.983	0.993	0.000358	0.0295	0.107	0.0189	0.0986	0.249
Cerebral Aqueduct	−0.00855	0.224	0.422	0.000254	0.0816	0.221	0.0175	0.0677	0.195
Cerebral Peduncle	−0.0155	0.341	0.542	0.000434	0.154	0.337	0.0433	0.0516	0.163
Colliculus: Inferior	−0.0606	0.133	0.304	0.000343	0.675	0.814	0.0843	0.126	0.293
Colliculus: Superior	0.0394	0.69	0.827	−0.000285	0.886	0.947	0.0197	0.884	0.946
Corpus Callosum	−0.0673	0.42	0.615	0.00265	0.0857	0.229	0.0941	0.41	0.605
Corticospinal Tract/Pyramids	−0.0168	0.157	0.341	0.000166	0.474	0.662	0.0169	0.296	0.501
Cuneate Nucleus	−0.00318	0.149	0.329	7.23e-05	0.122	0.286	−0.00285	0.343	0.545
Dentate Gyrus Of Hippocampus	0.000317	0.989	0.995	4.4e-06	0.992	0.995	0.0279	0.392	0.59
Facial Nerve (Cranial Nerve 7)	−0.00428	0.0496	0.159	2.9e-05	0.521	0.702	0.00332	0.265	0.469
Fasciculus Retroflexus	0.0012	0.532	0.712	3.46e-06	0.925	0.967	0.000801	0.759	0.871
Fimbria	0.00243	0.932	0.971	0.000803	0.144	0.322	0.0407	0.297	0.502
Fornix	0.00252	0.558	0.73	5e-05	0.538	0.715	0.00969	0.0993	0.25
Fourth Ventricle	−0.0174	0.0971	0.247	0.000381	0.0883	0.232	0.00784	0.584	0.752
Fundus Of Striatum	0.00116	0.243	0.448	−1.17e-05	0.549	0.724	−0.00153	0.262	0.467
Globus Pallidus	−0.0389	0.0752	0.209	0.00025	0.534	0.713	0.0883	0.00323	0.017
Habenular Commissure	0.000292	0.763	0.874	4.48e-05	0.0169	0.0692	7.72e-05	0.954	0.98
Hippocampus	−0.113	0.348	0.55	0.00151	0.492	0.677	0.162	0.325	0.527
Hypothalamus	0.0357	0.597	0.763	0.00051	0.68	0.818	0.123	0.181	0.371
Inferior Olivary Complex	−0.00332	0.0333	0.117	3.31e-05	0.296	0.501	0.00164	0.441	0.632
Internal Capsule	−0.0257	0.262	0.467	0.000544	0.202	0.398	0.0996	0.00152	0.00866
Interpedunclar Nucleus	0.000615	0.818	0.906	−2.48e-05	0.639	0.792	−0.000917	0.802	0.897
Lateral Olfactory Tract	0.00054	0.918	0.964	−4.66e-05	0.638	0.792	0.00073	0.918	0.965
Lateral Septum	−0.013	0.527	0.708	0.000175	0.641	0.794	0.022	0.434	0.626
Lateral Ventricle	−0.0271	0.521	0.702	0.000851	0.305	0.508	0.0293	0.611	0.773
Mammillary Bodies	−0.00235	0.568	0.739	−2.13e-05	0.791	0.891	0.00997	0.0773	0.213
Mammilothalamic Tract	0.00191	0.292	0.498	−2.31e-05	0.498	0.683	0.0011	0.656	0.803
Medial Lemniscus/Medial Longitudinal Fasciculus	−0.0203	0.34	0.541	0.00013	0.748	0.863	0.0314	0.279	0.485
Medial Septum	0.00488	0.541	0.717	3.68e-05	0.804	0.898	9.78e-05	0.993	0.995
Medulla	−0.47	0.0377	0.129	0.000484	0.915	0.963	0.108	0.726	0.849
Midbrain	0.0346	0.709	0.839	0.00167	0.331	0.532	0.112	0.379	0.578
Nucleus Accumbens	0.0047	0.882	0.946	−0.000535	0.379	0.578	−0.0529	0.22	0.419
Olfactory Bulbs	0.0837	0.638	0.792	−0.00429	0.218	0.417	−0.313	0.199	0.395
Olfactory Tubercle	0.0405	0.158	0.342	−0.000705	0.22	0.418	−0.0789	0.0441	0.146
Optic Tract	−0.00159	0.882	0.946	0.000227	0.25	0.455	0.0249	0.0875	0.231
Periaqueductal Grey	0.00949	0.791	0.891	0.000432	0.542	0.717	0.0415	0.395	0.591
Pons	−0.234	0.115	0.277	0.00358	0.223	0.421	0.315	0.12	0.285
Pontine Nucleus	−0.00604	0.416	0.61	−1.19e-05	0.936	0.972	0.0165	0.103	0.257
Posterior Commissure	0.00212	0.184	0.375	−7.77e-07	0.98	0.993	−0.00122	0.577	0.746
Pre-Para Subiculum	0.00151	0.941	0.975	0.000141	0.719	0.845	−0.0218	0.431	0.623
Stratum Granulosum Of Hippocampus	0.00122	0.849	0.926	−4.82e-05	0.697	0.829	0.009	0.304	0.508
Stria Medullaris	0.00884	0.212	0.409	0.000117	0.393	0.59	0.00118	0.903	0.955
Stria Terminalis	−0.00286	0.688	0.825	0.000135	0.303	0.507	0.0256	0.00864	0.0397
Striatum	−0.222	0.129	0.297	0.00287	0.288	0.496	0.168	0.401	0.597
Subependymale Zone / Rhinocele	0.00012	0.843	0.922	−8.4e-06	0.492	0.677	−0.00107	0.194	0.389
Superior Olivary Complex	−0.0163	0.00638	0.0305	0.000166	0.177	0.367	0.00918	0.259	0.466

Structure	β_{MET19}	p_{MET19}	q_{MET19}	$\beta_{MET19:Growth}$	$p_{MET19:Growth}$	$q_{MET19:Growth}$	$\beta_{MET19:7Gy}$	$p_{MET19:7Gy}$	$q_{MET19:7Gy}$
Thalamus	0.0316	0.813	0.903	0.00117	0.642	0.794	0.136	0.455	0.644
Third Ventricle	0.0197	0.124	0.289	0.000398	0.126	0.293	−0.0044	0.801	0.896
Ventral Tegmental Decussation	0.000401	0.79	0.89	3.91e-05	0.185	0.377	0.00165	0.422	0.616
Lobules 1-2: Lingula And Central Lobule (Ventral)	−0.0494	0.0329	0.116	0.00153	0.000894	0.00533	0.0444	0.159	0.343
Lobule 3: Central Lobule (Dorsal)	−0.0472	0.0504	0.161	0.00103	0.0474	0.154	0.0603	0.0671	0.194
Lobules 4-5: Culmen (Ventral And Dorsal)	−0.0673	0.114	0.276	0.00111	0.208	0.405	0.0204	0.726	0.849
Lobule 6: Declive	−0.0506	0.0694	0.198	0.000631	0.284	0.49	−0.00913	0.81	0.902
Lobule 7: Tuber (Or Folium)	−0.0151	0.167	0.353	8.64e-05	0.71	0.84	−0.00249	0.867	0.938
Lobule 8: Pyramis	−0.0155	0.434	0.626	0.00107	0.0103	0.046	0.0126	0.64	0.793
Lobule 9: Uvula	−0.0283	0.332	0.533	0.00138	0.0273	0.101	0.00911	0.819	0.906
