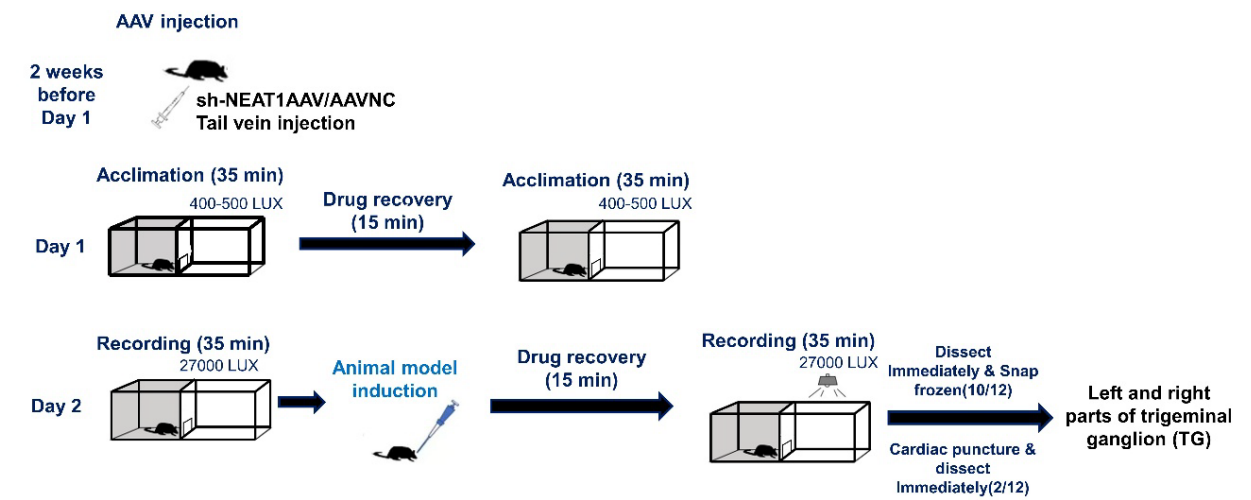
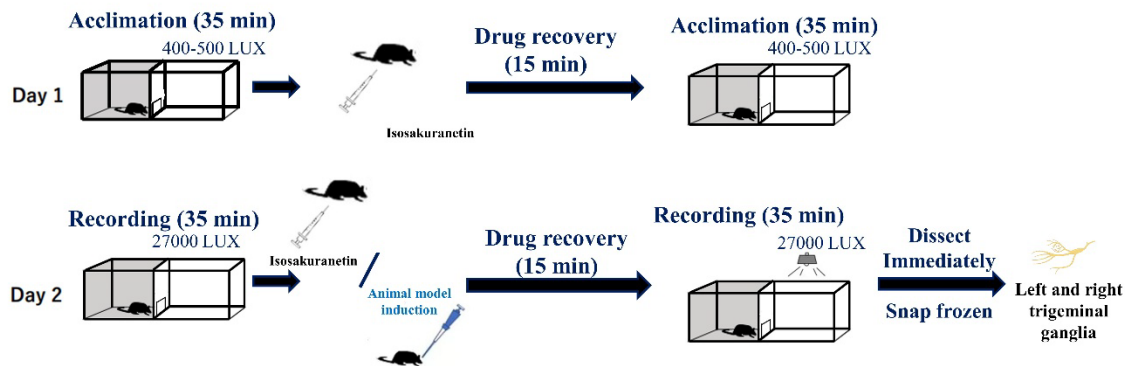


Supplementary material 1: Experimental flowchart on examining whether knocking down NEAT1 by shNEAT1-AAV vector could alleviate photophobia-like behavior induced by intranasal injection of UMB in male mice (Series 1).

