

Is there substantial subcortical control of cortical functions?

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Is there dynamic 5HT modulation of decision making processes

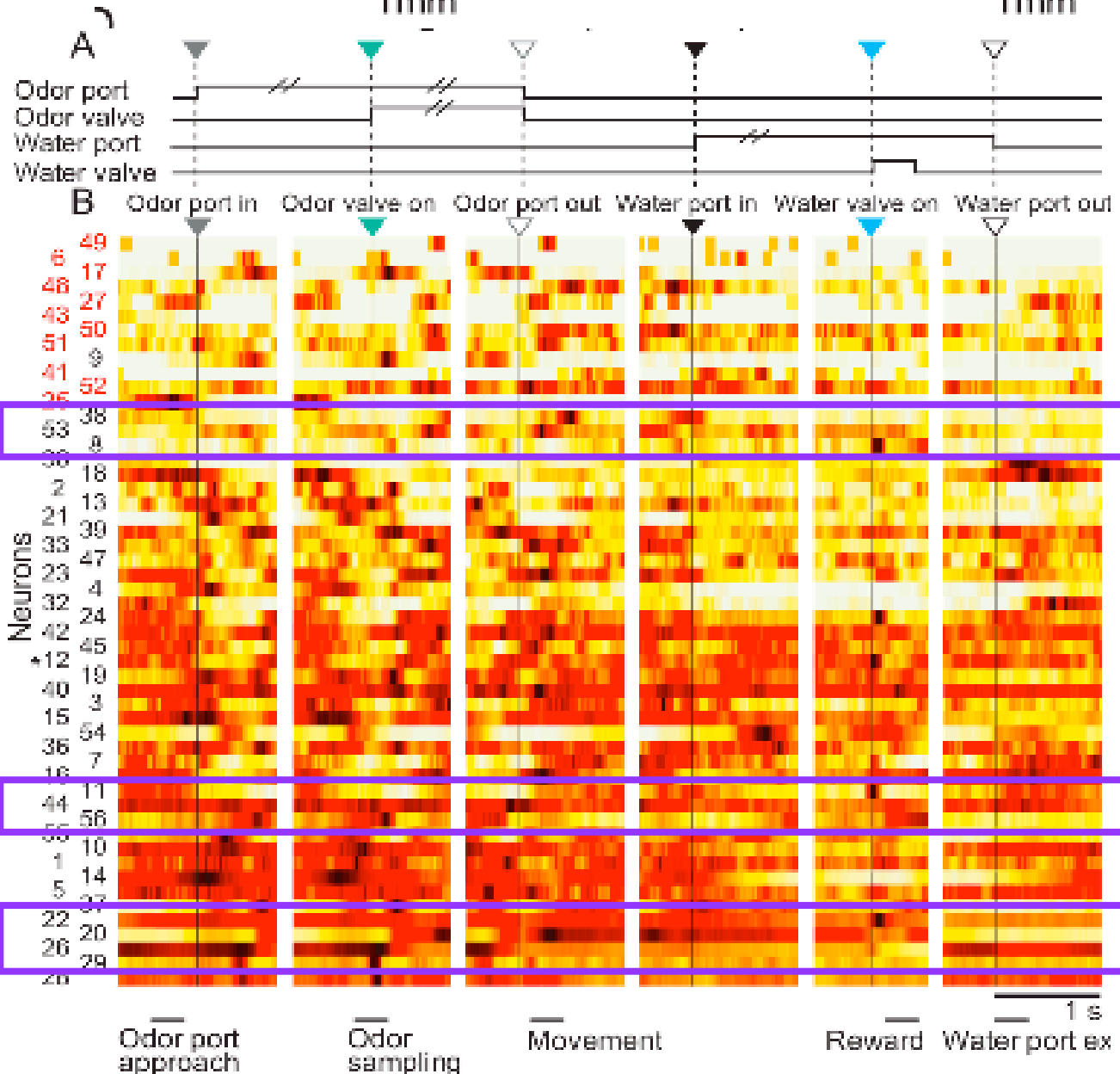
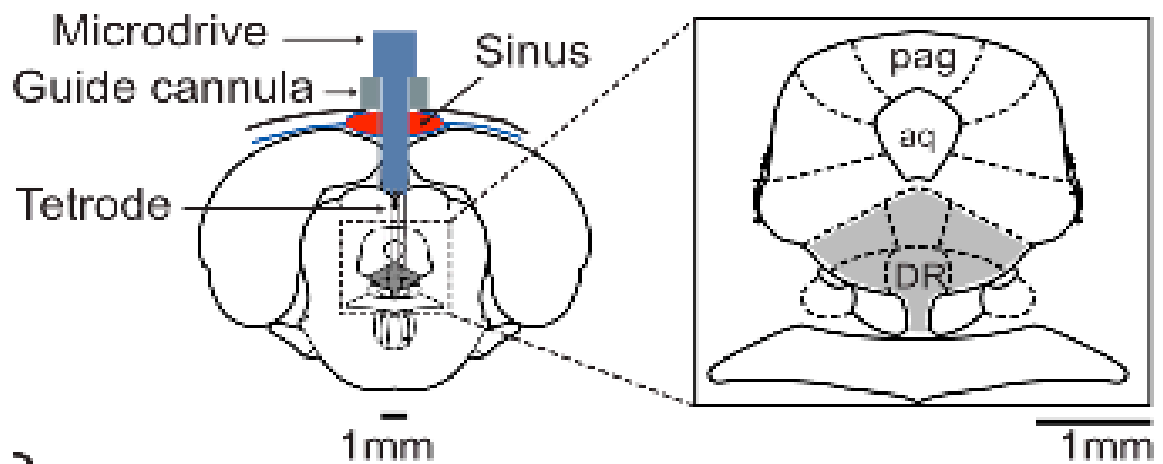