Lobule 10: Nodulus	−0.0365	0.0463	0.151	0.000354	0.366	0.565	−0.0134	0.592	0.759
Anterior Lobule (Lobules 4-5)	−0.0194	0.162	0.347	0.000388	0.179	0.369	0.0251	0.184	0.375
Simple Lobule (Lobule 6)	−0.0352	0.306	0.508	0.00055	0.44	0.631	0.0158	0.737	0.858
Crus 1: Ansiform Lobule (Lobule 6)	−0.0396	0.276	0.482	0.000159	0.831	0.914	0.0179	0.719	0.845
Crus 2: Ansiform Lobule (Lobule 7)	−0.0743	0.0237	0.0903	0.000582	0.397	0.593	0.027	0.546	0.721
Paramedian Lobule (Lobule 7)	−0.0957	0.0403	0.136	0.00277	0.00425	0.0216	0.0873	0.17	0.356
Copula: Pyramis (Lobule 8)	−0.0482	0.0527	0.165	0.00153	0.00331	0.0172	0.042	0.216	0.414
Flocculus (Fl)	−0.009	0.343	0.545	0.000169	0.362	0.562	0.000597	0.963	0.984
Paraflocculus (Pfl)	0.0439	0.379	0.578	0.000171	0.86	0.933	−0.132	0.0531	0.166
Trunk Of Arbor Vita	−0.0695	0.103	0.257	0.00156	0.0821	0.221	0.052	0.372	0.57
Lobule 1-2 White Matter	−0.00318	0.0578	0.176	0.000106	0.00121	0.00702	0.00171	0.454	0.643
Lobule 3 White Matter	−0.00593	0.0797	0.217	0.000176	0.0171	0.0699	0.00842	0.0683	0.196
Trunk Of Lobules 1-3 White Matter	−0.00243	0.292	0.497	0.000147	0.00256	0.0139	0.00261	0.407	0.603
Lobules 4-5 White Matter	−0.00932	0.278	0.484	0.000299	0.114	0.275	0.0131	0.264	0.469
Lobules 6-7 White Matter	−0.0193	0.0241	0.0914	0.000303	0.0978	0.248	0.00735	0.529	0.71
Lobule 8 White Matter	−0.00111	0.43	0.622	5.08e-05	0.0881	0.232	0.000685	0.721	0.847
Trunk Of Lobules 6-8 White Matter	−0.00253	0.0567	0.174	5.47e-05	0.0622	0.184	0.00243	0.179	0.369
Lobule 9 White Matter	−0.0024	0.429	0.621	8.22e-05	0.207	0.403	0.0011	0.79	0.89
Lobule 10 White Matter	−0.00288	0.0477	0.154	8.97e-06	0.774	0.882	−0.00141	0.476	0.664
Anterior Lobule White Matter	−0.000488	0.675	0.814	2.4e-05	0.325	0.527	0.00123	0.44	0.631
Simple Lobule White Matter	−0.0033	0.421	0.616	8.51e-05	0.32	0.523	0.00344	0.539	0.716
Crus 1 White Matter	−0.00371	0.426	0.618	6.21e-05	0.518	0.701	0.00396	0.533	0.712
Trunk Of Simple And Crus 1 White Matter	−0.00302	0.144	0.321	9.97e-05	0.0227	0.0871	0.0042	0.137	0.31
Crus 2 White Matter	−0.00691	0.0321	0.114	0.000118	0.0839	0.225	0.00377	0.391	0.588
Paramedian Lobule	−0.00356	0.0551	0.171	9.13e-05	0.0176	0.0712	0.00331	0.19	0.384
Trunk Of Crus 2 And Paramedian White Matter	−0.00742	0.0548	0.17	0.000152	0.0619	0.184	0.00621	0.238	0.442
Copula White Matter	−0.00172	0.104	0.258	6.28e-05	0.00502	0.0247	0.000756	0.6	0.765
Paraflocculus White Matter	0.00135	0.732	0.854	−1.04e-05	0.894	0.952	−0.00673	0.212	0.409
Flocculus White Matter	−0.000964	0.184	0.375	2.38e-05	0.0913	0.237	0.000484	0.625	0.785
Dentate Nucleus	−0.00592	0.0981	0.248	8.95e-05	0.246	0.451	0.00409	0.402	0.598
Nucleus Interpositus	−0.0108	0.0639	0.188	0.000155	0.221	0.419	0.00512	0.519	0.702
Fastigial Nucleus	−0.0098	0.0662	0.193	0.000192	0.0893	0.234	0.00372	0.609	0.772
Cingulate Cortex: Area 24A	−0.00944	0.557	0.73	9.69e-05	0.746	0.861	−0.014	0.524	0.706
Cingulate Cortex: Area 24A'	0.00474	0.458	0.646	0.000169	0.174	0.363	−0.0198	0.0233	0.0889
Cingulate Cortex: Area 24B	−0.00474	0.717	0.844	−8.66e-05	0.73	0.853	−0.0156	0.382	0.58
Cingulate Cortex: Area 24B'	−0.00249	0.651	0.8	−6.87e-05	0.529	0.71	−0.00187	0.804	0.898
Cingulate Cortex: Area 25	0.00493	0.233	0.436	1.81e-05	0.814	0.903	−0.00711	0.209	0.406
Cingulate Cortex: Area 29A	0.000171	0.987	0.994	−1.89e-05	0.928	0.969	−0.0116	0.407	0.603
Cingulate Cortex: Area 29B	0.00163	0.722	0.847	−2.81e-05	0.757	0.869	−0.00586	0.35	0.552
Cingulate Cortex: Area 29C	0.0165	0.263	0.468	−0.000409	0.167	0.353	−0.0439	0.0293	0.107
Cingulate Cortex: Area 30	0.0082	0.74	0.858	−0.000624	0.199	0.395	−0.0328	0.33	0.532
Cingulate Cortex: Area 32	0.0111	0.645	0.796	−0.000391	0.403	0.599	−0.0378	0.25	0.455
Amygdalopiriform Transition Area	−0.0141	0.0457	0.149	0.000239	0.0978	0.248	0.00932	0.332	0.533

Structure	β_{MET19}	p_{MET19}	q_{MET19}	$\beta_{MET19:Growth}$	$p_{MET19:Growth}$	$q_{MET19:Growth}$	$\beta_{MET19:7Gy}$	$p_{MET19:7Gy}$	$q_{MET19:7Gy}$
Primary Auditory Cortex	−0.0163	0.146	0.325	0.000327	0.136	0.309	0.00665	0.663	0.807
Secondary Auditory Cortex: Dorsal Area	−0.0057	0.639	0.792	0.000253	0.28	0.486	−0.0115	0.489	0.675
Secondary Auditory Cortex: Ventral Area	−0.0176	0.248	0.454	0.000317	0.294	0.5	0.00887	0.67	0.811
Caudomedial Entorhinal Cortex	0.024	0.645	0.796	−0.000145	0.886	0.947	−0.0317	0.657	0.803
Cingulum	−0.000764	0.903	0.955	0.000148	0.213	0.411	−0.00483	0.573	0.743
Claustrum	0.000295	0.936	0.972	1.09e-05	0.884	0.946	−0.00658	0.189	0.381
Cortex-Amygdala Transition Zones	0.018	0.0235	0.0896	−0.000198	0.211	0.409	−0.0258	0.0172	0.0703