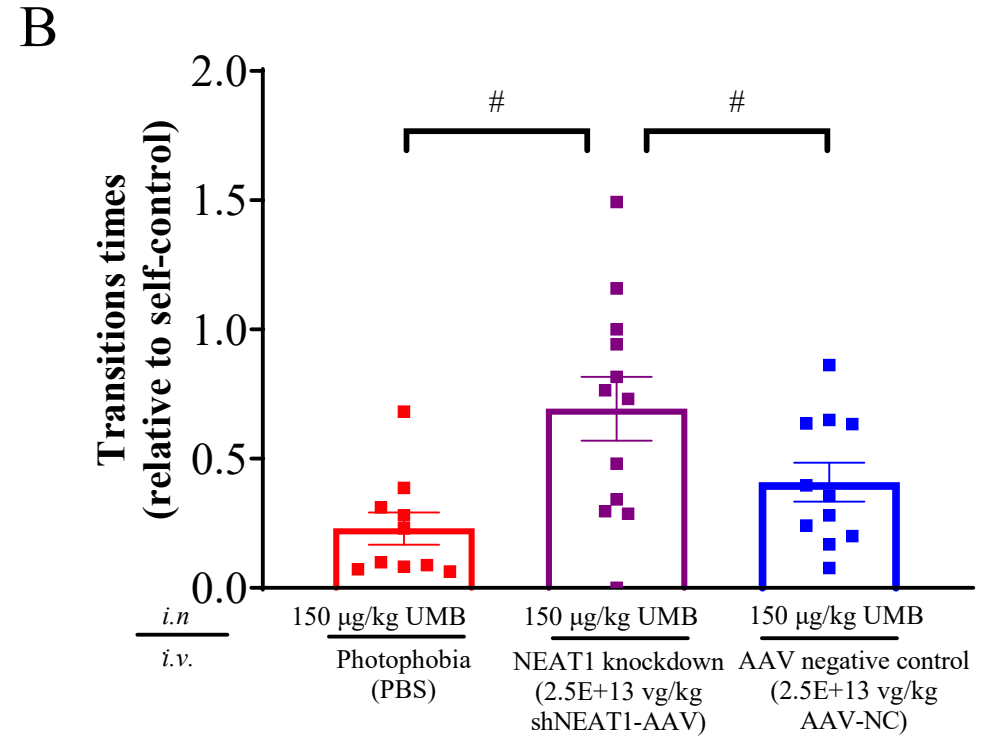
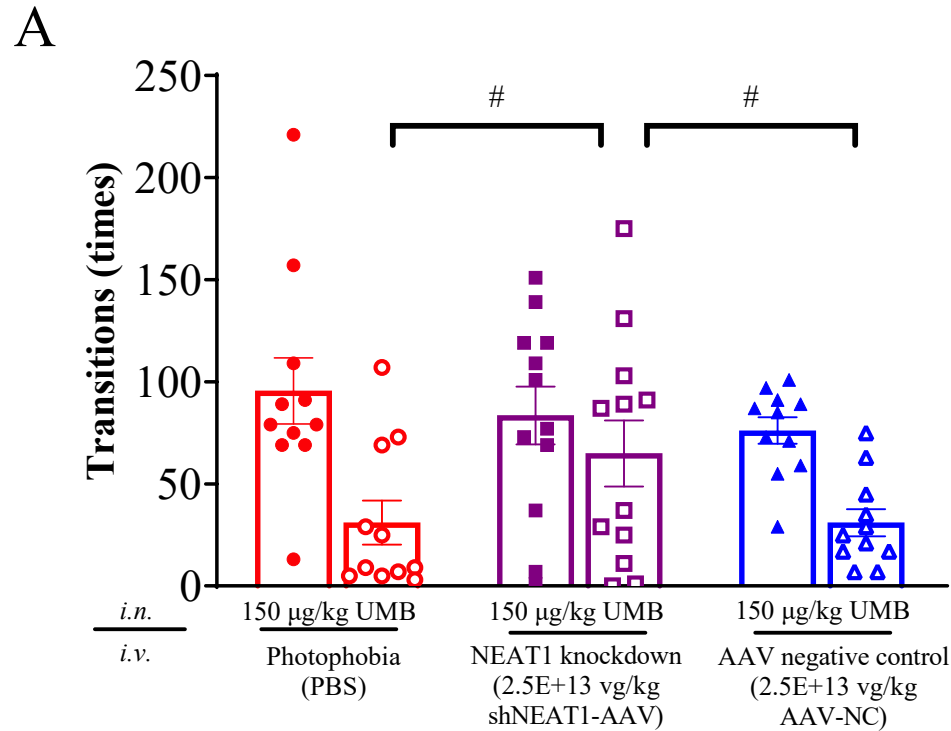