Fig. 7 Zach Mainen's recordings of dorsal raphe. Above, the tetrode implantation. Below, response of each of a population of DR neurons during the course of the task.

Behavior Readout:
Setup: Olfactometer
Candidate Behavior: Temporal Discounting

Non-Behavioral Readout:
Voltammetry

There is dynamic 5HT modulation of decision making processes



Chronic changes in 5HT pre/postsynaptic activity affect olfactory decision making

Acute Changes in 5HT presynaptic activity affect olfactory decision making

5HT levels change dynamically and meaningfully in relevant target area(s) during decision making tasks

Gain of function testing in behaviour

Loss of function testing in behaviour

Show real time optical control of 5HT presynaptic activity can influence behaviour

Show real time optical control of 5HT presynaptic activity can alter 5HT levels in target site during task

Confirm there are 5HT projections in areas previously implicated in decision making processes

Find most densely innervated targets by 5HT neurons

IP/IC SSRI (Citalopram) injection

IC injection of 5HTR antagonists (esp 5HT3A antagonists)

DR-Cre + AAV8-pCBA-DIO-DTA

DR-Cre + AAV8-pCBA-DIO-ChR2(/NpHR):GFP

In vivo Voltammetry (Wightman)

DR-Cre x Rosa-GFP

DR-Cre x RGL

DR-Cre + AAV8-pCBA-DIO-ChR2:GFP

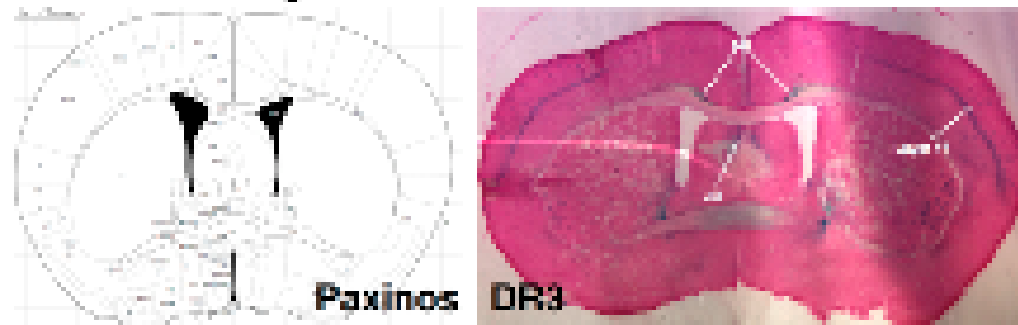
Genetic Targeting:
Cre Transgenic + Viral Delivery of DIO Constructs