Claustrum: Dorsal Part	−0.0014	0.508	0.691	2.48e-05	0.529	0.71	0.00274	0.344	0.546
Dorsal Nucleus Of The Endopiriform	−0.00287	0.745	0.861	4.34e-05	0.791	0.891	−0.000533	0.965	0.985
Dorsal Intermediate Entorhinal Cortex	−0.0307	0.0424	0.141	0.000239	0.424	0.618	0.019	0.357	0.558
Dorsolateral Entorhinal Cortex	−0.0357	0.0647	0.189	−0.000141	0.706	0.837	0.0163	0.538	0.715
Dorsolateral Orbital Cortex	0.00631	0.542	0.717	−0.000144	0.513	0.695	−0.0176	0.213	0.411
Dorsal Tenia Tecta	0.00921	0.106	0.261	−0.000142	0.182	0.373	−0.0166	0.0335	0.118
Ectorhinal Cortex	−0.00789	0.675	0.814	−7.84e-06	0.983	0.993	0.00327	0.899	0.954
Frontal Cortex: Area 3	−9.75e-05	0.987	0.995	7.35e-06	0.951	0.979	−0.00723	0.38	0.578
Frontal Association Cortex	−0.00598	0.941	0.975	−0.000493	0.768	0.877	−0.0982	0.372	0.571
Intermediate Nucleus Of The Endopiriform Claustrum	0.0038	0.368	0.567	−7.93e-05	0.358	0.56	−0.00847	0.142	0.319
Insular Region: Not Subdivided	0.0427	0.436	0.628	−3.39e-05	0.974	0.99	−0.0372	0.619	0.779
Lateral Orbital Cortex	−0.0026	0.949	0.979	−4.41e-05	0.959	0.982	−0.0624	0.265	0.469
Lateral Parietal Association Cortex	0.00141	0.461	0.649	−4.8e-05	0.209	0.406	−0.00127	0.627	0.786
Primary Motor Cortex	−0.0224	0.693	0.828	0.000585	0.593	0.76	−0.0574	0.459	0.647
Secondary Motor Cortex	0.0025	0.961	0.982	−0.000603	0.533	0.712	−0.0971	0.16	0.344
Medial Entorhinal Cortex	−0.00327	0.696	0.829	0.00013	0.43	0.622	0.00448	0.694	0.829
Medial Orbital Cortex	0.00946	0.636	0.79	−4.3e-05	0.915	0.963	−0.0288	0.291	0.497
Medial Parietal Association Cortex	0.00462	0.216	0.414	−0.000111	0.144	0.322	−0.00594	0.244	0.45
Piriform Cortex	0.0703	0.303	0.507	−0.00111	0.394	0.59	−0.0998	0.284	0.491
Posterolateral Cortical Amygdaloid Area	0.00306	0.778	0.883	−4.31e-05	0.842	0.922	−0.0152	0.305	0.508
Posteromedial Cortical Amygdaloid Area	−0.0153	0.162	0.346	7.85e-05	0.709	0.839	0.0142	0.34	0.541
Perirhinal Cortex	−0.0113	0.53	0.711	−0.000155	0.651	0.8	0.00876	0.721	0.847
Parietal Cortex: Posterior Area: Rostral Part	0.000557	0.499	0.683	−7.96e-06	0.626	0.786	−0.00116	0.305	0.508
Rostral Amygdalopiriform Area	−0.00205	0.679	0.818	1.1e-05	0.915	0.963	−0.00415	0.54	0.717
Primary Somatosensory Cortex	−0.00601	0.852	0.928	0.000269	0.664	0.808	−0.0314	0.477	0.664
Primary Somatosensory Cortex: Barrel Field	−0.00245	0.971	0.989	0.000288	0.82	0.907	−0.053	0.56	0.732
Primary Somatosensory Cortex: Dysgranular Zone	−0.000311	0.905	0.956	2.43e-05	0.625	0.785	−0.00235	0.507	0.69
Primary Somatosensory Cortex: Forelimb Region	−0.0168	0.612	0.774	0.000401	0.532	0.712	−0.0226	0.616	0.777
Primary Somatosensory Cortex: Hindlimb Region	−0.00138	0.952	0.979	−1.33e-06	0.998	0.998	−0.0217	0.485	0.672
Primary Somatosensory Cortex: Jaw Region	−0.00538	0.339	0.541	6.81e-05	0.538	0.715	0.0013	0.865	0.936
Primary Somatosensory Cortex: Shoulder Region	0.000209	0.92	0.966	−7.88e-06	0.846	0.924	−0.0023	0.419	0.613
Primary Somatosensory Cortex: Trunk Region	0.00358	0.429	0.622	−7.74e-05	0.387	0.586	−0.00605	0.328	0.53
Primary Somatosensory Cortex: Upper Lip Region	−0.0055	0.882	0.946	−4.15e-05	0.953	0.979	−0.00749	0.883	0.946
Secondary Somatosensory Cortex	0.00276	0.948	0.979	9.23e-06	0.991	0.995	0.000659	0.991	0.995
Temporal Association Area	−0.0169	0.45	0.638	0.000292	0.499	0.683	−0.00383	0.9	0.955
Primary Visual Cortex	0.0194	0.394	0.59	−0.000332	0.451	0.64	−0.0283	0.363	0.563
Primary Visual Cortex: Binocular Area	0.00219	0.897	0.953	0.000282	0.384	0.582	−0.0188	0.415	0.609
Primary Visual Cortex: Monocular Area	−8.84e-05	0.996	0.998	4.79e-05	0.892	0.95	−0.00844	0.734	0.855
Secondary Visual Cortex: Lateral Area	−0.00581	0.795	0.892	0.000489	0.254	0.459	−0.0278	0.363	0.562
Secondary Visual Cortex: Mediolateral Area	0.000176	0.985	0.994	−8.42e-05	0.654	0.802	−0.00221	0.865	0.936
Secondary Visual Cortex: Mediomedial Area	0.00571	0.783	0.886	−0.000179	0.66	0.805	−0.00872	0.758	0.87
Claustrum: Ventral Part	−0.00391	0.425	0.618	5e-05	0.577	0.746	0.0103	0.123	0.289
Ventral Nucleus Of The Endopiriform Claustrum	−0.00172	0.623	0.783	1.87e-07	0.998	0.998	0.0017	0.722	0.847
Ventral Intermediate Entorhinal Cortex	−0.0134	0.185	0.377	0.000168	0.408	0.603	0.0128	0.353	0.554
Ventral Orbital Cortex	0.00651	0.633	0.79	−4.13e-05	0.878	0.944	−0.0262	0.16	0.344
Ventral Tenia Tecta	0.00075	0.455	0.644	−1.89e-05	0.349	0.551	−0.00236	0.0858	0.229

Supplementary Table S.3 Table of 159 segmented atlas structures affected by metformin treatment (MET19). Columns of the table contain information for the coefficient estimates for metformin treatment, interactions with age or radiation and corresponding test statistics: p value (p) and FDR adjusted p values (q).