Group	Animal model	Test drugs	Sample numbers
Group 1 (PBS)	Photophobia (<i>i.n.</i> 150 µg/kg UMB)	<i>i.v.</i> vehicle(PBS)	n = 12
Group 2 (shNEAT1-AAV)	Photophobia (<i>i.n.</i> 150 µg/kg UMB)	<i>i.v.</i> shNEAT1 AAV(2.50E+13v.g./kg)	n = 12
Group 3 (AAVNC)	Photophobia (<i>i.n.</i> 150 µg/kg UMB)	<i>i.v.</i> AAVNC (2.50E+13v.g./kg)	n = 12

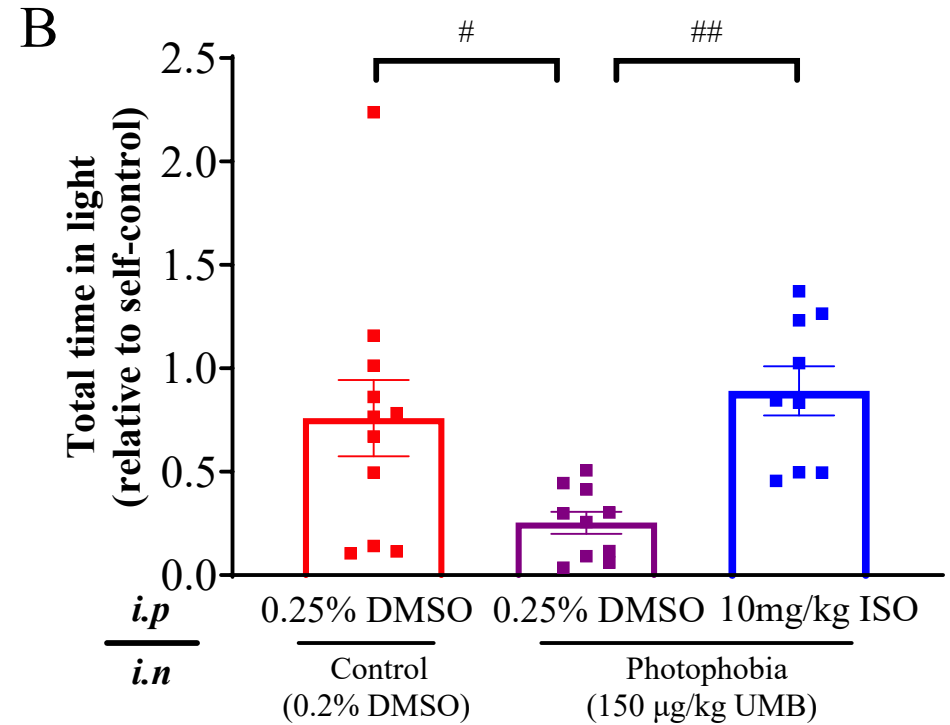
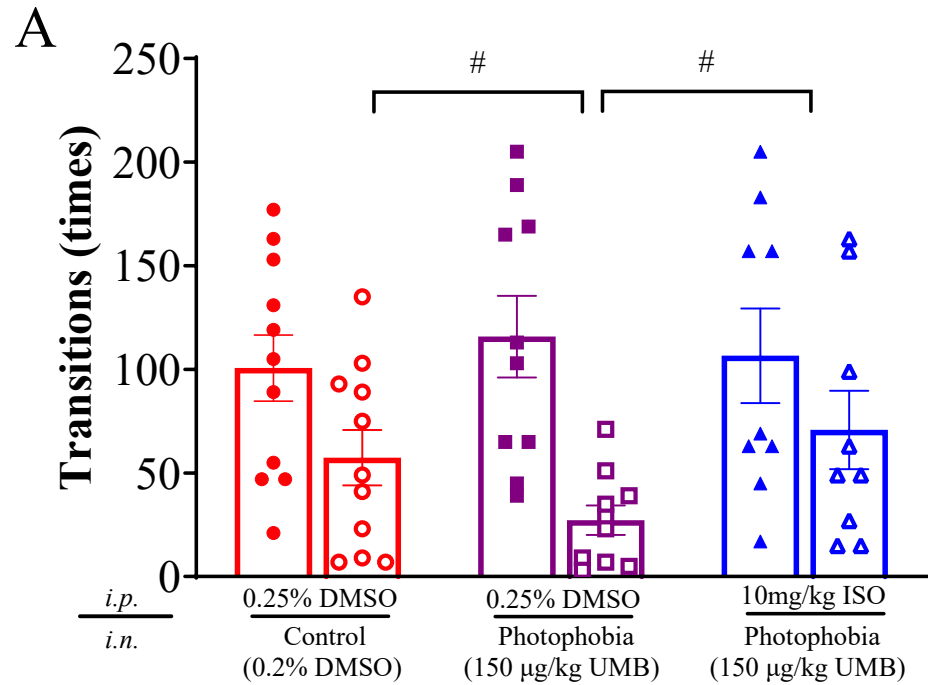
Supplementary material 2: Experimental procedure on examining whether TRPM3 inhibition by ISO could reduce photophobia-like behavior induced by by intranasal injection of UMB in male mice (Series 2).



