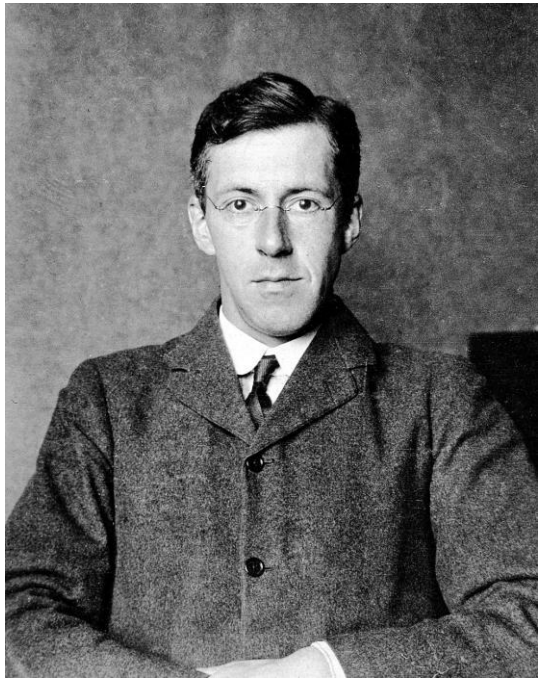
Oxytocin modulation of neural circuits

Lennart Oettl

2.11.2018

Oxytocin

- Discovered by Sir Henry H. Dale in 1906



Sir Henry Dale, 1904

Wellcome Physiological Laboratories

Oxytocin

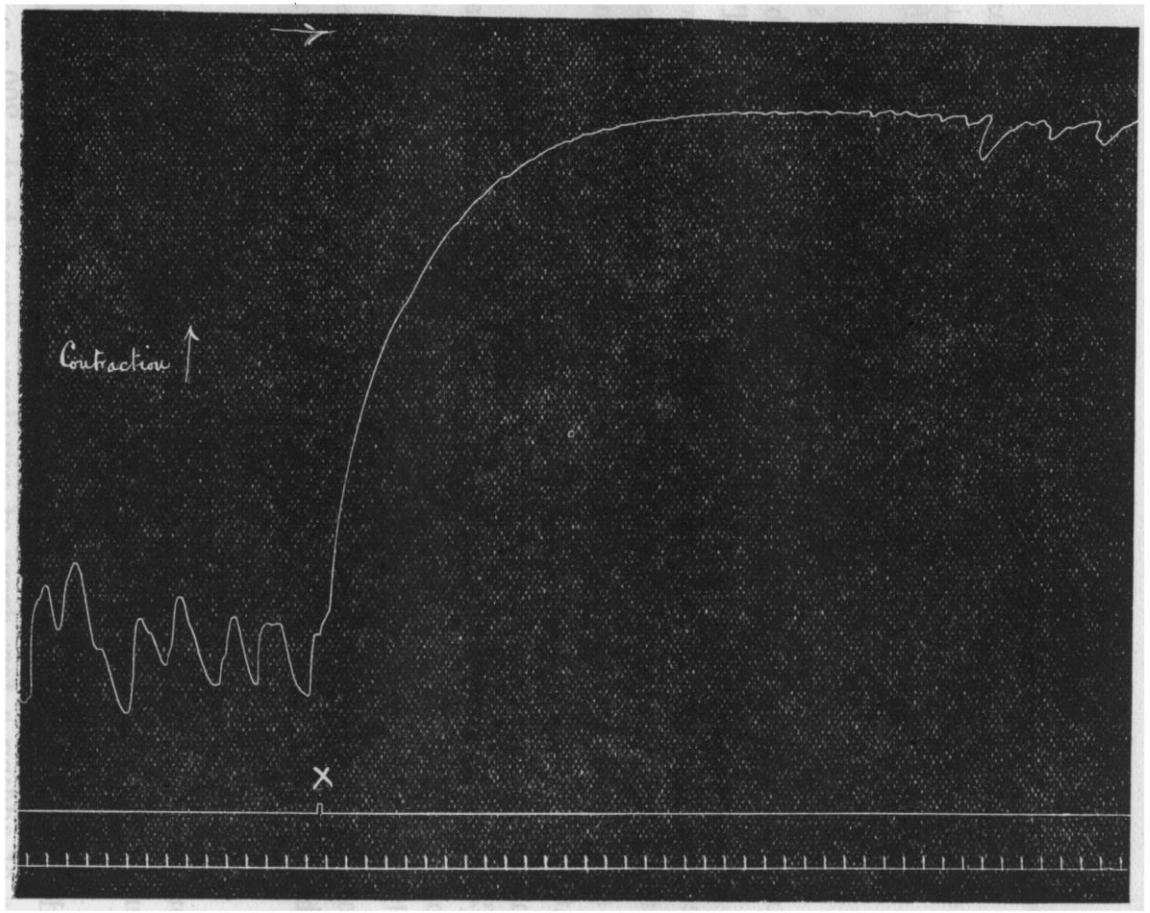
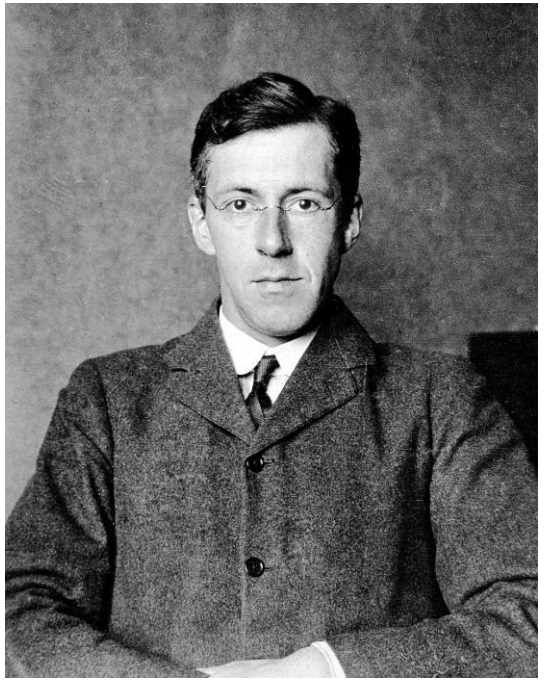


Figure 3.—Contractions of isolated horn of cat's uterus (not pregnant). At × 3 drops of pituitary extract were added to the 200 c.c. of Ringer's solution in the bath. Time = 10 seconds. Scale, ½ linear.



Sir Henry Dale, 1904

Wellcome Physiological Laboratories

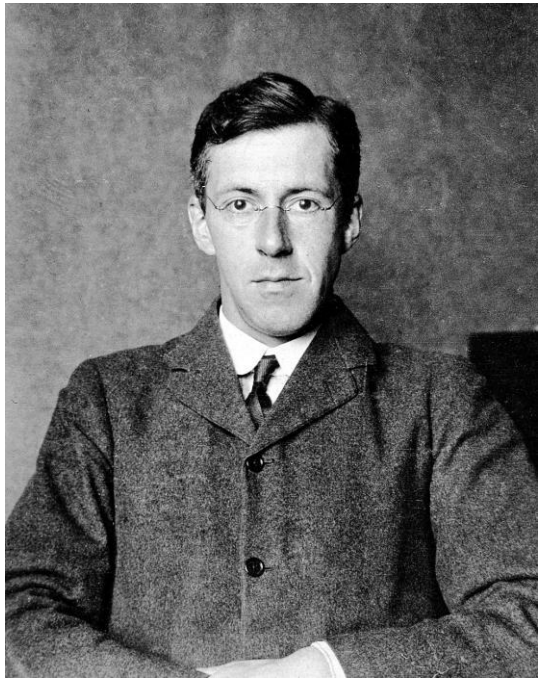
Oxytocin

- Discovered by Sir Henry H. Dale in 1906

- nine-amino-acid neuropeptide, (sequence elucidated in 1953)

- Greek meaning: ‘‘quick birth’’

- Mainly known for its physiological roles :
  uterine contractions during parturition
  and milk ejection.