Structure	$\beta_{SEX:7Gy:MET16}$	$p_{SEX:7Gy:MET16}$	$q_{SEX:7Gy:MET16}$	$\beta_{SEX:7Gy:MET16:Growth}$	$p_{SEX:7Gy:MET16:Growth}$	$q_{SEX:7Gy:MET16:Growth}$
Amygdala	0.232	0.159	0.343	−0.00497	0.111	0.27
Anterior Commissure: Pars Anterior	0.0243	0.317	0.519	0.000308	0.514	0.698
Anterior Commissure: Pars Posterior	0.00788	0.311	0.512	3.42e-05	0.825	0.91
Basal Forebrain	0.175	0.0527	0.165	−0.00171	0.321	0.524
Bed Nucleus Of Stria Terminalis	0.0827	0.00118	0.00689	−0.000638	0.194	0.389
Cerebellar Peduncle: Inferior	0.0398	0.0397	0.135	−0.000949	0.0173	0.0706
Cerebellar Peduncle: Middle	0.0711	0.0255	0.0952	−0.000963	0.129	0.297
Cerebellar Peduncle: Superior	0.0466	0.0249	0.0936	−0.000864	0.0363	0.126
Cerebral Aqueduct	0.0213	0.224	0.422	−0.000253	0.486	0.673
Cerebral Peduncle	0.0697	0.0839	0.225	−0.00076	0.32	0.523
Colliculus: Inferior	0.169	0.091	0.236	−0.00233	0.256	0.461
Colliculus: Superior	0.635	0.00979	0.0441	−0.00509	0.308	0.51
Corpus Callosum	0.579	0.00522	0.0255	−0.0045	0.246	0.451
Corticospinal Tract/Pyramids	0.0812	0.0058	0.0281	−0.00168	0.0038	0.0195
Cuneate Nucleus	0.0092	0.0934	0.24	−0.000196	0.0936	0.24
Dentate Gyrus Of Hippocampus	0.18	0.00242	0.0131	−0.00154	0.176	0.366
Facial Nerve (Cranial Nerve 7)	0.0164	0.00263	0.0142	−0.000321	0.00476	0.0237
Fasciculus Retroflexus	0.0143	0.00261	0.0141	−0.000173	0.06	0.18
Fimbria	0.218	0.00215	0.0118	−0.00349	0.0117	0.0511
Fornix	0.0365	0.000637	0.00386	−0.000304	0.136	0.309
Fourth Ventricle	0.0527	0.0441	0.146	−0.00111	0.0481	0.155
Fundus Of Striatum	−0.000288	0.907	0.957	3.79e-05	0.44	0.631
Globus Pallidus	0.131	0.0156	0.0654	−0.00132	0.194	0.389
Habenular Commissure	0.0063	0.009	0.041	−4.12e-05	0.38	0.579
Hippocampus	0.632	0.034	0.12	−0.00725	0.191	0.385
Hypothalamus	0.497	0.00295	0.0157	−0.00348	0.263	0.468
Inferior Olivary Complex	0.00618	0.111	0.27	−0.000235	0.00316	0.0167
Internal Capsule	0.106	0.0628	0.185	−0.000764	0.475	0.663
Interpedunclar Nucleus	0.00943	0.156	0.339	−7.28e-05	0.582	0.751
Lateral Olfactory Tract	0.022	0.0889	0.233	−0.00012	0.631	0.789
Lateral Septum	0.181	0.000413	0.00257	−0.0025	0.00839	0.0387
Lateral Ventricle	0.246	0.019	0.076	−0.00539	0.00982	0.0442
Mammillary Bodies	0.00745	0.466	0.653	0.000106	0.6	0.766
Mammilothalamic Tract	0.00923	0.0399	0.135	−4.42e-06	0.959	0.982
Medial Lemniscus/Medial Longitudinal Fasciculus	0.118	0.0255	0.0954	−0.00266	0.00893	0.0408
Medial Septum	0.0462	0.0196	0.0772	−0.000302	0.418	0.612
Medulla	1.45	0.00972	0.0439	−0.036	0.0016	0.00905
Midbrain	0.504	0.0284	0.104	−0.00491	0.256	0.461
Nucleus Accumbens	0.063	0.422	0.616	3.17e-05	0.983	0.993
Olfactory Bulbs	0.433	0.327	0.53	0.0073	0.404	0.6
Olfactory Tubercle	0.0446	0.531	0.711	0.00041	0.775	0.882
Optic Tract	0.063	0.0172	0.0703	−0.000742	0.135	0.308
Periaqueductal Grey	0.22	0.0133	0.0569	−0.0021	0.237	0.441
Pons	1.23	0.000921	0.00546	−0.021	0.00445	0.0224
Pontine Nucleus	0.0594	0.00131	0.00756	−0.000805	0.0306	0.111
Posterior Commissure	0.00996	0.0121	0.0529	−0.000121	0.119	0.282
Pre-Para Subiculum	0.0816	0.105	0.26	−0.000708	0.473	0.661
Stratum Granulosum Of Hippocampus	0.044	0.00577	0.0279	−0.000322	0.3	0.505
Stria Medullaris	0.0442	0.012	0.0524	−0.000684	0.0467	0.152
Stria Terminalis	0.0383	0.0301	0.109	−0.000282	0.393	0.59
Striatum	1.09	0.00271	0.0145	−0.00746	0.272	0.478
Subependymale Zone / Rhinocele	0.00038	0.8	0.896	2.55e-05	0.405	0.601
Superior Olivary Complex	0.0553	2e-04	0.00127	−0.000722	0.0191	0.0762

Structure	$\beta_{SEX:7Gy:MET16}$	$p_{SEX:7Gy:MET16}$	$q_{SEX:7Gy:MET16}$	$\beta_{SEX:7Gy:MET16:Growth}$	$p_{SEX:7Gy:MET16:Growth}$	$q_{SEX:7Gy:MET16:Growth}$
Thalamus	1.04	0.00179	0.01	−0.0094	0.136	0.308
Third Ventricle	0.0695	0.0291	0.106	−0.00077	0.238	0.442
Ventral Tegmental Decussation	0.00583	0.118	0.281	−5.86e-05	0.429	0.622
Lobules 1-2: Lingula And Central Lobule (Ventral)	0.0531	0.354	0.556	0.000456	0.69	0.827
Lobule 3: Central Lobule (Dorsal)	0.103	0.0874	0.231	−0.00138	0.29	0.496
Lobules 4-5: Culmen (Ventral And Dorsal)	0.311	0.00344	0.0179	−0.00881	7.87e-05	0.000518
Lobule 6: Declive	0.131	0.0579	0.176	−0.00479	0.00119	0.00689
Lobule 7: Tuber (Or Folium)	0.00145	0.958	0.981	−5.59e-05	0.923	0.967
Lobule 8: Pyramis	0.000651	0.989	0.995	0.00108	0.301	0.506
Lobule 9: Uvula	0.0959	0.187	0.379	−0.000525	0.737	0.858
Lobule 10: Nodulus	0.116	0.0107	0.0474	−0.00127	0.194	0.389
Anterior Lobule (Lobules 4-5)	0.0619	0.0722	0.203	−0.000319	0.658	0.804
Simple Lobule (Lobule 6)	0.205	0.0164	0.0678	−0.00385	0.0314	0.112
Crus 1: Ansiform Lobule (Lobule 6)	0.225	0.013	0.0561	−0.00531	0.00464	0.0232
Crus 2: Ansiform Lobule (Lobule 7)	0.176	0.0314	0.112	−0.00559	0.00121	0.00702
