Genotype —	Brain Vacuole Area (Median), %		
	5 day	30 day	45 day
w ¹¹¹⁸ ; UAS-sws-RNAi	0.45	0.64	0.89
w ¹¹¹⁸ ; repo-GAL4	0.26	0.71	0.54
repo-GAL4; UAS-sws- RNAi	0.49	1.20	2.58
^{w1118} ; NPP-GAL4	0.33	0.54	0.53
NPP-GAL4; UAS-sws- RNAi	0.59	1.09	1.60
w ¹¹¹⁸ ; NPS-GAL4	0.20	0.78	0.48
NPS-GAL4; UAS-sws- RNAi	0.81	0.97	0.80
w ¹¹¹⁸ ; NPC-GAL4	0.19	0.72	0.85
NPC-GAL4; UAS-sws- RNAi	0.47	1.13	1.92

Table S1. The neuropile degeneration index (total vacuole area in brain neuropile) in flies with different genotypes and three ages.



Figure S1. Automated analysis of the SPG nuclei in ImageJ. (A) the minimum size of nuclei is 5 μ m² in the Control and *sws* KD (*UAS-sws-RNAi*). (B) the minimum size of normal nuclei is 10 μ m² in the Control and *sws* KD (*UAS-sws-RNAi*). Scale bar: 25 μ m.



Figure S2. Subperineurial glia morphology under *sws* knockdown in the CNS. (**A**) Visualisation of subperineurial glia in brains of 30-day-old flies marked with membrane GFP (green, UAS-CD8-GFP) and nuclear RFP (red, UAS-RedStinger) expression in SPG (NPS-GAL4) in control and knockdown (UAS-sws-RNAi) flies. White arrows indicate Red-Stinger-positive fragmented nuclei of glia. Scale bar; 25 μ m. (**B**) Analysis number of SPG nuclei (5 μ m² size) in fly brains with *sws* KD(UAS-sws-RNAi). Student t-test, mean ± 95% CI, n = 25.



Figure S3. Longevity assay. (A-D) Survival curves for flies with *sws* KD in all glia (**A**), CG+WG (**B**), PG (**C**) and SPG (**D**). Controls are F1 males from crossing w^{1118} female and *UAS-sws-RNAi* male (dark grey lines) and F1 males from crossing w^{1118} females and one of each of the four used *GAL4* males (light grey lines).



Figure S4. Processes under control of upregulated genes in 30-day-old SPG *sws* KD males compared to *CantonS* control and respective FDR-adjusted p-values of functional enrichment analysis in g:Profiler software.



Figure S5. Processes under control of upregulated genes in 30-day-old SPG *sws* KD males compared to *CantonS* control and respective query gene number from functional enrichment analysis in g:Profiler software.



Figure S6. Processes under control of downregulated genes in 30-day-old SPG *sws* KD males compared to *CantonS* control and respective FDR-adjusted p-values of functional enrichment analysis in g:Profiler software.



Figure S7. Processes under control of downregulated genes in 30-day-old SPG *sws* KD males compared to *CantonS* control and respective query gene number from functional enrichment analysis in g:Profiler software.



Figure S8. Processes under control of upregulated genes in 30-day-old CG+WG *sws* KD males compared to *CantonS* control and respective FDR-adjusted p-values of functional enrichment analysis in g:Profiler software.



oxoacid metabolic process organic acid metabolic process oxidation-reduction process monocarboxylic acid metabolic process lipid metabolic process organic acid biosynthetic process carboxylic acid biosynthetic process small molecule metabolic process fatty acid metabolic process organic acid catabolic process carboxylic acid catabolic process small molecule catabolic process alpha-amino acid metabolic process metabolic process sulfur compound metabolic process cellular lipid metabolic process lipid catabolic process pigment metabolic process pigment biosynthetic process small molecule biosynthetic process cellular amino acid metabolic process cellular response to xenobiotic stimulus xenobiotic metabolic process response to xenobiotic stimulus cellular amino acid catabolic process defense response cellular lipid catabolic process fatty acid biosynthetic process alpha-amino acid catabolic process cellular amino acid biosynthetic process monocarboxylic acid catabolic process monocarboxylic acid biosynthetic process glutathione metabolic process fatty acid beta-oxidation cellular modified amino acid metabolic process carbohydrate metabolic process toxin metabolic process insecticide metabolic process flavonoid metabolic process flavonoid biosynthetic process uronic acid metabolic process glucuronate metabolic process cellular glucuronidation flavonoid glucuronidation secondary metabolite catabolic process toxin catabolic process xenobiotic catabolic process insecticide catabolic process fatty acid catabolic process alpha-amino acid biosynthetic process fatty acid oxidation

carboxylic acid metabolic process

lipid oxidation

Figure S9. Processes under control of upregulated genes in 30-day-old CG+WG *sws* KD males compared to *CantonS* control and respective query gene number from functional enrichment analysis in g:Profiler software.



Figure S10. Processes under control of downregulated genes in 30-day-old CG+WG *sws* KD males compared to *CantonS* control and respective FDR-adjusted p-values of functional enrichment analysis in g:Profiler software.

CG+WG *sws* KD DOWN



Figure S11. Processes under control of downregulated genes in 30-day-old CG+WG *sws* KD males compared to *CantonS* control and respective query gene number from functional enrichment analysis in g:Profiler software.



150 µm.

Figure S12. The typical images of H&E stained paraffin brain sections of *sws* KD brain (*repo-GAL4;UAS-sws-RNAi*) males and respective F1 males from crossing w^{1118} females and *repo-GAL4* males (*white*¹¹¹⁸;*repo-GAL4*) of different age (5, 30, 45 day of imago's life, +25 °C). Vacuoles (areas with no tissue due to neurodegeneration) are marked with arrows. Scale bar: 150 µm.