Group	Animal model	Test drugs	Sample numbers
Group 1 (Vehicle)	Control (<i>i.n.</i> 0.2% DMSO)	<i>i.p.</i> 0.25% DMSO	n = 12
Group 2 (UMB)	Photophobia (<i>i.n.</i> 150 µg/kg UMB)	<i>i.p.</i> 0.25% DMSO	n = 12
Group 3 (ISO)	Photophobia (<i>i.n.</i> 150 µg/kg UMB)	<i>i.p.</i> 10 mg/kg Isosakuranetin	n = 12



Supplemental material 3: NEAT1 knock down by shNEAT1-AAV restored transition times between the light and dark compartments in male C57BL/6J photophobia mice induced by intranasal injection of UMB. Transition times data was collected the same as the total time in light from the same mice shown in Fig. 2. (A) Transition (times) between the light and dark compartments before and after light aversion induction in the PBS, shNEAT1-AAV and shNEAT1-AAV-NC groups. (B) Transition times recorded after light aversion induction relative to self-control. Data are shown as mean $\pm$ SEM. Significant difference was shown by # $P < 0.05$.



Supplemental material 4: Inhibition of TRPM3 by intraperitoneal injection of ISO restored the reduced transition times between the light and dark compartments in male C57BL/6J photophobia mice induced by intranasal injection of UMB.

Transition times data was collected the same as the total time in light from the same mice shown in Fig. 5. (A) Transition (times) between the light and dark compartments before and after light aversion induction in the model control and photophobia groups with or without pretreatment of ISO (*i.p.*). (B) Transition times recorded after light aversion induction relative to respective self-control. Data are shown as mean $\pm$ SEM. Significant difference was shown by # $P < 0.05$.

Supplementary Table - Statistic data for Figures 1-5 & Supplemental materials 3&4

Figures	Groups	Passed normality (Shapiro-Wilk test)?	Statistic and calculations	Significance	Mean $\pm$ SEM, sample number
Fig.1 C (NEAT1 fold change by RNA-seq)	UMB vs DMSO	Yes	Wald test	* padj = 0.0151	UMB: 5809 $\pm$ 810.1 (n=7) DMSO: 3401 $\pm$ 271 (n=7)
Fig.1 D (NEAT1 fold change by qPCR)	UMB vs DMSO	Yes	Unpaired t test (one-tailed)	* $p = 0.0489$	UMB: 1.253 $\pm$ 0.1050 (n=7) DMSO: 1.000 $\pm$ 0.09371 (n=7)
Fig.2 A (Total time in light)	Self-control vs PBS	No	Wilcoxon test (one-tailed)	*** $p = 0.0005$	Self-control: 427.1 $\pm$ 58.93 (n=11) PBS: 147.8 $\pm$ 58.96 (n=11)
Fig.2 B (Total time in light)	Self-control vs shNEAT1-AAV	No	Wilcoxon test (one-tailed)	ns $p=0.1083$	Self-control: 621.8 $\pm$ 149.2 (n=12) shNEAT1-AAV: 730.4 $\pm$ 187.5 (n=12)
Fig.2 C (Total time in light)	Self-control vs AAV-NC	No	Wilcoxon test (one-tailed)	*** $p = 0.0005$	Self-control: 326.7 $\pm$ 34.63 (n=11) AAV-NC: 156.5 $\pm$ 41.42 (n=11)
Fig.2 D (Total time in light)	shNEAT1-AAV vs PBS	No	Kruskal-Wallis one-way ANOVA followed by Mann-Whitney test	### $p = 0.0002$	PBS: 98.10 $\pm$ 35.04 (n=10) shNEAT1-AAV: 468.7 $\pm$ 76.23 (n=10)
	AAV-NC vs shNEAT1-AAV	Yes	Kruskal-Wallis one-way ANOVA followed by Welch's t test	### $p = 0.0007$	AAV-NC: 126.2 $\pm$ 31.27 (n=10) shNEAT1-AAV: 468.7 $\pm$ 76.23 (n=10)
Fig.2 E (Total time in light fold change)	shNEAT1-AAV vs PBS	Yes	Ordinary one-way ANOVA followed by Welch's t test	#### $p < 0.0001$	PBS: 0.1617 $\pm$ 0.04581 (n=9) shNEAT1-AAV: 1.013 $\pm$ 0.1281 (n=11)
	AAV-NC vs shNEAT1-AAV	Yes	Ordinary one-way ANOVA followed by unpaired t test	## $p = 0.0012$	AAV-NC: 0.4592 $\pm$ 0.09446 (n=11) shNEAT1-AAV: 1.013 $\pm$ 0.1281 (n=11)
Fig.2 G (NEAT1 fold change by qPCR)	shNEAT1-AAV vs PBS	Yes	Ordinary one-way ANOVA followed by unpaired t test	## $p = 0.0018$	PBS: 1.000 $\pm$ 0.08208 (n=7) shNEAT1-AAV: 0.6527 $\pm$ 0.05710 (n=8)