Paramedian Lobule (Lobule 7)	0.145	0.21	0.407	−0.0036	0.136	0.309
Copula: Pyramis (Lobule 8)	0.0748	0.226	0.425	−0.00137	0.291	0.497
Flocculus (Fl)	0.0519	0.0276	0.102	−0.00109	0.0196	0.0773
Paraflocculus (Pfl)	0.395	0.00147	0.00839	−0.00202	0.407	0.603
Trunk Of Arbor Vita	0.251	0.0182	0.0731	−0.00408	0.0695	0.198
Lobule 1-2 White Matter	0.0027	0.516	0.699	9.93e-05	0.225	0.423
Lobule 3 White Matter	0.00723	0.391	0.588	−2.86e-05	0.876	0.943
Trunk Of Lobules 1-3 White Matter	0.00732	0.202	0.398	−7.14e-06	0.953	0.979
Lobules 4-5 White Matter	0.0478	0.0258	0.0959	−0.00115	0.0151	0.0637
Lobules 6-7 White Matter	0.0357	0.0942	0.241	−0.0011	0.016	0.0666
Lobule 8 White Matter	−0.00159	0.649	0.799	8.35e-05	0.262	0.467
Trunk Of Lobules 6-8 White Matter	0.00286	0.385	0.583	−6.38e-06	0.93	0.97
Lobule 9 White Matter	0.00684	0.365	0.564	7.14e-05	0.66	0.805
Lobule 10 White Matter	0.00932	0.0102	0.0456	−7.89e-05	0.312	0.514
Anterior Lobule White Matter	0.00459	0.113	0.274	−2.34e-05	0.701	0.833
Simple Lobule White Matter	0.0212	0.0378	0.13	−0.000355	0.0984	0.249
Crus 1 White Matter	0.0277	0.017	0.0698	−0.000511	0.0341	0.12
Trunk Of Simple And Crus 1 White Matter	0.0107	0.0376	0.129	−0.000181	0.097	0.246
Crus 2 White Matter	0.0161	0.0445	0.146	−0.000455	0.00796	0.037
Paramedian Lobule	0.0039	0.397	0.593	−0.000165	0.0864	0.23
Trunk Of Crus 2 And Paramedian White Matter	0.0146	0.128	0.297	−0.000356	0.0813	0.22
Copula White Matter	0.00225	0.392	0.589	−2.12e-05	0.704	0.835
Paraflocculus White Matter	0.0255	0.00938	0.0426	−0.000264	0.178	0.368
Flocculus White Matter	0.00291	0.106	0.261	−7.63e-05	0.0312	0.112
Dentate Nucleus	0.0194	0.0293	0.107	−0.00047	0.0152	0.0639
Nucleus Interpositus	0.0365	0.0122	0.053	−0.000705	0.0258	0.096
Fastigial Nucleus	0.0331	0.0127	0.0547	−0.000546	0.0535	0.167
Cingulate Cortex: Area 24A	0.0958	0.0161	0.0669	−0.000742	0.324	0.526
Cingulate Cortex: Area 24A'	0.0426	0.00722	0.0339	−0.000337	0.278	0.484
Cingulate Cortex: Area 24B	0.0739	0.0226	0.0869	−0.000572	0.365	0.564
Cingulate Cortex: Area 24B'	0.0327	0.0168	0.0692	−0.000243	0.376	0.575
Cingulate Cortex: Area 25	0.0247	0.0163	0.0672	−0.000153	0.43	0.622
Cingulate Cortex: Area 29A	0.0605	0.0179	0.072	−0.000485	0.356	0.557
Cingulate Cortex: Area 29B	0.022	0.0538	0.168	−0.000136	0.549	0.724
Cingulate Cortex: Area 29C	0.0489	0.181	0.371	7.48e-06	0.992	0.995
Cingulate Cortex: Area 30	0.132	0.031	0.112	−0.000762	0.531	0.711
Cingulate Cortex: Area 32	0.16	0.00739	0.0346	−0.00185	0.115	0.277
Amygdalopiriform Transition Area	0.012	0.494	0.678	−0.000161	0.656	0.803

Structure	$\beta_{SEX:7Gy:MET16}$	$p_{SEX:7Gy:MET16}$	$q_{SEX:7Gy:MET16}$	$\beta_{SEX:7Gy:MET16:Growth}$	$p_{SEX:7Gy:MET16:Growth}$	$q_{SEX:7Gy:MET16:Growth}$
Primary Auditory Cortex	0.0646	0.02	0.0785	−0.000561	0.307	0.51
Secondary Auditory Cortex: Dorsal Area	0.0751	0.0128	0.0552	−0.000718	0.223	0.421
Secondary Auditory Cortex: Ventral Area	0.064	0.0908	0.236	−0.000496	0.513	0.695
Caudomedial Entorhinal Cortex	0.105	0.416	0.61	−0.00175	0.49	0.676
Cingulum	0.0501	0.00129	0.00745	−0.000456	0.126	0.293
Claustrum	0.0169	0.0627	0.185	−0.000132	0.478	0.666
Cortex-Amygdala Transition Zones	−0.00695	0.724	0.848	−0.000214	0.59	0.757
Claustrum: Dorsal Part	0.0102	0.0517	0.163	9.08e-07	0.993	0.995
Dorsal Nucleus Of The Endopiriform	0.024	0.271	0.476	0.000282	0.495	0.68
Dorsal Intermediate Entorhinal Cortex	0.0481	0.2	0.395	−0.00123	0.101	0.254
Dorsolateral Entorhinal Cortex	0.0916	0.0561	0.173	−0.00155	0.0986	0.249
Dorsolateral Orbital Cortex	0.0355	0.168	0.354	−0.000755	0.17	0.358
Dorsal Tenia Tecta	0.0131	0.352	0.554	−4.4e-05	0.869	0.939
Ectorhinal Cortex	0.0359	0.442	0.632	−0.000455	0.614	0.775
Frontal Cortex: Area 3	0.0377	0.0118	0.0515	−0.000549	0.0652	0.19
Frontal Association Cortex	0.431	0.0317	0.113	−0.00741	0.0767	0.212
Intermediate Nucleus Of The Endopiriform Claustrum	0.00323	0.758	0.87	0.000254	0.241	0.447
Insular Region: Not Subdivided	0.321	0.0182	0.0733	−0.00181	0.483	0.67
Lateral Orbital Cortex	0.194	0.0566	0.174	−0.00409	0.0556	0.172
Lateral Parietal Association Cortex	0.0136	0.0043	0.0217	−0.000122	0.202	0.398
Primary Motor Cortex	0.433	0.00217	0.0119	−0.00381	0.166	0.352
Secondary Motor Cortex	0.408	0.00116	0.00678	−0.00247	0.309	0.511
Medial Entorhinal Cortex	0.012	0.561	0.732	−0.000659	0.11	0.269
Medial Orbital Cortex	0.114	0.0217	0.0842	−0.002	0.0476	0.154
Medial Parietal Association Cortex	0.0312	0.000814	0.00489	−0.000273	0.153	0.334
Piriform Cortex	0.124	0.463	0.651	0.000188	0.954	0.98
Posterolateral Cortical Amygdaloid Area	0.0297	0.27	0.475	−0.000688	0.206	0.402