DR-Cre





Not much staining in DR



Cerebellum staining seems to be purkinje cells

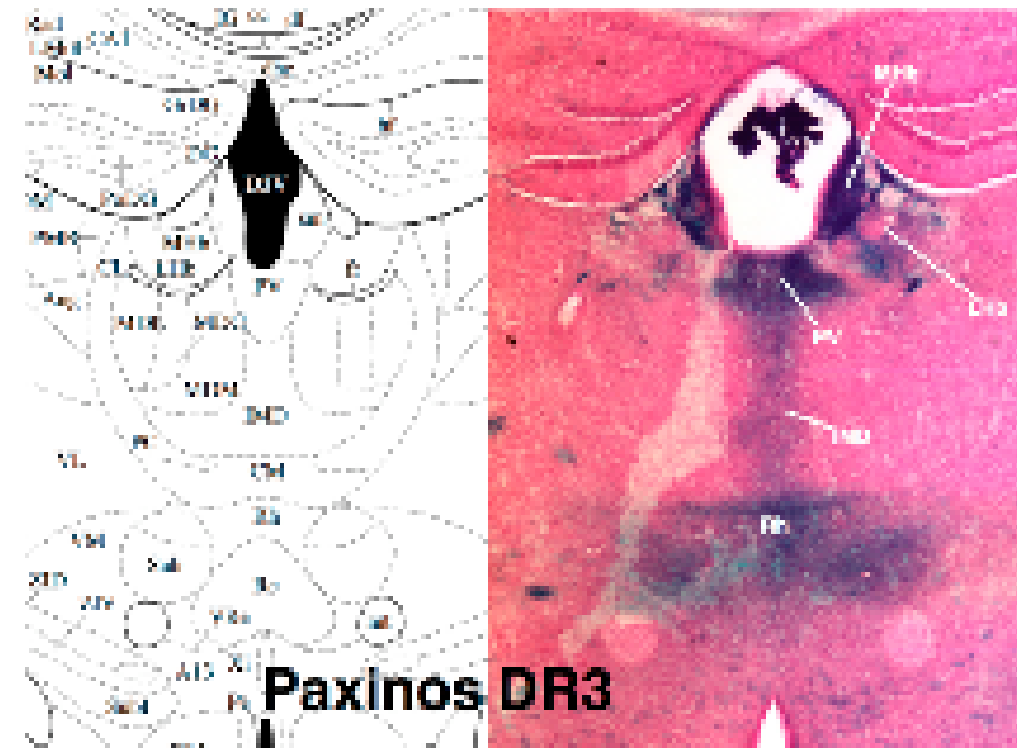


The staining in layer 4 of the cortex is unclear in nature (cell? Projection?)

Faint staining in prefrontal cortex

Fig. 2 DR3-Cre x ROSA-RGL

LacZ Staining (unsure of nature, cellular or axonal) in Dorsal Raphe, purkinje cells of the cerebellum, Layer 4 of somatosensory cortex, singulate cortex(Cgl), paraventricular thalamic nucleus(PV), medial and lateral habenula(M and L H) and reunions thalamic nucleus(Rh).