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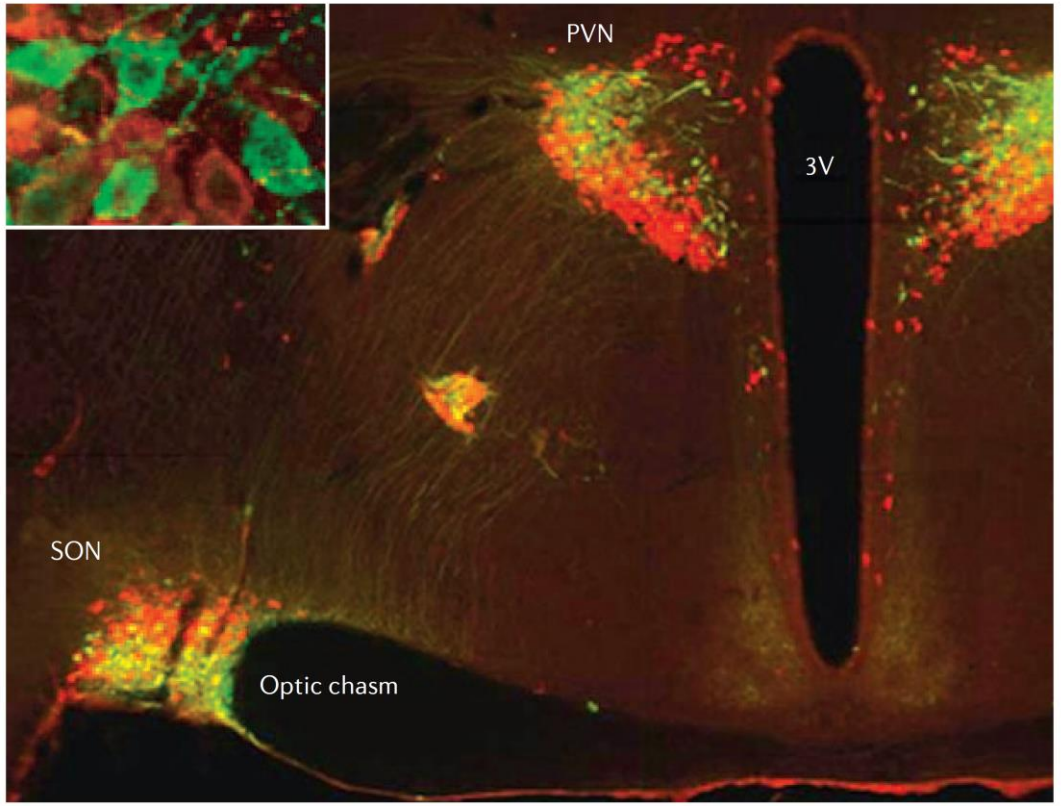
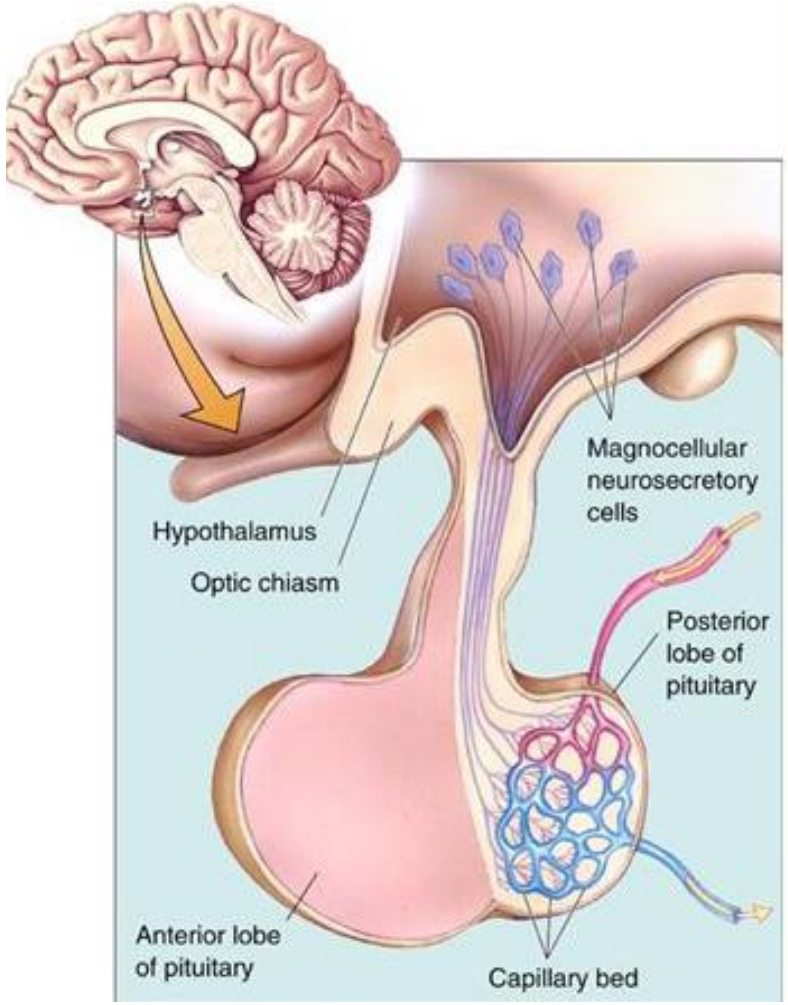
Sir Henry Dale and Otto Loewi



Ludwig & Leng, 2006

- synthesized in the paraventricular (PVN) and supraoptic (SON) nuclei of the hypothalamus

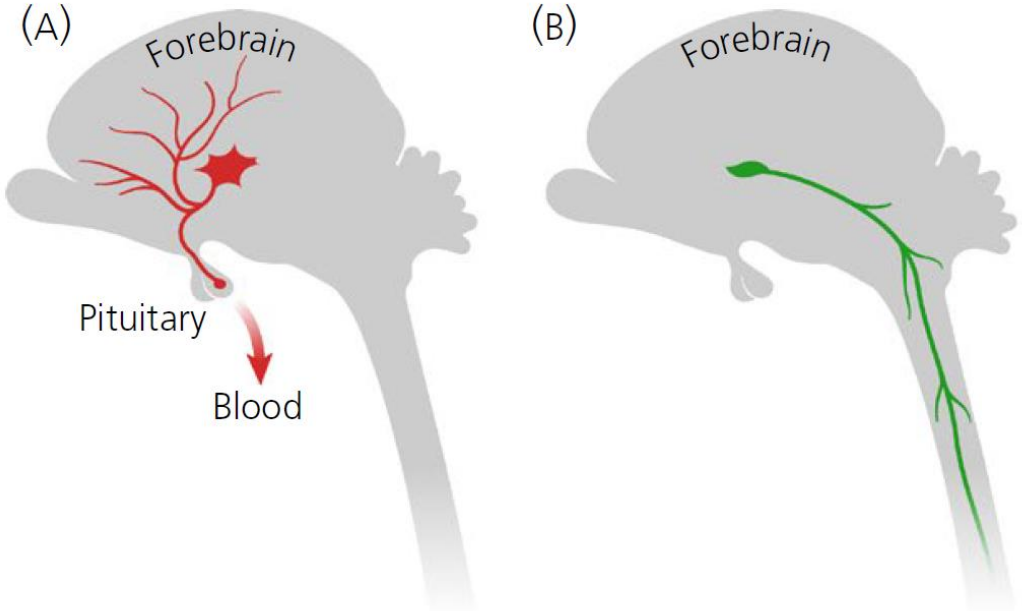
- two types of OT neurons (magnocellular and parvocellular neurons) have been identified (Swanson and Kuypers, 1980)



- classical view:
  - magnocellular OT neurons -> posterior pituitary (release OT into the blood circulation)
  - parvocellular OT neurons -> exclusively to hindbrain areas, where local release of OT modulates vital body functions.