Posteromedial Cortical Amygdaloid Area	0.0232	0.391	0.588	−0.000857	0.105	0.26
Perirhinal Cortex	0.038	0.393	0.59	−0.000533	0.536	0.714
Parietal Cortex: Posterior Area: Rostral Part	0.0056	0.00638	0.0305	−4.36e-05	0.287	0.494
Rostral Amygdalopiriform Area	0.00558	0.651	0.8	−8.6e-05	0.738	0.858
Primary Somatosensory Cortex	0.229	0.00423	0.0215	−0.00304	0.0514	0.163
Primary Somatosensory Cortex: Barrel Field	0.473	0.00427	0.0217	−0.00457	0.15	0.331
Primary Somatosensory Cortex: Dysgranular Zone	0.0189	0.00331	0.0172	−0.000137	0.27	0.475
Primary Somatosensory Cortex: Forelimb Region	0.256	0.00189	0.0106	−0.00232	0.15	0.331
Primary Somatosensory Cortex: Hindlimb Region	0.177	0.00174	0.00979	−0.00189	0.091	0.236
Primary Somatosensory Cortex: Jaw Region	0.0402	0.00411	0.0209	−0.000457	0.0996	0.251
Primary Somatosensory Cortex: Shoulder Region	0.0125	0.0162	0.0669	−0.00012	0.238	0.442
Primary Somatosensory Cortex: Trunk Region	0.0318	0.0048	0.0238	−0.000251	0.263	0.467
Primary Somatosensory Cortex: Upper Lip Region	0.251	0.00656	0.0313	−0.0041	0.0207	0.0811
Secondary Somatosensory Cortex	0.26	0.0132	0.0564	−0.00325	0.101	0.252
Temporal Association Area	0.047	0.397	0.593	−0.000219	0.84	0.921
Primary Visual Cortex	0.0646	0.253	0.458	−0.000494	0.655	0.802
Primary Visual Cortex: Binocular Area	0.0807	0.0535	0.167	−0.000839	0.303	0.507
Primary Visual Cortex: Monocular Area	0.13	0.00397	0.0203	−0.00138	0.12	0.285
Secondary Visual Cortex: Lateral Area	0.0895	0.107	0.262	−0.000604	0.575	0.744
Secondary Visual Cortex: Mediolateral Area	0.0648	0.00623	0.0299	−0.000334	0.479	0.666
Secondary Visual Cortex: Mediomedial Area	0.1	0.0515	0.163	−0.00045	0.66	0.805
Claustrum: Ventral Part	0.0253	0.0371	0.128	9.73e-05	0.666	0.808
Ventral Nucleus Of The Endopiriform Claustrum	0.00763	0.378	0.578	−5.87e-06	0.972	0.989
Ventral Intermediate Entorhinal Cortex	0.0179	0.474	0.662	−0.000992	0.051	0.162
Ventral Orbital Cortex	0.0765	0.0239	0.0907	−0.00129	0.0574	0.175
Ventral Tenia Tecta	0.00171	0.492	0.677	−3.45e-05	0.495	0.68

Supplementary Table S.4 Table of 159 segmented atlas structures. Columns of the table contain information for the coefficients estimates for the three-way or four-way interaction effects of sex, radiation, age and metformin treatment (MET16) and corresponding test statistics: p value (p) and FDR adjusted p values (q).

Structure	$\beta_{SEX:7Gy:MET19}$	$p_{SEX:7Gy:MET19}$	$q_{SEX:7Gy:MET19}$	$\beta_{SEX:7Gy:MET19:Growth}$	$p_{SEX:7Gy:MET19:Growth}$	$q_{SEX:7Gy:MET19:Growth}$
Amygdala	0.15	0.366	0.565	−0.00196	0.55	0.724
Anterior Commissure: Pars Anterior	0.00631	0.797	0.894	0.000419	0.399	0.595
Anterior Commissure: Pars Posterior	0.00201	0.799	0.895	3.94e-05	0.808	0.901
Basal Forebrain	0.257	0.00493	0.0243	−0.00215	0.235	0.438
Bed Nucleus Of Stria Terminalis	0.043	0.0945	0.242	−0.000408	0.429	0.622
Cerebellar Peduncle: Inferior	0.027	0.168	0.354	−0.00078	0.0623	0.184
Cerebellar Peduncle: Middle	0.00872	0.786	0.889	−0.000502	0.451	0.64
Cerebellar Peduncle: Superior	0.0188	0.371	0.57	−0.000512	0.237	0.441
Cerebral Aqueduct	0.0162	0.359	0.56	−0.000431	0.26	0.467
Cerebral Peduncle	−0.00228	0.955	0.98	0.000347	0.666	0.808
Colliculus: Inferior	0.102	0.312	0.513	−0.00209	0.333	0.533
Colliculus: Superior	0.385	0.122	0.286	−0.00609	0.245	0.451
Corpus Callosum	0.126	0.546	0.721	−0.000255	0.95	0.979
Corticospinal Tract/Pyramids	0.0493	0.0971	0.247	−0.000526	0.388	0.587
Cuneate Nucleus	0.0105	0.0595	0.179	−0.000251	0.0406	0.137
Dentate Gyrus Of Hippocampus	0.0618	0.302	0.506	−0.00147	0.22	0.418
Facial Nerve (Cranial Nerve 7)	0.00452	0.409	0.605	−0.00016	0.178	0.368
Fasciculus Retroflexus	0.0146	0.00237	0.0129	−0.000209	0.0311	0.112
Fimbria	0.00222	0.975	0.991	−2.6e-05	0.986	0.994
Fornix	0.0146	0.174	0.363	−0.000209	0.33	0.532
Fourth Ventricle	0.0532	0.0444	0.146	−0.00134	0.0226	0.0869
Fundus Of Striatum	0.00148	0.554	0.727	2.19e-05	0.671	0.813
Globus Pallidus	−0.0253	0.644	0.796	0.000632	0.553	0.726
Habenular Commissure	0.0036	0.139	0.313	−4.63e-05	0.349	0.551
Hippocampus	0.143	0.634	0.79	−0.0041	0.482	0.669
Hypothalamus	0.308	0.0682	0.196	−0.0021	0.521	0.702
Inferior Olivary Complex	0.00573	0.144	0.32	−0.000103	0.216	0.413
Internal Capsule	−0.0358	0.533	0.712	0.00125	0.266	0.47
Interpeduncular Nucleus	0.00574	0.393	0.59	−5.49e-05	0.693	0.828
Lateral Olfactory Tract	0.0012	0.927	0.968	0.000167	0.523	0.704
Lateral Septum	0.0348	0.499	0.683	−0.00138	0.165	0.351
Lateral Ventricle	−0.00935	0.93	0.97	7.09e-05	0.974	0.991
Mammillary Bodies	0.00853	0.41	0.605	−2.57e-05	0.904	0.956
Mammilothalamic Tract	0.00752	0.0973	0.247	−7.42e-05	0.41	0.605