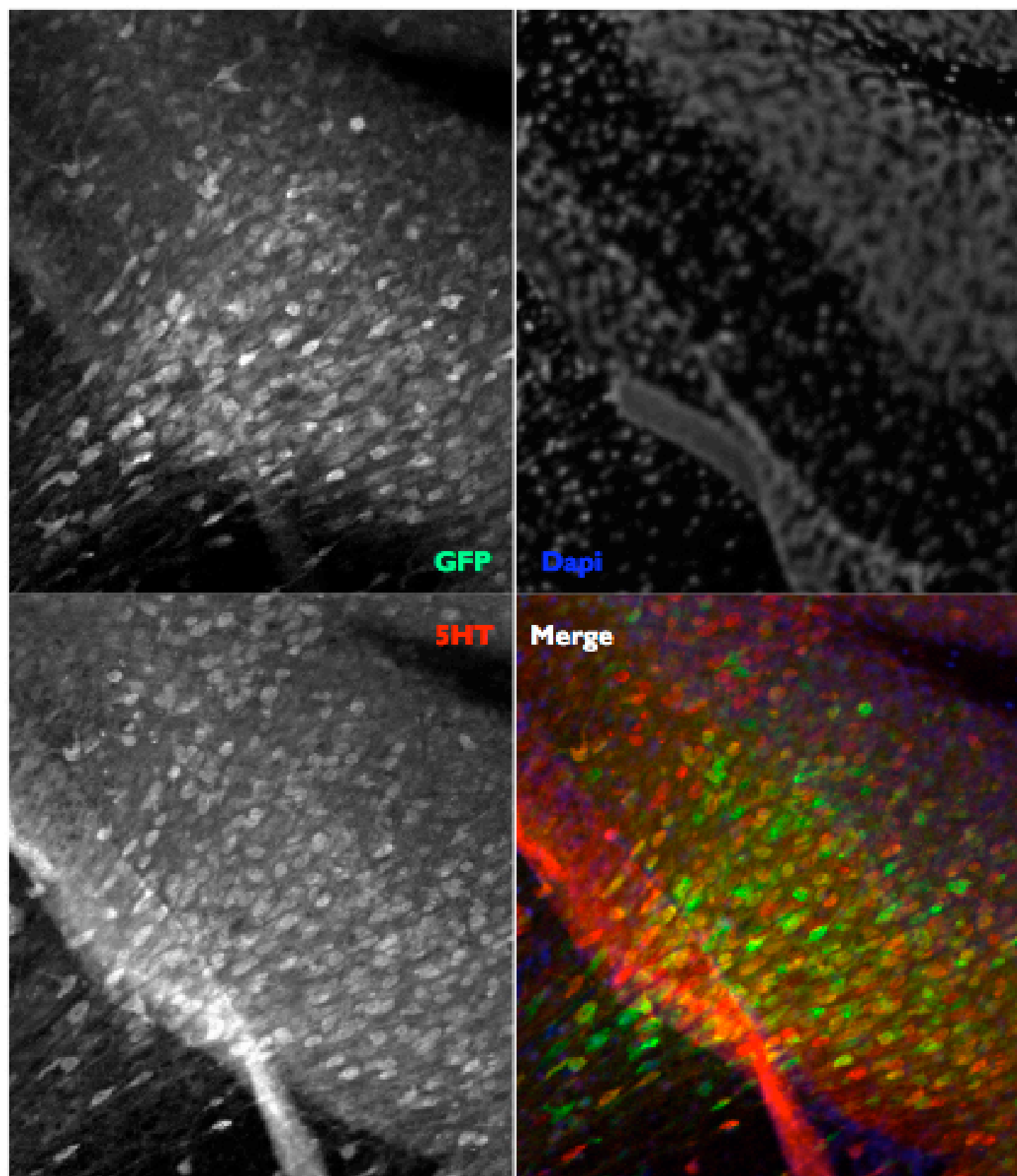


Fig. 6 Sagittal view of dorsal raphe, 7 days after microinjection of 1 μ L of AAV8-pCBA-DIO-ChR2.GFP into DR37 heterozygous male. Age: 8 weeks.