Supplementary Table - Statistic data for Figures 1-5 & Supplemental material 3&4

	AAV-NC vs shNEAT1-AAV	Yes	Ordinary one-way ANOVA followed by unpaired t test	# $p = 0.0242$	AAV-NC: 0.8711 ± 0.2254 (n=7) shNEAT1-AAV: 0.6527 ± 0.05710 (n=8)
Fig.3 D (<i>Trpm3</i> fold change by RNA-seq)	UMB vs DMSO	Yes	Wald test	* padj = 0.0233	UMB: 109.3 ± 10.62 (n=7) DMSO: 54.75 ± 12.31 (n=7)
Fig.3 E (<i>Rnf38</i> fold change by RNA-seq)	UMB vs DMSO	Yes	Wald test	* padj = 0.0444	UMB: 405.4 ± 78.32 (n=7) DMSO: 176.7 ± 21.36 (n=7)
Fig.3 F (<i>Slc7a2</i> fold change by RNA-seq)	UMB vs DMSO	Yes	Wald test	* padj = 0.0107	UMB: 88.78 ± 5.502 (n=7) DMSO: 58.70 ± 4.637 (n=7)
Fig.3 G (Mir196a-1 fold change by RNA-seq)	UMB vs DMSO	Yes	Wald test	*** padj = 0.0006	UMB: 2.143 ± 1.534 (n=7) DMSO: 73.14 ± 35.16 (n=7)
Fig.3 H (Mir196a-2 fold change by RNA-seq)	UMB vs DMSO	Yes	Wald test	** padj = 0.0028	UMB: 0 ± 0 (n=7) DMSO: 5.286 ± 2.157 (n=7)
Fig.3 I (<i>Trpm3</i> fold change by pPCR)	UMB vs DMSO	Yes	Unpaired t test (one-tailed)	* $p = 0.0489$	UMB: 1.253 ± 0.1050 (n=7) DMSO: 1.000 ± 0.09371 (n=7)
Fig.3 J (<i>Rnf38</i> fold change by qPCR)	UMB vs DMSO	Yes	Welch's t test (one-tailed)	* $p = 0.0223$	UMB: 405.4 ± 78.32 (n=7) DMSO: 176.7 ± 21.36 (n=7)
Fig.3 K (<i>Slc7a2</i> fold change by qPCR)	UMB vs DMSO	Yes	Welch's t test (one-tailed)	ns $p = 0.0296$	UMB: 1.974 ± 0.4177 (n=7) DMSO: 1.000 ± 0.08711 (n=7)
Fig.4 A (<i>Trpm3</i> fold change by qPCR)	shNEAT1-AAV vs PBS	Yes	Welch's ANOVA test followed by Welch's t test	# $p = 0.0158$	PBS: 1.000 ± 0.1375 (n=7) shNEAT1-AAV: 0.6146 ± 0.05270 (n=8)
	AAV-NC vs shNEAT1-AAV	Yes	Welch's ANOVA test followed by Welch's t test	# $p = 0.0193$	AAV-NC: 1.007 ± 0.1524 (n=8) shNEAT1-AAV: 0.6146 ± 0.05270 (n=8)
Fig.4 B (miR-196a-5p fold change by qPCR)	shNEAT1-AAV vs PBS	No	Kruskal-Wallis one-way ANOVA followed by Mann-Whitney test	# $p = 0.0296$	PBS: 0.4431 ± 0.1501 (n=6) shNEAT1-AAV: 1.230 ± 0.3486 (n=8)