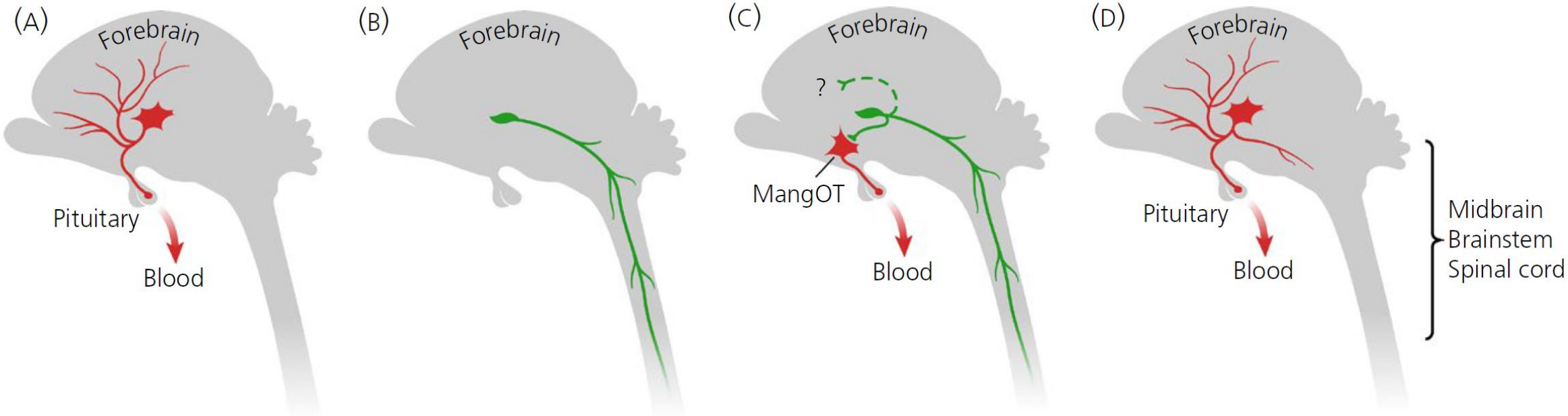
magnocellular

parvocellular



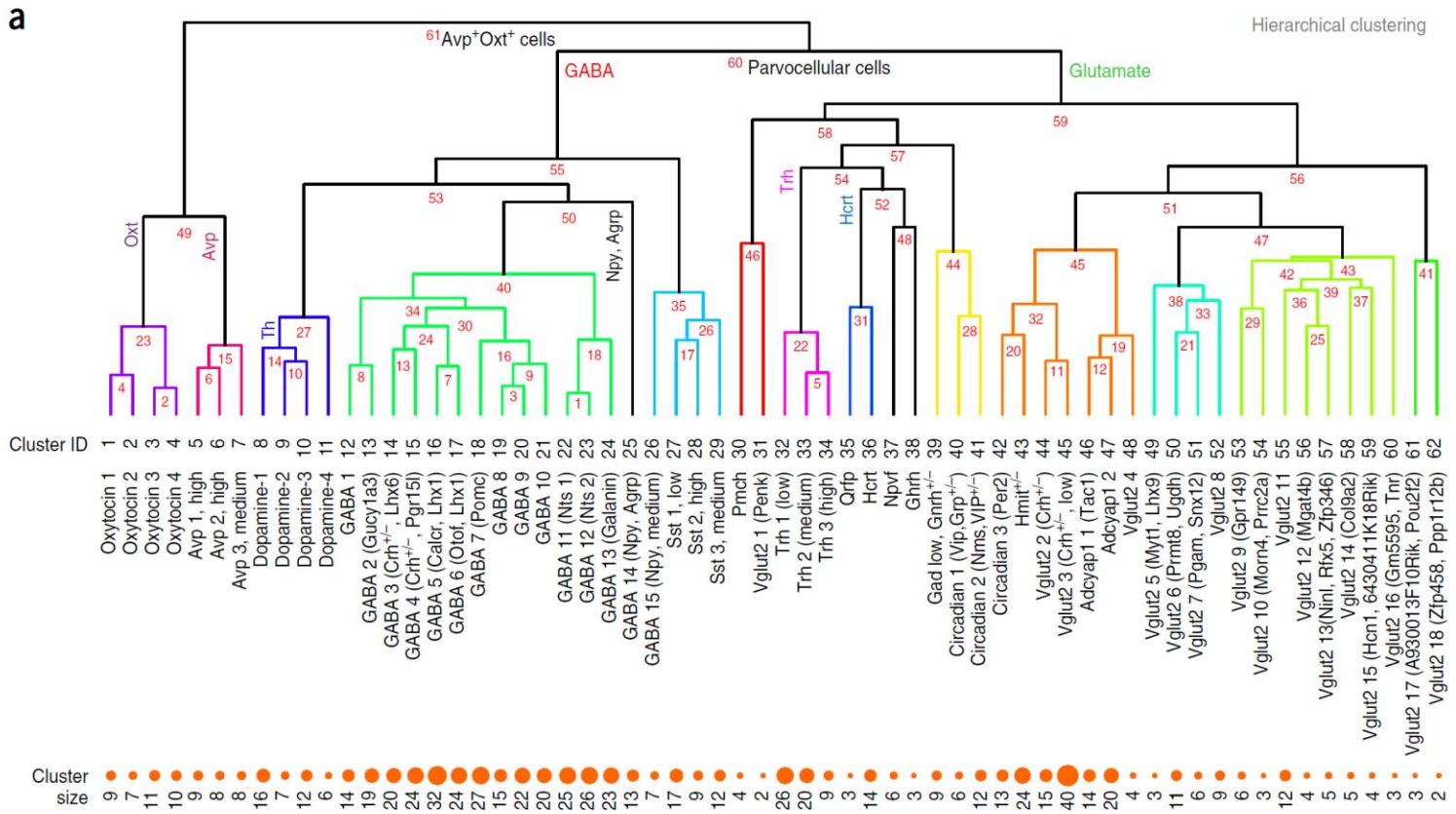
magnocellular

parvocellular



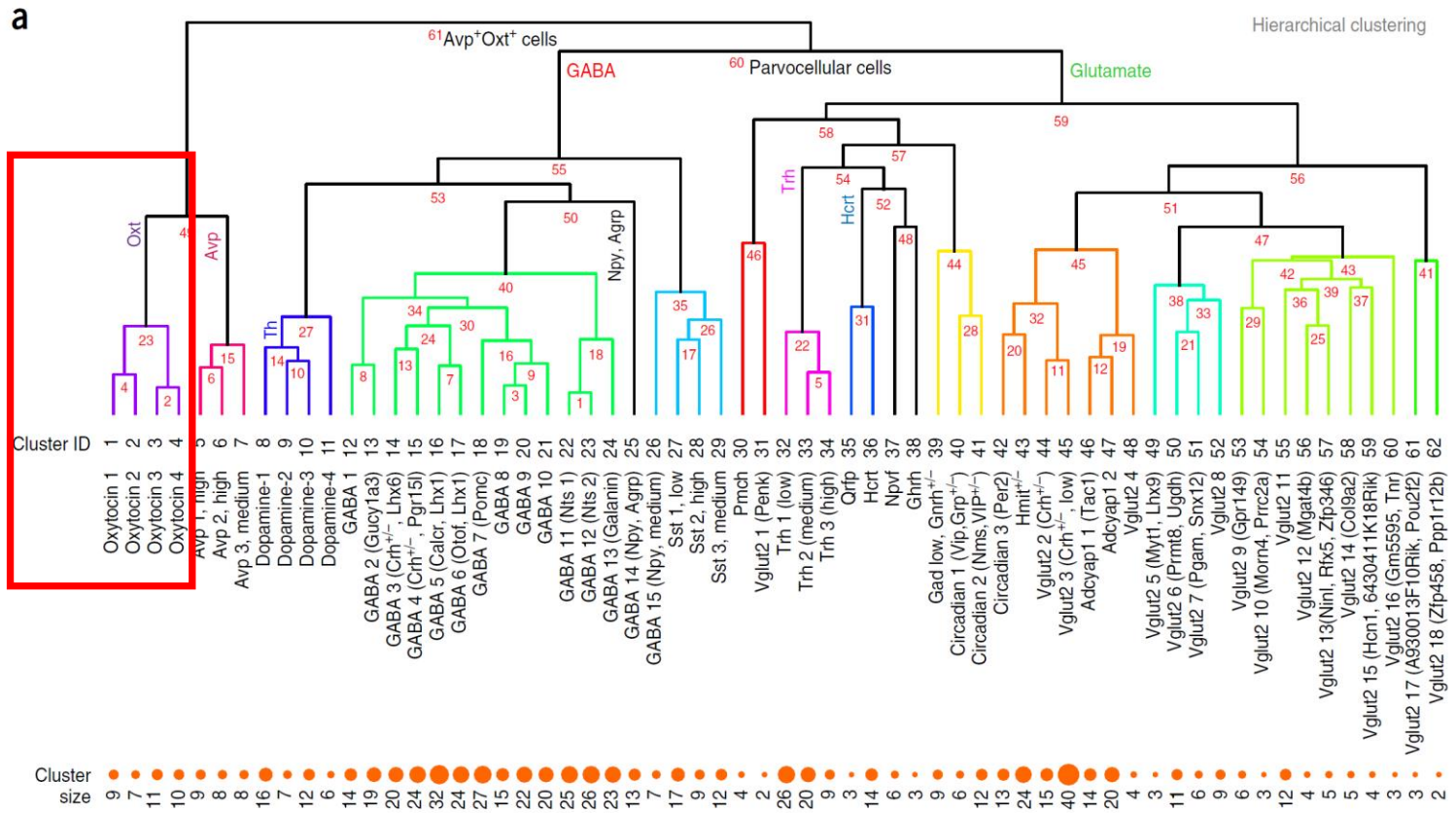
