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2 **Supplementary figure 1. Histological characterization of adeno-associated virus (AAV)-**
 3 **infected cells in the centrally projecting Edinger-Westphal nucleus (EWcp) and FOS**
 4 **immunoreactive cells in the mesencephalic lateral periaqueductal gray matter (IPAG).**

5 (A) AAV-infected cells in the EWcp were visualized by immunofluorescence for green
 6 fluorescence protein (GFP, green in A and B). Note that the green GFP immunopositive cells
 7 contain also the neuronal nuclear marker (NeuN, red) as shown also by the higher
 8 magnification insert in A. Most of the GFP and NeuN immunopositive cells co-express
 9 urocortin1 (UCN1, white in A) also, proving the neuronal identity of AAV-infected peptidergic
 10 cells in the EWcp. (B) The AAV-infected, GFP-immunopositive cell bodies in the EWcp do
 11 not correspond to glial cells as they contain neither the microglial marker ionized calcium-
 12 binding adapter molecule 1 (IBA1, white in B) nor the astroglial marker, glial fibrillary acidic
 13 protein (GFAP, red in B). (C) Immunohistological confirmation of neuronal identity of FOS-
 14 immunoreactive cells (green in C and D) in the periaqueductal gray matter upon CGRP

15 treatment as the FOS signal fully co-localizes with the neuronal marker NeuN (red in C). (D)
16 The nuclear FOS (green) signal is not localized to micro- (IBA1, white) or astroglial (GFAP,
17 red) cells.

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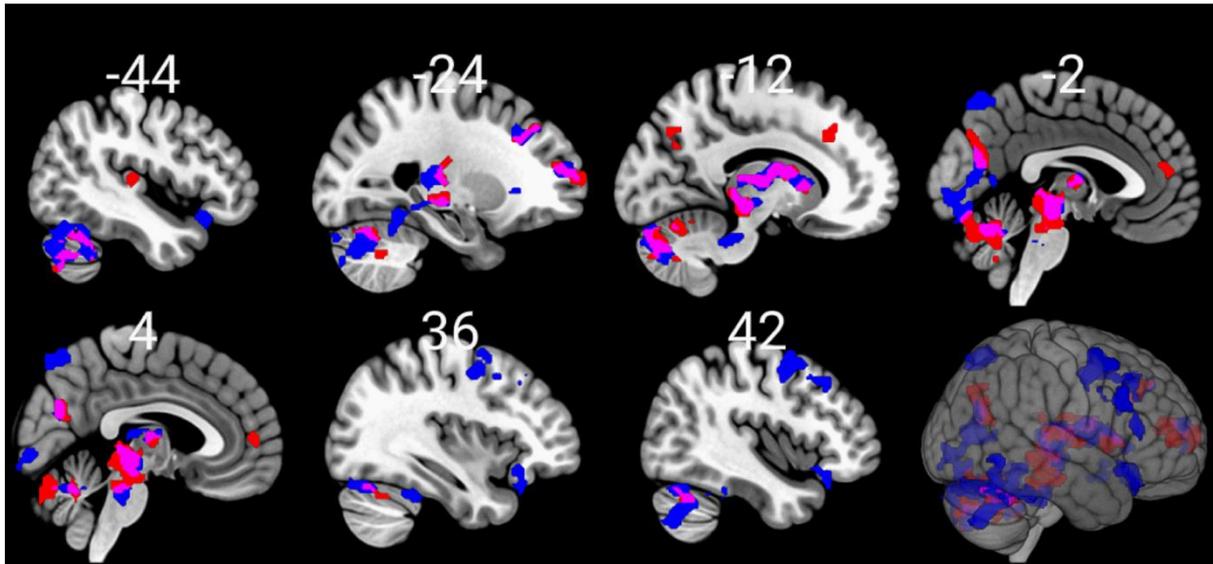
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33 **Supplementary figure 2. Similarities and differences in functional connectivity of**
34 **Edinger-Westphal nucleus and periaqueductal gray matter.** Blue color represents
35 functional connectivity of Edinger-Westphal nucleus; red color represents functional
36 connectivity of periaqueductal gray matter; pink color represents overlapping connectivity.
37 Initial threshold of $p < 0.001$ uncorrected for multiple comparison and at least twenty
38 contiguous voxels was used in the analysis. All connections were positive.

Case code	Gender	Age	<i>Post mortem time (min)</i>
SKO27	Female	76 Years	195
SKO28	Female	93 Years	224
SKO29	Female	69 Years	212

39 **Supplementary table 1. Characteristics of human brain samples used for RNAscope *in***
40 ***situ* hybridization.**

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Cluster size (voxel)	Region	Peak coordinates			Peak
		x	y	z	T-value
2855	Midbrain	4	-28	-6	16.100
	Midbrain	18	-22	-8	5.677
	Midbrain	-24	-22	-6	4.810
222	L Superior frontal gyrus	-26	62	10	5.328
	L Middle frontal gyrus	-24	50	16	4.097
1468	R Vermis_7	2	-74	-26	4.66
	R Cerebelum_IX	12	-54	-34	4.62
	L Cerebelum_VI	-26	-60	-36	4.499
171	L Cerebelum_Crus1	-40	-46	-36	4.506
170	R Anterior cingulate cortex	12	50	8	4.318
	L Anterior cingulate cortex	-2	48	12	3.593
318	L Calcarine	-2	-68	22	4.313
	L Precuneus	-2	-72	32	3.849
	R Precuneus	8	-66	30	3.601
173	L Superior frontal gyrus	-12	28	36	4.111
	L Middle frontal gyrus	-24	36	40	3.659
192	L Cerebelum_Crus1	-46	-58	-38	4.111
	L Cerebelum_Crus2	-40	-74	-46	4.015

42 **Supplementary table 2. Regions with positive functional connectivity of periaqueductal**
43 **gray matter.** Reported results are significant at cluster-level $p_{\text{FWE}} < 0.05$. Coordinates are in
44 Montreal Neurological Institute (MNI) space. R: right hemisphere, L: left hemisphere.