Supplementary Table - Statistic data for Figures 1-5 & Supplemental material 3&4

	AAV-NC vs shNEAT1-AAV	Yes	Kruskal–Walli one-way ANOVA followed by unpaired t test	ns $p = 0.1670$	AAV-NC: 0.8329 ± 0.1904 (n=8) shNEAT1-AAV: 1.230 ± 0.3486 (n=8)
Fig.4 G (Relative Luciferase Activity)	miR-196a-5p-NC-mimics + NEAT1-WT vs miR-196a-5p-mimics + NEAT1-WT	Yes	Unpaired t test (two-tailed)	**** $p < 0.0001$	miR-196a-5p-NC-mimics + NEAT1-WT: 1.00 ± 0.02104 (n=6) miR-196a-5p-mimics + NEAT1-WT: 0.6855 ± 0.005067 (n=6)
	miR-196a-5p-NC -mimics + NEAT1-MT Vs miR-196a-5p-mimics + NEAT1-MT	Yes	Unpaired t test (two-tailed)	ns $p = 0.8821$	miR-196a-5p-NC -mimics + NEAT1-MT: 1.019 ± 0.02403 (n=6) miR-196a-5p-mimics + NEAT1-MT: 1.014 ± 0.02112 (n=6)
Fig.4 H (Relative Luciferase Activity)	miR-196a-5p-NC-mimics + <i>Trpm3</i> -WT vs miR-196a-5p-mimics + <i>Trpm3</i> -WT	Yes	Unpaired t test (two-tailed)	**** $p < 0.0001$	miR-196a-5p-NC-mimics + <i>Trpm3</i> -WT: 1.00 ± 0.01712 (n=6) miR-196a-5p-mimics + <i>Trpm3</i> -WT: 0.9062 ± 0.01039 (n=6)
	miR-196a-5p-NC -mimics + <i>Trpm3</i> -MT Vs miR-196a-5p-mimics + <i>Trpm3</i> -MT	Yes	Unpaired t test (two-tailed)	ns $p = 0.7004$	miR-196a-5p-NC -mimics + <i>Trpm3</i> -MT: 1.038 ± 0.03092 (n=6) miR-196a-5p-mimics + <i>Trpm3</i> -MT: 1.022 ± 0.02587 (n=6)
Fig.5 A (Total time in light)	Self-control vs DMSO	Yes	Paired t test (one-tailed)	* $p = 0.0213$	Self-control: 361.9 ± 64.84 (n=11) DMSO: 266.5 ± 68.29 (n=11)
Fig.5 B (Total time in light)	Self-control vs UMB	Yes	Paired t test (one-tailed)	* $p = 0.0002$	Self-control: 496.8 ± 76.94 (n=10) UMB: 129.7 ± 32.97 (n=10)
Fig.5 C (Total time in light)	Self-control vs UMB+ISO	No	Wilcoxon test (one-tailed)	ns $p = 0.3262$	Self-control: 384.1 ± 78.98 (n=9) UMB+ISO: 360.2 ± 109.9 (n=9)
Fig.5 D (Total time in light)	UMB vs DMSO	Yes	Kruskal–Walli one-way ANOVA followed by Welch's t test	# $p = 0.0461$	DMSO: 266.5 ± 68.29 (n=11) UMB: 129.7 ± 32.97 (n=10)
	UMB+ISO vs UMB	Yes	Kruskal–Walli one-way ANOVA followed by Welch's t test	### $p = 0.0007$	UMB+ISO: 360.2 ± 109.9 (n=9) UMB: 129.7 ± 32.97 (n=10)