Althammer & Grinevich 2017

More than 2 types of Oxytocin neurons?



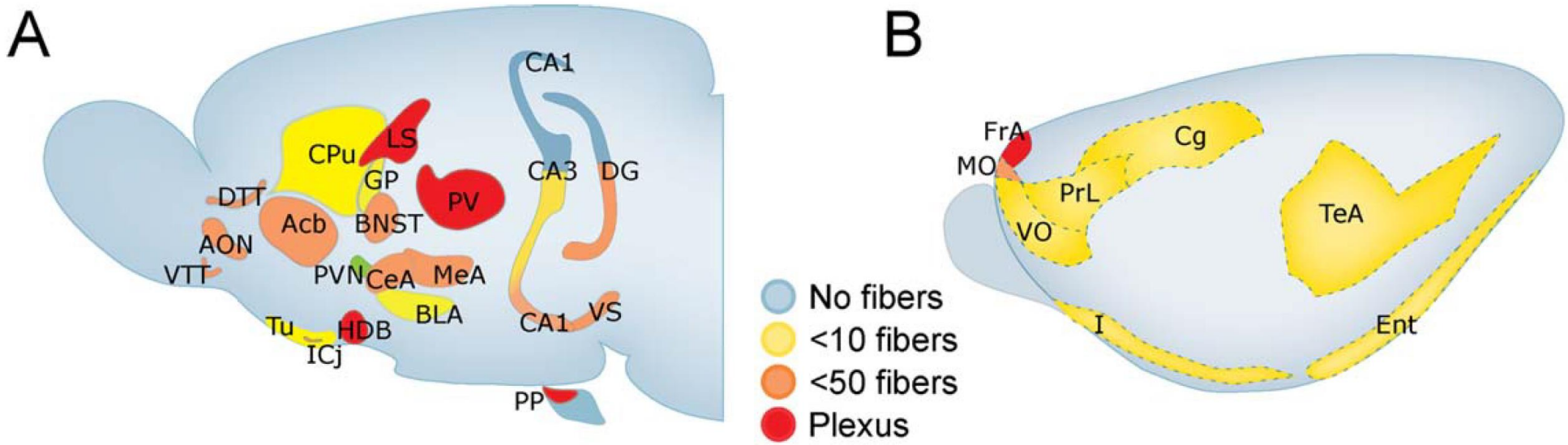
Romanov et al 2016

More than 2 types of Oxytocin neurons?