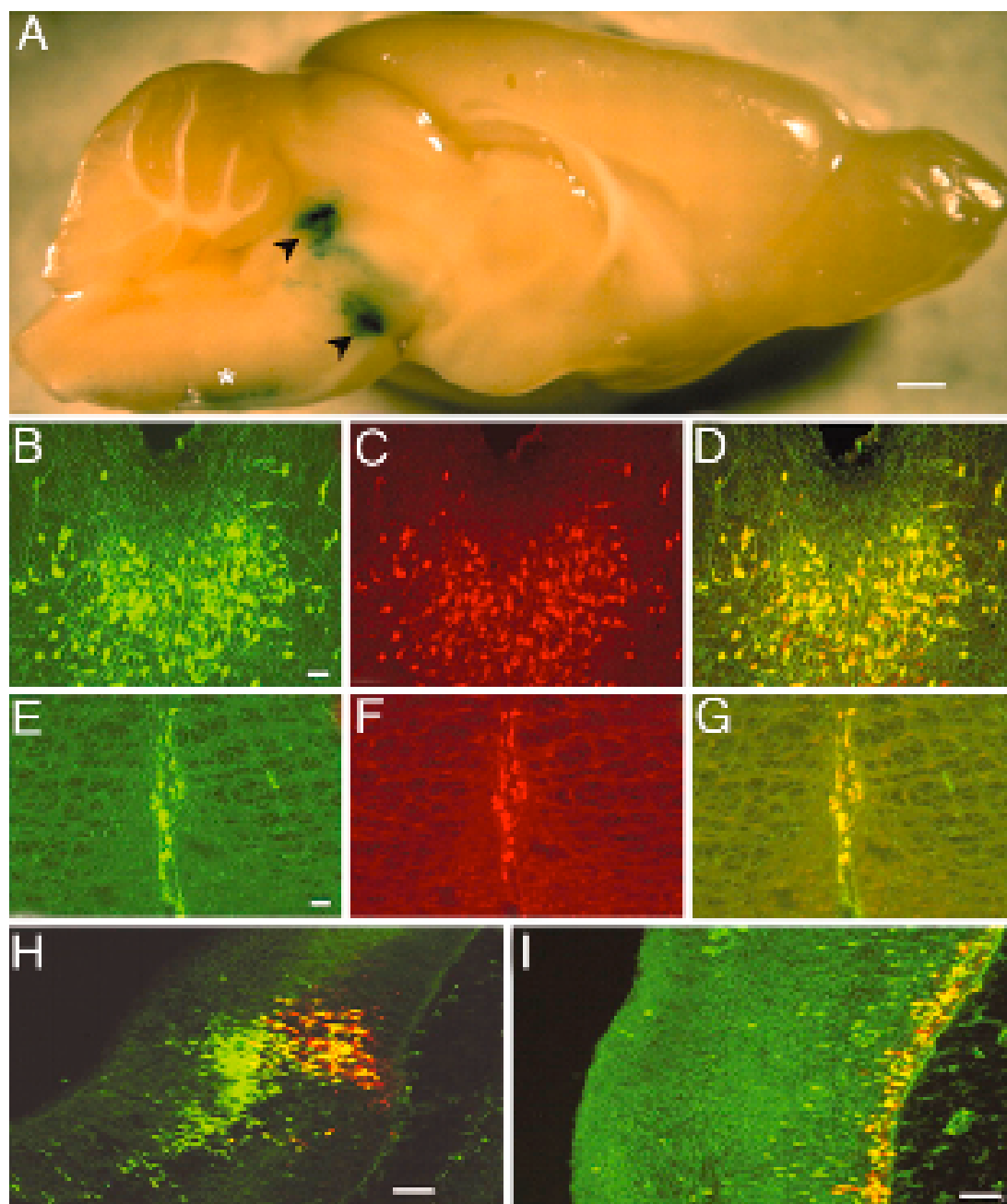


Fig. 5 cPec-Cre. (A) Whole-mount X-gal stain showing LacZ expression directed by cPec-Cre in adult R26R^{cPec-Cre} brain. Black arrowheads, dorsal and median raphe. Asterisk, ventral medullary raphe. (B-I) cPec-Cre activity is restricted to developing and adult 5-HT neurons. Colocalization (D and G) of TPH (B and E) (FITC, and-TPH 1:200) and β-gal (C and F) (Texas red, anti-β-gal 1:5,000) in B7 dorsal raphe nucleus (B-D) and B2 raphe obscurus nucleus (E-G). (H and I) Colocalization of Cre recombinase (FITC, and-Cre recombinase 1:100) with 5-HT (Texas red, and-5-HT 1:10,000) in rostral (H) and caudal (I) E12 hindbrain. (Scale bars: 800 μm, A; 50 μm, B-I.)