Medial Lemniscus/Medial Longitudinal Fasciculus	0.0817	0.125	0.291	−0.000641	0.548	0.723
Medial Septum	0.0396	0.0476	0.154	−0.000252	0.52	0.702
Medulla	1	0.0775	0.214	−0.0195	0.103	0.257
Midbrain	0.317	0.173	0.361	−0.00378	0.405	0.601
Nucleus Accumbens	0.136	0.0856	0.228	−0.000722	0.653	0.801
Olfactory Bulbs	−0.136	0.761	0.872	0.00651	0.479	0.666
Olfactory Tubercle	0.142	0.0483	0.155	−0.00119	0.431	0.623
Optic Tract	0.00888	0.739	0.858	−9.79e-05	0.851	0.927
Periaqueductal Grey	0.162	0.0713	0.201	−0.0026	0.164	0.349
Pons	0.52	0.163	0.349	−0.0147	0.057	0.175
Pontine Nucleus	0.0283	0.129	0.297	−0.000612	0.117	0.28
Posterior Commissure	0.00817	0.0419	0.14	−0.000121	0.138	0.311
Pre-Para Subiculum	0.0297	0.559	0.731	−0.00103	0.322	0.525
Stratum Granulosum Of Hippocampus	0.0193	0.229	0.43	−0.000393	0.228	0.429
Stria Medullaris	0.0321	0.0708	0.2	−0.00042	0.245	0.451
Stria Terminalis	−0.000621	0.972	0.989	0.000385	0.267	0.471
Striatum	0.278	0.448	0.637	−0.000102	0.989	0.995
Subependymale Zone / Rhinocele	0.000193	0.898	0.954	5.56e-05	0.084	0.225
Superior Olivary Complex	0.0361	0.0161	0.0669	−0.000608	0.0601	0.18

Structure	$\beta_{SEX:7Gy:MET19}$	$p_{SEX:7Gy:MET19}$	$q_{SEX:7Gy:MET19}$	$\beta_{SEX:7Gy:MET19:Growth}$	$p_{SEX:7Gy:MET19:Growth}$	$q_{SEX:7Gy:MET19:Growth}$
Thalamus	0.591	0.0776	0.214	−0.00885	0.181	0.372
Third Ventricle	0.0245	0.447	0.636	1.86e-05	0.978	0.993
Ventral Tegmental Decussation	0.00112	0.765	0.876	−5.55e-05	0.476	0.664
Lobules 1-2: Lingula And Central Lobule (Ventral)	0.0071	0.902	0.955	−0.000841	0.485	0.672
Lobule 3: Central Lobule (Dorsal)	0.0378	0.534	0.713	−0.00137	0.314	0.515
Lobules 4-5: Culmen (Ventral And Dorsal)	0.237	0.0269	0.0995	−0.00532	0.0225	0.0867
Lobule 6: Declive	0.128	0.068	0.196	−0.00261	0.0915	0.237
Lobule 7: Tuber (Or Folium)	0.0448	0.103	0.257	−8.11e-05	0.894	0.952
Lobule 8: Pyramis	0.0535	0.283	0.49	−0.000402	0.713	0.842
Lobule 9: Uvula	0.106	0.149	0.328	−0.00179	0.276	0.482
Lobule 10: Nodulus	0.096	0.0374	0.129	−0.00241	0.0194	0.0766
Anterior Lobule (Lobules 4-5)	0.0213	0.54	0.717	1.95e-05	0.979	0.993
Simple Lobule (Lobule 6)	0.0929	0.283	0.49	−0.00192	0.305	0.508
Crus 1: Ansiform Lobule (Lobule 6)	0.126	0.168	0.353	−0.00394	0.0449	0.147
Crus 2: Ansiform Lobule (Lobule 7)	0.128	0.122	0.287	−0.0031	0.0863	0.23
Paramedian Lobule (Lobule 7)	0.114	0.331	0.532	−0.00362	0.154	0.336
Copula: Pyramis (Lobule 8)	0.0582	0.352	0.554	−0.00201	0.141	0.316
Flocculus (Fl)	0.0241	0.312	0.513	−0.000846	0.0838	0.225
Paraflocculus (Pfl)	0.304	0.0153	0.0642	−0.00445	0.0824	0.222
Trunk Of Arbor Vita	0.152	0.157	0.342	−0.00281	0.233	0.436
Lobule 1-2 White Matter	−0.000408	0.923	0.967	−5.77e-05	0.502	0.685
Lobule 3 White Matter	0.00246	0.773	0.882	−0.000174	0.366	0.565
Trunk Of Lobules 1-3 White Matter	0.00199	0.731	0.854	−6.14e-05	0.63	0.789
Lobules 4-5 White Matter	0.0368	0.0895	0.234	−0.000713	0.15	0.33
Lobules 6-7 White Matter	0.0452	0.0365	0.127	−0.000689	0.151	0.332
Lobule 8 White Matter	0.00456	0.199	0.395	−5.04e-05	0.519	0.701
Trunk Of Lobules 6-8 White Matter	0.00433	0.196	0.391	−5.2e-05	0.499	0.683
Lobule 9 White Matter	0.00544	0.476	0.664	−0.000126	0.461	0.649
Lobule 10 White Matter	0.00619	0.0913	0.237	−0.000166	0.043	0.143
Anterior Lobule White Matter	0.00192	0.512	0.695	−1.36e-05	0.832	0.915
Simple Lobule White Matter	0.0117	0.258	0.465	−0.000159	0.479	0.666
Crus 1 White Matter	0.0176	0.133	0.304	−0.000432	0.0875	0.231
Trunk Of Simple And Crus 1 White Matter	0.00763	0.143	0.32	−0.000173	0.132	0.303
Crus 2 White Matter	0.0107	0.186	0.378	−0.000283	0.115	0.277
Paramedian Lobule	0.00448	0.336	0.537	−0.000129	0.202	0.398
Trunk Of Crus 2 And Paramedian White Matter	0.00945	0.33	0.532	−0.000297	0.165	0.351
Copula White Matter	0.0029	0.276	0.482	−6.32e-05	0.28	0.486
Paraflocculus White Matter	0.0186	0.0609	0.182	−0.000426	0.0393	0.134
Flocculus White Matter	0.00187	0.305	0.508	−7.46e-05	0.0448	0.147
Dentate Nucleus	0.0102	0.26	0.466	−0.000281	0.165	0.351
Nucleus Interpositus	0.0229	0.12	0.284	−0.00032	0.335	0.535
Fastigial Nucleus	0.0246	0.0667	0.193	−0.000411	0.166	0.352
Cingulate Cortex: Area 24A	0.0924	0.0218	0.0843	−0.000866	0.273	0.478
Cingulate Cortex: Area 24A'	0.0354	0.0271	0.0999	−0.000421	0.198	0.394
Cingulate Cortex: Area 24B	0.0968	0.0032	0.0169	−0.000814	0.22	0.418
Cingulate Cortex: Area 24B'	0.0381	0.00597	0.0288	−0.000351	0.223	0.421
Cingulate Cortex: Area 25	0.0145	0.161	0.346	−0.000189	0.352	0.554
Cingulate Cortex: Area 29A	0.0685	0.00816	0.0377	−0.00131	0.0179	0.072
Cingulate Cortex: Area 29B	0.0263	0.0225	0.0867	−0.000499	0.0369	0.128