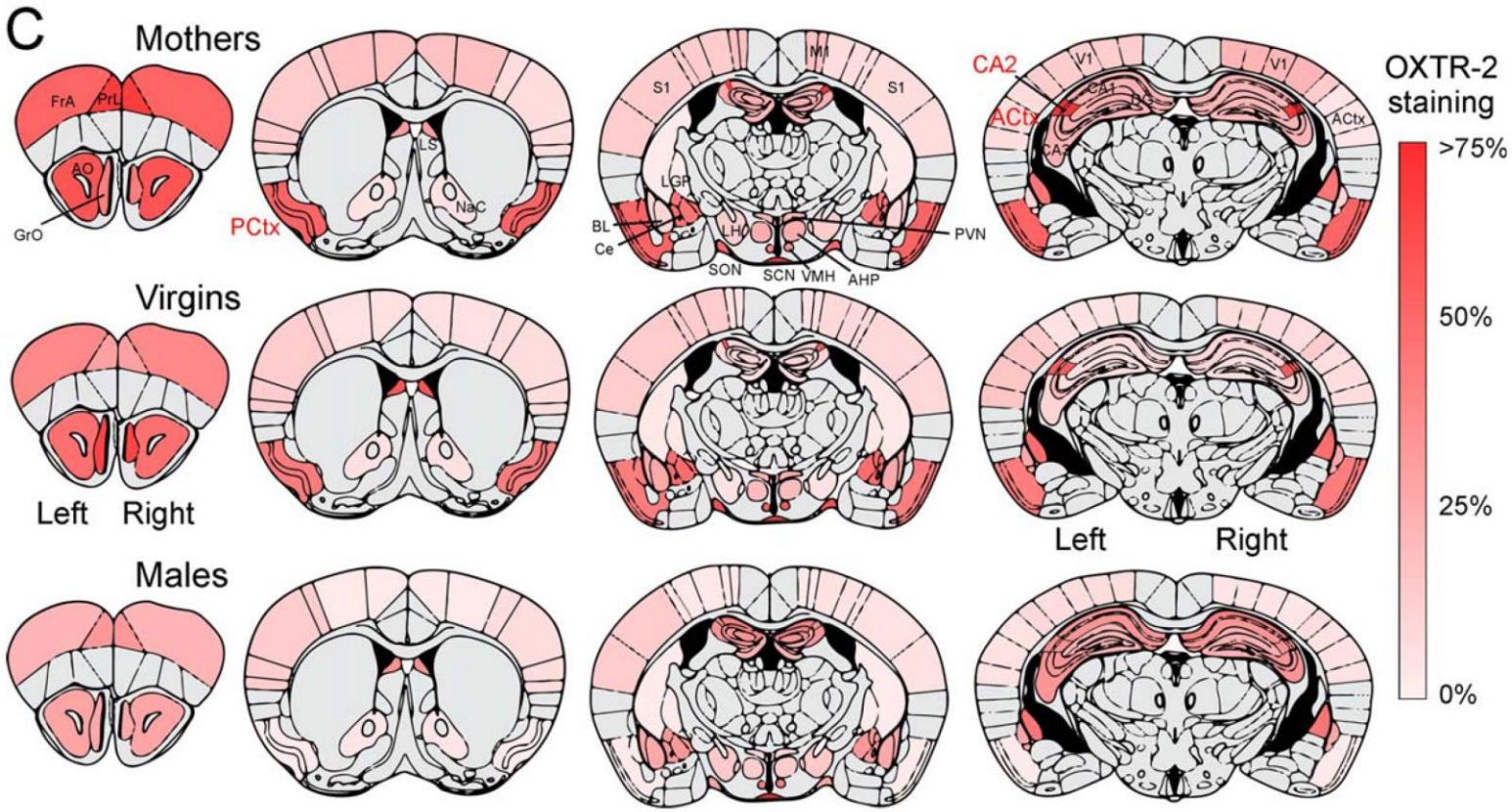
Romanov et al 2016

Distribution of oxytocin fibers in the brain



Knobloch et al 2012

Distribution of oxytocin receptors in the brain



Mitre et al 2016

How does OT reach its targets in the brain?

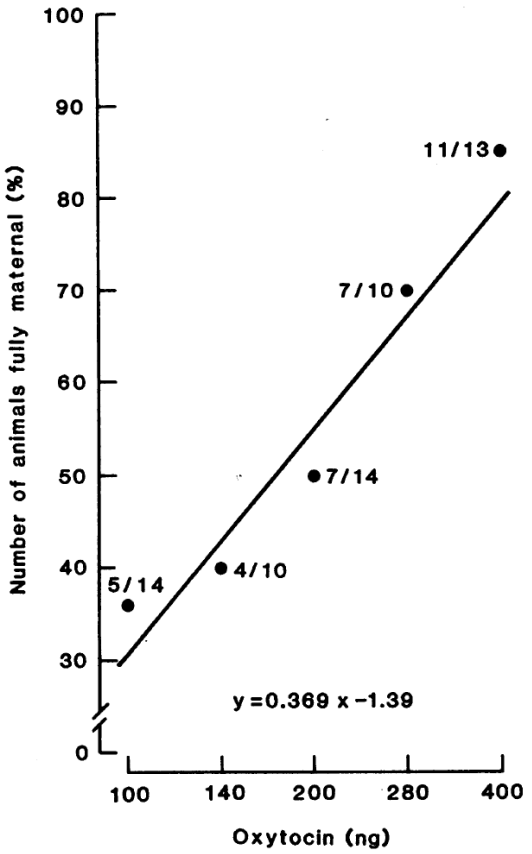
- volume transmission (release from hypothalamic dendrites followed by diffusion in the extracellular space to other brain areas)

- local axonal release

Oxytocin Modulation of Behaviour

Substance	N	Percentage of animals fully maternal		
		0 to 60 minutes	60 to 120 minutes	240 to 300 minutes
Oxytocin	107	72*	72*	72* (N = 58)†
Tocinoic acid	24	50‡	50‡	54‡
β-Endorphin	11	27	27	
Luteinizing hormone–releasing hormone	23	26	26	
Thyrotropin-releasing hormone	12	25	25	
Pro-Leu-Gly-NH_2	12	25	25	
Prolactin	12	25	25	
17β-Estradiol	12	25	25	
Progesterone	12	25	25	
Prostaglandin E_2	14	21	21	36
Lysine vasopressin	29	21	24	24
Pressinoic acid	15	20	20	20
Bradykinin	10	20	20	
Arginine vasotocin	11	18	27	
Saline	51	18	18	19 (N = 26)†
Prostaglandin $F_{2\alpha}$	19	16	16	21
Arginine vasopressin	31	16	42§	55‡
No ICV injection	20	15	15	15
Substance P	17	12	12	
Neurotensin	11	9	9	

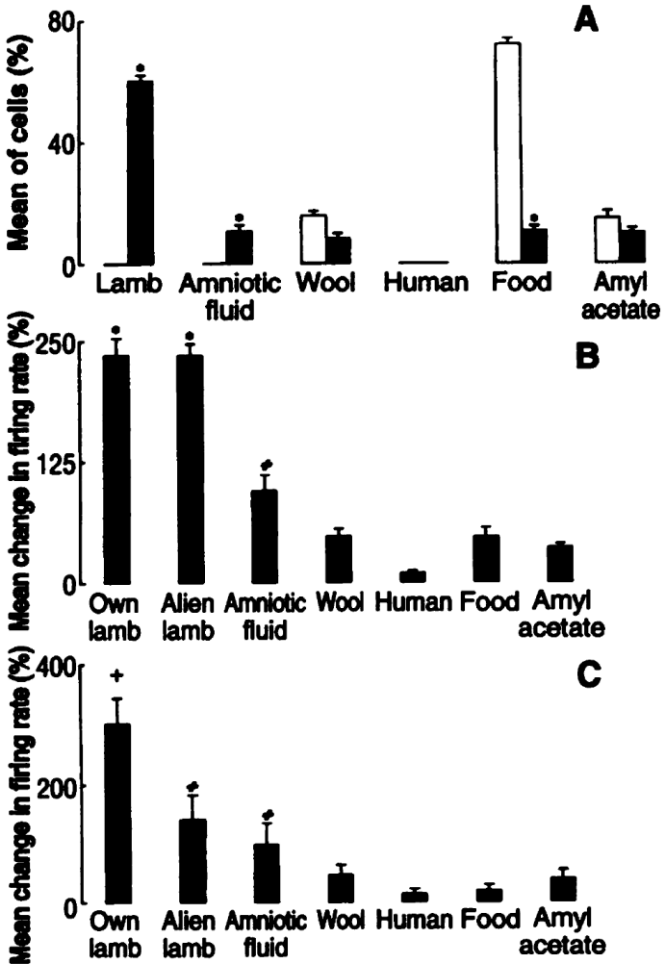
*$P < .001$. †N shows the number of animals observed during the third observation period added part way through the experiment. ‡$P < .01$. §$P < .05$ compared to the group treated with saline (Fisher's exact probability test).