Fig 4a. *slc6a4-ER:Cre*

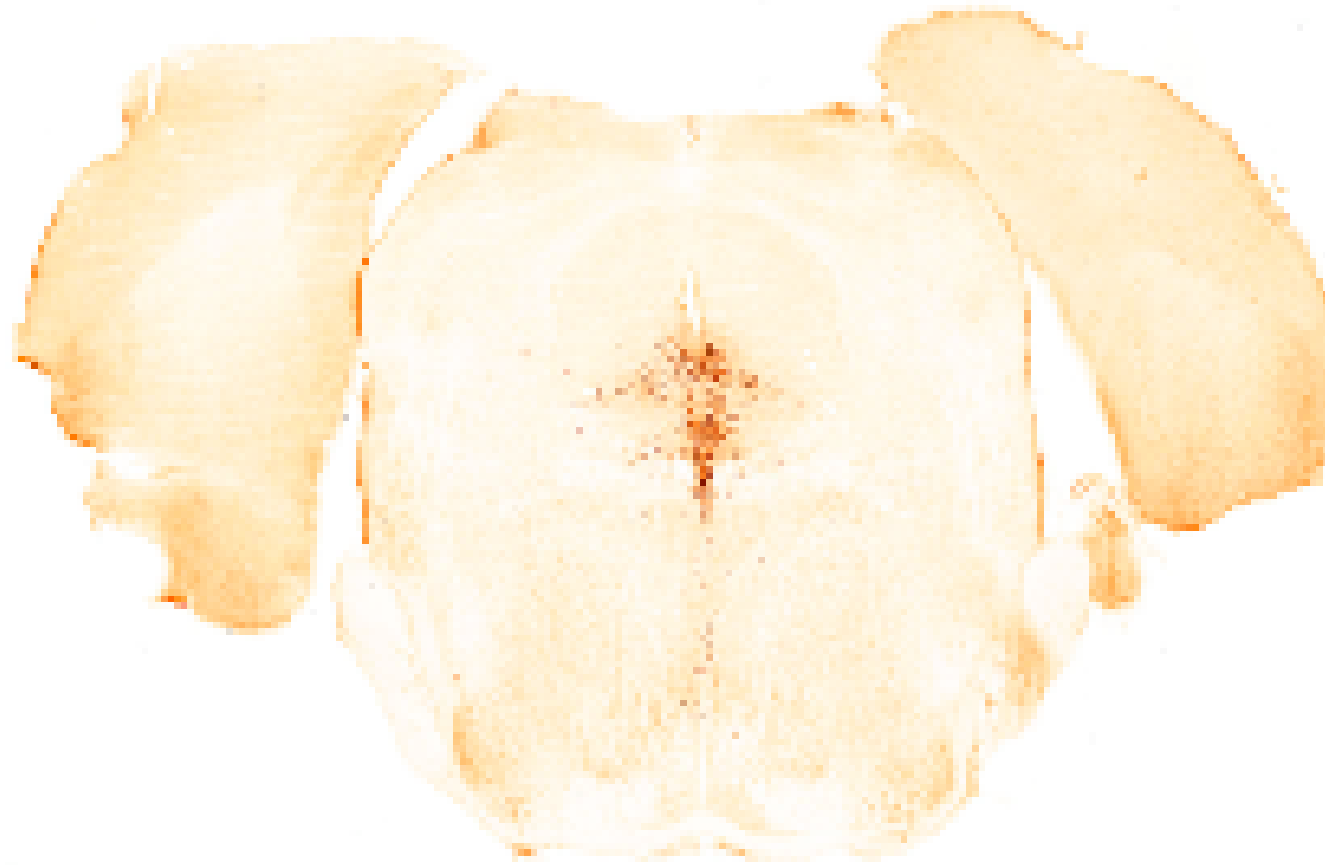


Fig 4b. *slc6a4-Cre*



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Hypothesis

Sub Goals

To Do

In Progress

Done

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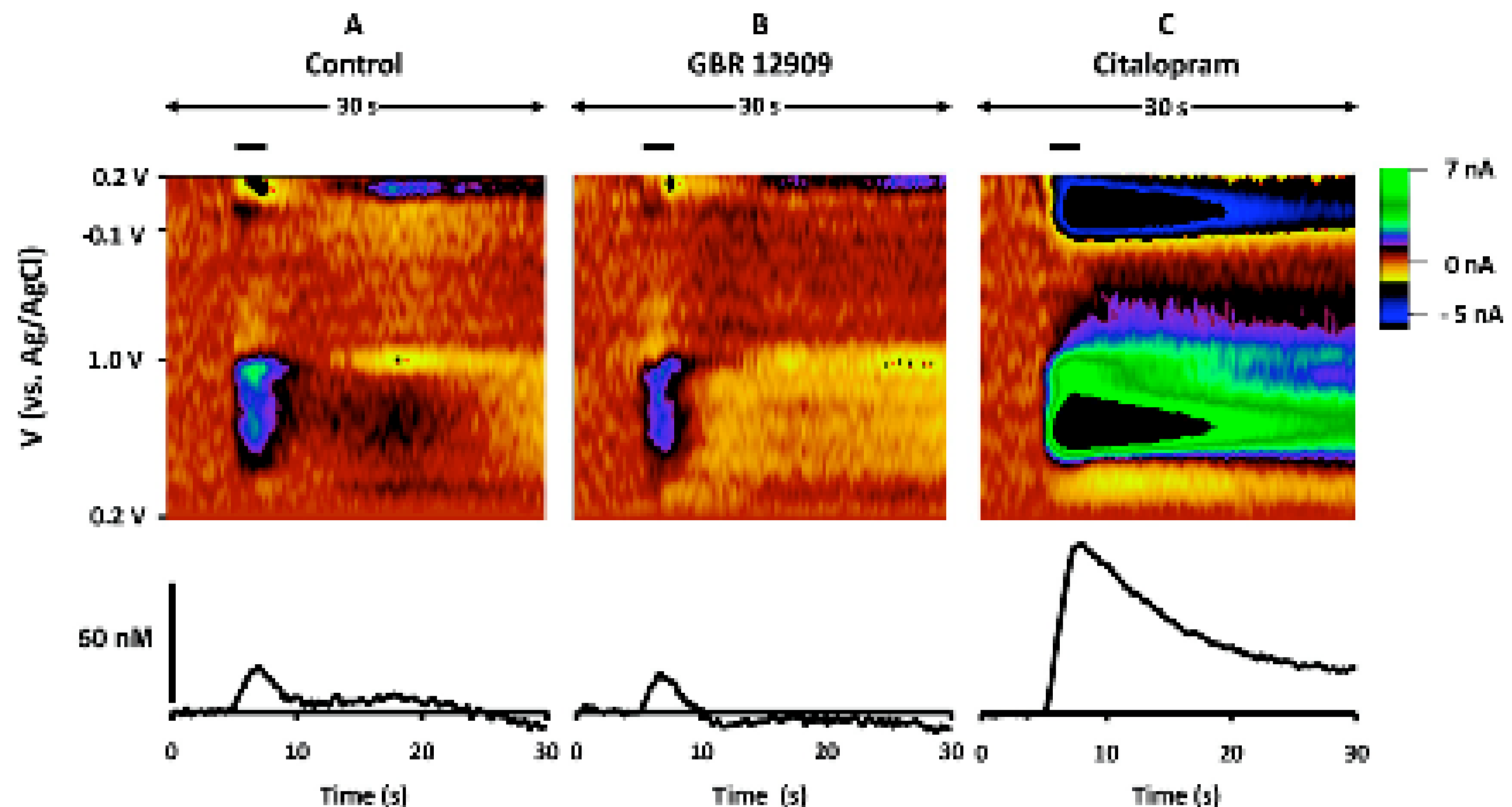


Fig. 8. Validation of 5-HT signal with GBR 12909 (15 mg kg^{-1}) and citalopram (10 mg kg^{-1}). The top panel shows the potential on the y-axis plotted against time on the x-axis; the current response is represented in false color. The black blocks horizontal to the x-axis are the durations of the stimulations. The bottom traces show concentration vs time. These responses are for (A) stimulation-evoked control response, (B) 40 min after systemic administration of GBR 12909, and (C) 40 min after systemic administration of citalopram.