Supplementary Table - Statistic data for Figures 1-5 & Supplemental material 3&4

Fig.5 E (Total time in light fold change)	UMB vs DMSO	Yes	Kruskal–Walli one-way ANOVA followed by Welch's t test	# $p = 0.0110$	DMSO: 0.7592 ± 0.1840 (n=11) UMB: 0.2532 ± 0.05387 (n=10)
	UMB+ISO vs UMB	No	Kruskal–Walli one-way ANOVA followed by Mann-Whitney test	# $p = 0.0326$	UMB+ISO: 0.8916 ± 0.1186 (n=9) UMB: 0.2532 ± 0.05387 (n=10)
Supplemental Material 3 A (Transition times)	PBS self-control vs shNEAT1-AAV self-control	Yes	Ordinary one-way ANOVA followed by unpaired t test	ns $p = 0.2898$	PBS self-control: 95.55 ± 16.22 (n=11) shNEAT1-AAV self-control: 83.50 ± 14.11 (n=12)
	shNEAT1-AAV self-control vs AAVNC self-control	Yes	Ordinary one-way ANOVA followed by Welch's t test	ns $p = 0.3201$	shNEAT1-AAV self-control: 83.50 ± 14.11 (n=12) AAVNC self-control: 76.09 ± 6.491 (n=11)
	PBS vs shNEAT1-AAV	Yes	Ordinary one-way ANOVA followed by unpaired t test	# $p = 0.0485$	PBS: 31.00 ± 10.75 (n=11) shNEAT1-AAV: 64.92 ± 16.18 (n=12)
	shNEAT1-AAV vs AAVNC	Yes	Ordinary one-way ANOVA followed by Welch's t test	# $p = 0.0361$	shNEAT1-AAV: 64.92 ± 16.18 (n=12) AAVNC: 31.00 ± 6.644 (n=11)
Supplemental Material 3 B (Transition times fold change)	PBS vs shNEAT1-AAV	No	Kruskal–Walli one-way ANOVA followed by Mann-Whitney test	## $p = 0.0028$	PBS: 0.2298 ± 0.06230 (n=10) shNEAT1-AAV: 0.6928 ± 0.1232 (n=12)
	shNEAT1-AAV vs AAVNC	Yes	Kruskal–Walli one-way ANOVA followed by unpaired t test	# $p = 0.0343$	shNEAT1-AAV: 0.6928 ± 0.1232 (n=12) AAVNC: 0.4093 ± 0.07536 (n=11)
Supplemental Material 4 A (Transition times)	DMSO self-control vs UMB self-control	Yes	Ordinary one-way ANOVA followed by unpaired t test	ns $p = 0.2767$	DMSO self-control: 100.6 ± 15.97 (n=11) UMB self-control: 115.8 ± 19.67 (n=10)
	UMB self-control vs UMB+ISO self-control	Yes	Ordinary one-way ANOVA followed by unpaired t test	ns $p = 0.3808$	UMB self-control: 115.8 ± 19.67 (n=10) UMB+ISO self-control: 106.6 ± 22.86 (n=9)

Supplementary Table - Statistic data for Figures 1-5 & Supplemental material 3&4

	DMSO vs UMB	Yes	Ordinary one-way ANOVA followed by unpaired t test	# $p = 0.0339$	DMSO: 57.36 ± 13.36 (n=11) UMB: 27.20 ± 7.090 (n=10)
	UMB vs UMB+ISO	Yes	Ordinary one-way ANOVA followed by Welch's t test	# $p = 0.0281$	UMB: 27.20 ± 7.090 (n=10) UMB+ISO 70.78 ± 18.96 (n=9)
Supplemental Material 4 B (Transition times fold change)	DMSO vs UMB	Yes	Ordinary one-way ANOVA followed by Welch's t test	# $p = 0.0170$	DMSO: 0.6089 ± 0.1372 (n=11) UMB: 0.2533 ± 0.06437 (n=10)
	UMB vs UMB+ISO	Yes	Ordinary one-way ANOVA followed by unpaired t test	### $p = 0.0005$	UMB+ISO: 0.6695 ± 0.08419 (n=9) UMB: 0.2533 ± 0.06437 (n=10)