Pedersen et al 1982

Oxytocin Modulation of Behaviour

Kendrick et al., Science, 1992



Oxytocin Modulation of Behaviour

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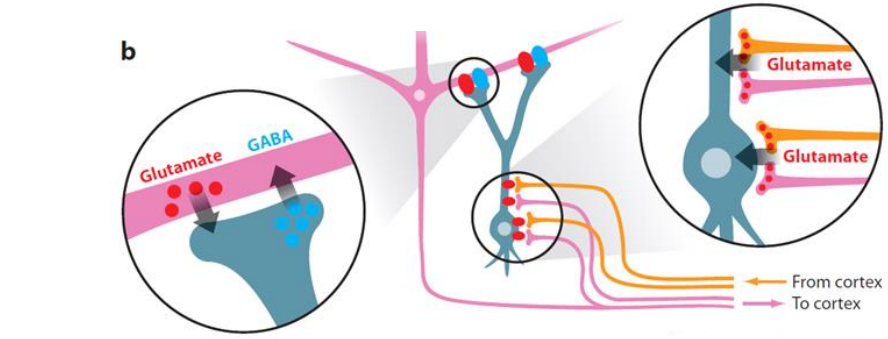
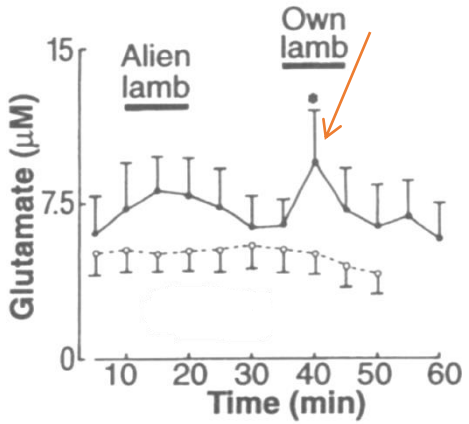
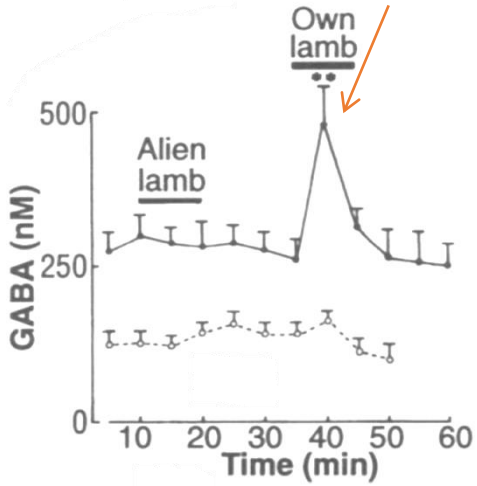
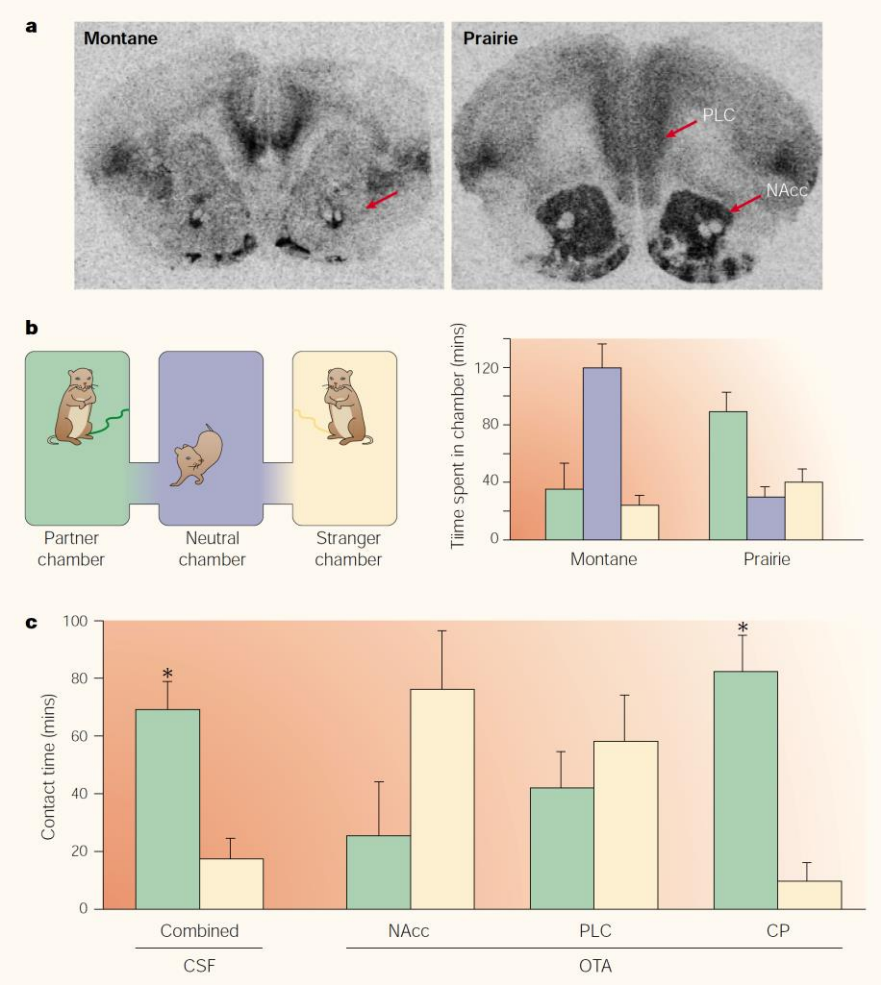






Oxytocin Modulation of Behaviour



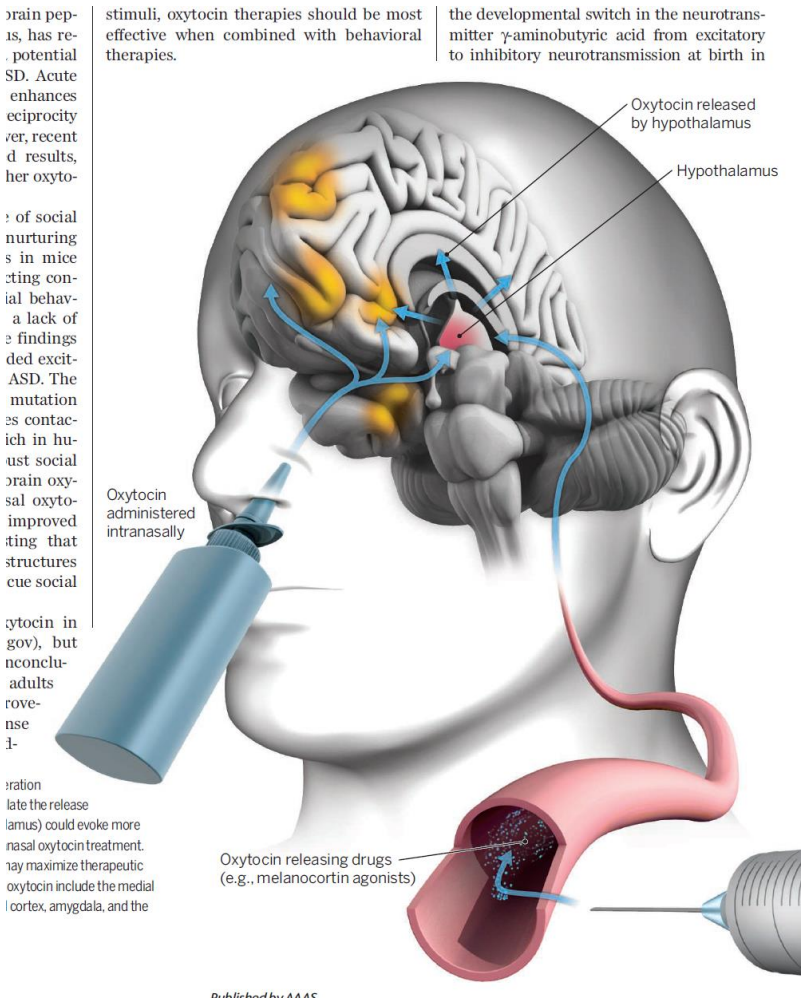
Prairie vole: monogamous
Montane vole: polygamous

(Prairie vole)