Cingulate Cortex: Area 29C	0.0955	0.00995	0.0446	−0.00144	0.0642	0.188
Cingulate Cortex: Area 30	0.131	0.0349	0.122	−0.00232	0.0699	0.198
Cingulate Cortex: Area 32	0.14	0.0201	0.0788	−0.00175	0.156	0.341
Amygdalopiriform Transition Area	0.00252	0.887	0.947	−0.000251	0.508	0.69

Structure	$\beta_{SEX:7Gy:MET19}$	$p_{SEX:7Gy:MET19}$	$q_{SEX:7Gy:MET19}$	$\beta_{SEX:7Gy:MET19:Growth}$	$p_{SEX:7Gy:MET19:Growth}$	$q_{SEX:7Gy:MET19:Growth}$
Primary Auditory Cortex	0.031	0.269	0.474	−0.00022	0.703	0.834
Secondary Auditory Cortex: Dorsal Area	0.0313	0.304	0.508	−0.000233	0.707	0.838
Secondary Auditory Cortex: Ventral Area	0.0399	0.297	0.502	−0.000464	0.56	0.732
Caudomedial Entorhinal Cortex	−0.0841	0.521	0.702	0.00121	0.65	0.799
Cingulum	0.0199	0.205	0.401	−0.00041	0.19	0.384
Claustrum	0.0119	0.194	0.389	−0.000173	0.376	0.575
Cortex-Amygdala Transition Zones	0.0192	0.334	0.535	−0.000306	0.465	0.652
Claustrum: Dorsal Part	0.00714	0.178	0.368	−3.47e-05	0.739	0.858
Dorsal Nucleus Of The Endopiriform	0.0313	0.156	0.34	8.89e-05	0.838	0.919
Dorsal Intermediate Entorhinal Cortex	−0.0168	0.658	0.804	−0.000804	0.307	0.51
Dorsolateral Entorhinal Cortex	−0.0324	0.503	0.686	−0.000427	0.665	0.808
Dorsolateral Orbital Cortex	0.0281	0.281	0.487	−0.000677	0.242	0.447
Dorsal Tenia Tecta	0.0262	0.0659	0.192	−0.000161	0.567	0.737
Ectorhinal Cortex	−0.00103	0.983	0.993	−2.87e-05	0.976	0.991
Frontal Cortex: Area 3	0.0306	0.043	0.143	−0.000591	0.0587	0.177
Frontal Association Cortex	0.356	0.0797	0.217	−0.00963	0.0287	0.105
Intermediate Nucleus Of The Endopiriform Claustrum	0.0135	0.203	0.398	1.63e-05	0.943	0.976
Insular Region: Not Subdivided	0.294	0.0322	0.115	−0.00348	0.199	0.395
Lateral Orbital Cortex	0.191	0.0646	0.189	−0.00355	0.113	0.273
Lateral Parietal Association Cortex	0.012	0.0125	0.0541	−0.000142	0.16	0.344
Primary Motor Cortex	0.428	0.00269	0.0145	−0.00549	0.0579	0.176
Secondary Motor Cortex	0.44	0.00054	0.00332	−0.0052	0.042	0.14
Medial Entorhinal Cortex	0.000792	0.97	0.989	−0.000129	0.766	0.876
Medial Orbital Cortex	0.0774	0.123	0.289	−0.00144	0.175	0.364
Medial Parietal Association Cortex	0.0256	0.0066	0.0315	−0.000379	0.0584	0.177
Piriform Cortex	0.125	0.464	0.652	0.000928	0.787	0.889
Posterolateral Cortical Amygdaloid Area	0.0346	0.203	0.399	−0.00091	0.111	0.271
Posteromedial Cortical Amygdaloid Area	0.0267	0.328	0.53	−0.000702	0.206	0.403
Perirhinal Cortex	0.000948	0.983	0.993	−0.000399	0.66	0.805
Parietal Cortex: Posterior Area: Rostral Part	0.005	0.016	0.0666	−4.14e-05	0.336	0.537
Rostral Amygdalopiriform Area	0.00531	0.671	0.812	−0.00033	0.223	0.421
Primary Somatosensory Cortex	0.179	0.0268	0.0992	−0.00326	0.0468	0.152
Primary Somatosensory Cortex: Barrel Field	0.31	0.0632	0.186	−0.00263	0.432	0.623
Primary Somatosensory Cortex: Dysgranular Zone	0.0179	0.00607	0.0291	−0.00023	0.0794	0.217
Primary Somatosensory Cortex: Forelimb Region	0.206	0.0135	0.0574	−0.00245	0.148	0.327
Primary Somatosensory Cortex: Hindlimb Region	0.128	0.0253	0.0947	−0.00137	0.246	0.451
Primary Somatosensory Cortex: Jaw Region	0.0384	0.00663	0.0316	−0.000585	0.0451	0.148
Primary Somatosensory Cortex: Shoulder Region	0.011	0.0363	0.126	−0.000104	0.328	0.53
Primary Somatosensory Cortex: Trunk Region	0.0269	0.0183	0.0734	−0.000244	0.3	0.505
Primary Somatosensory Cortex: Upper Lip Region	0.21	0.0244	0.092	−0.00319	0.0865	0.23
Secondary Somatosensory Cortex	0.173	0.102	0.255	−0.00223	0.284	0.49
Temporal Association Area	0.00229	0.967	0.987	1.05e-05	0.993	0.995
Primary Visual Cortex	0.0627	0.272	0.478	−0.000611	0.599	0.765
Primary Visual Cortex: Binocular Area	0.0848	0.0449	0.147	−0.000689	0.42	0.615
Primary Visual Cortex: Monocular Area	0.124	0.00683	0.0323	−0.00126	0.175	0.364
Secondary Visual Cortex: Lateral Area	0.0459	0.412	0.607	−0.00015	0.895	0.952
Secondary Visual Cortex: Mediolateral Area	0.0634	0.00815	0.0377	−0.000637	0.199	0.395
Secondary Visual Cortex: Mediomedial Area	0.0937	0.0725	0.203	−0.00108	0.315	0.517
Claustrum: Ventral Part	0.0216	0.0777	0.214	−5.91e-05	0.803	0.897
Ventral Nucleus Of The Endopiriform Claustrum	−0.00202	0.818	0.906	0.000161	0.36	0.561
Ventral Intermediate Entorhinal Cortex	0.0018	0.943	0.976	−0.000522	0.327	0.53
Ventral Orbital Cortex	0.0683	0.0461	0.15	−0.000657	0.356	0.557
Ventral Tenia Tecta	0.00441	0.0801	0.218	−6.61e-05	0.213	0.411

Supplementary Table S.5 Table of 159 segmented atlas structures. Columns of the table contain information for the coefficients estimates for the three-way or four-way interaction effects of sex, radiation, age and metformin treatment (MET19) and corresponding test statistics: p value (p) and FDR adjusted p values (q).