Insel & Young 2001

Oxytocin Modulation of Human Behaviour

Oxytocin Modulation of Human Behaviour

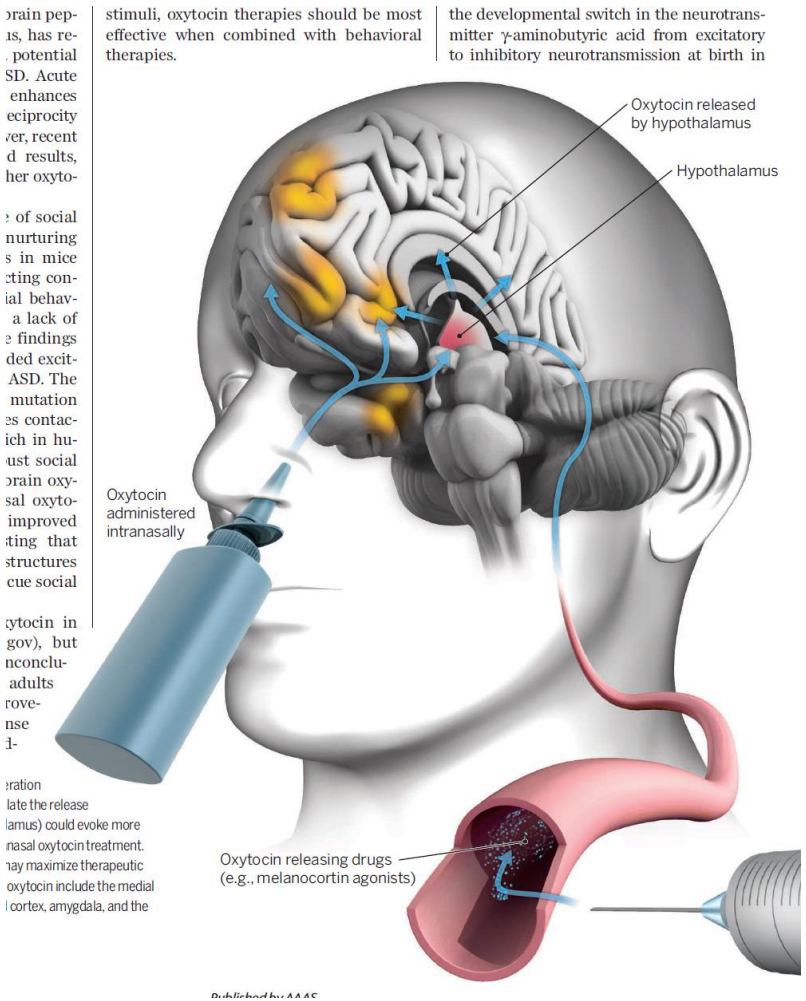


Young & Barrett 2014

Oxytocin increases trust in humans

Michael Kosfeld[1]*, Markus Heinrichs[2]*, Paul J. Zak[3], Urs Fischbacher[1] & Ernst Fehr[1,4]

Oxytocin Modulation of Human Behaviour



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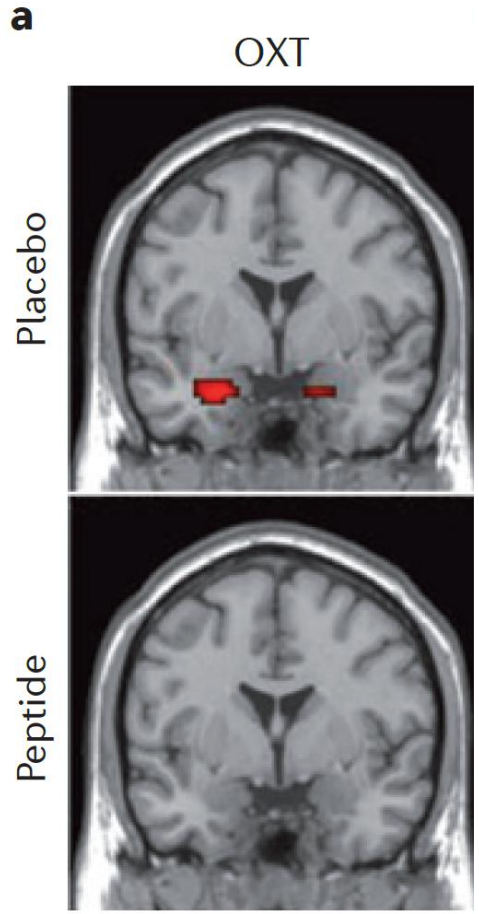
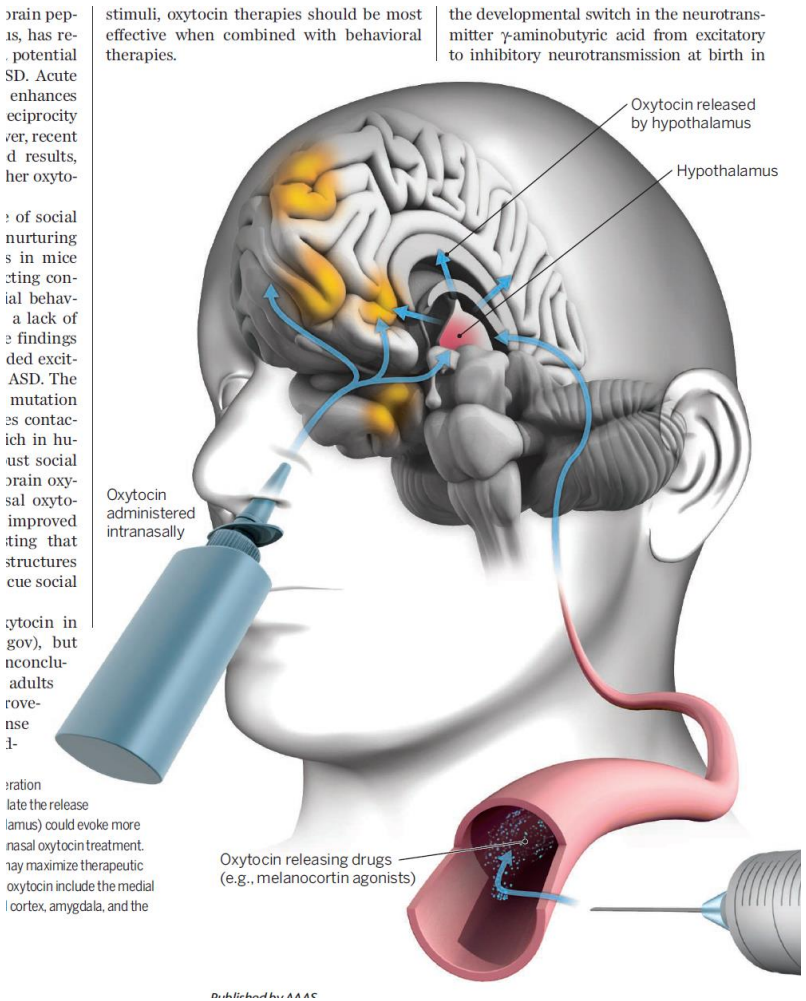


Kirsch et al 2005

Oxytocin Modulation of Human Behaviour



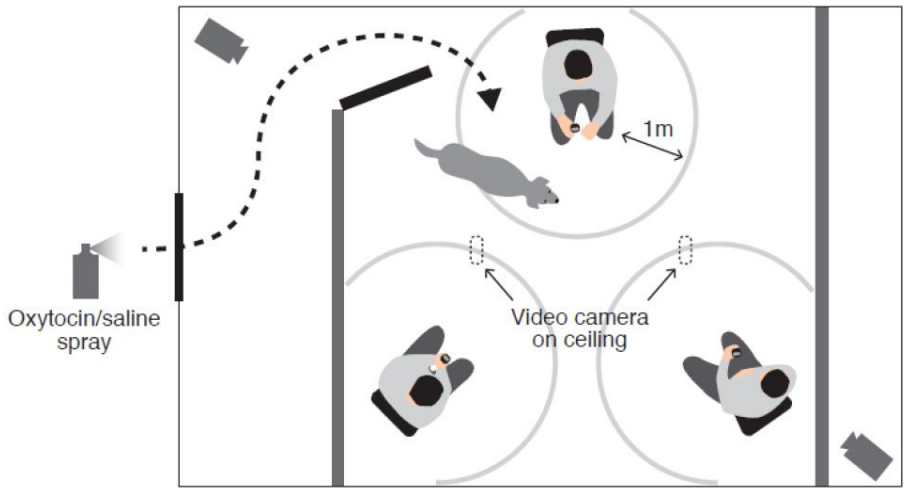
Young & Barrett 2014

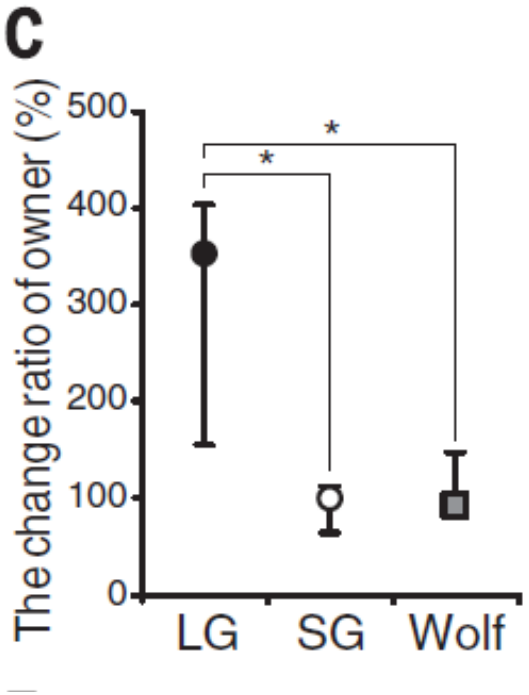
ORIGINAL ARTICLE

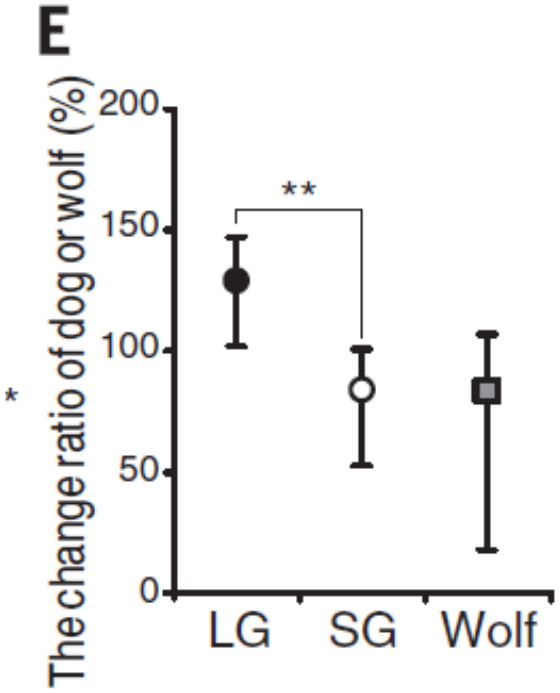
Oxytocin by intranasal and intravenous routes reaches the cerebrospinal fluid in rhesus macaques: determination using a novel oxytocin assay

MR Lee[1], KB Scheidweiler[2], XX Diao[2], F Akhlaghi[3], A Cummins[4], MA Huestis[2], L Leggio[1,5,6] and BB Averbeck[4,6]

Oxytocin Modulation of Human Behaviour

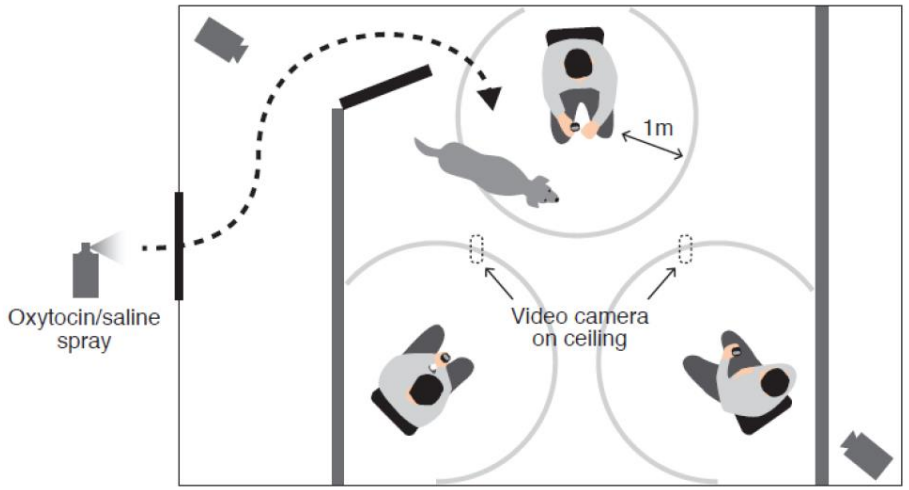


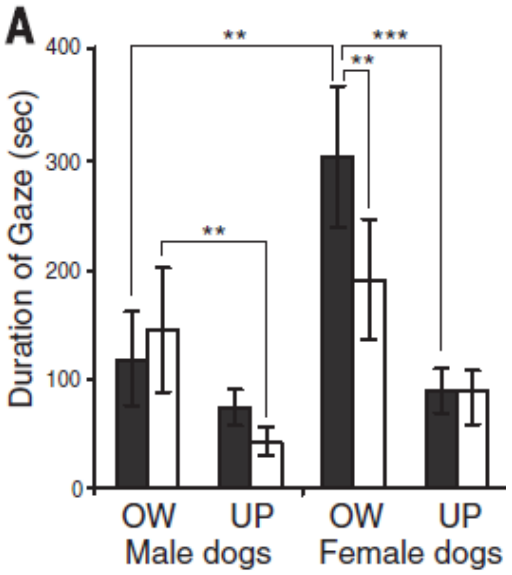


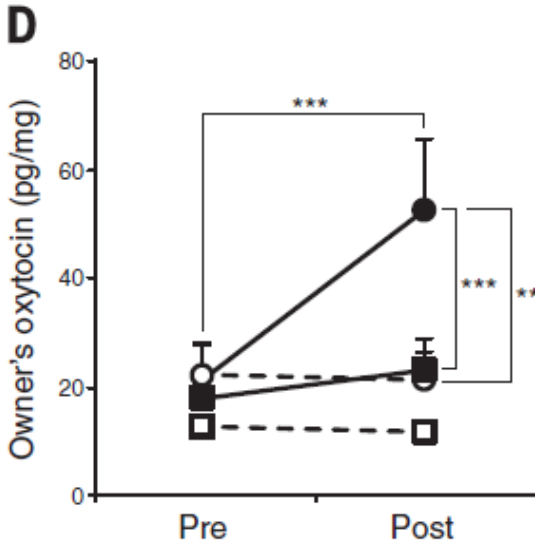


Nagasawa et al 2015

Oxytocin Modulation of Human Behaviour







Nagasawa et al 2015

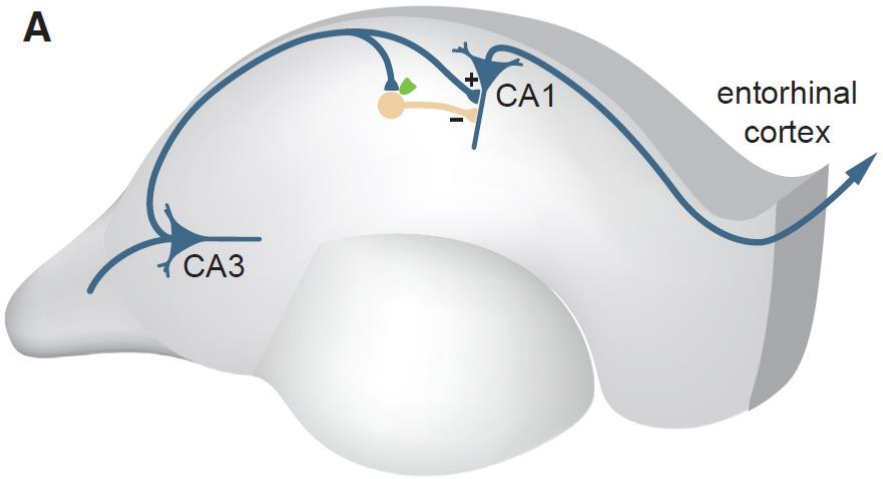
Oxytocin Modulation of Human Behaviour

Experiment 2
Oxytocin or Saline administration and owner-dog interactions.

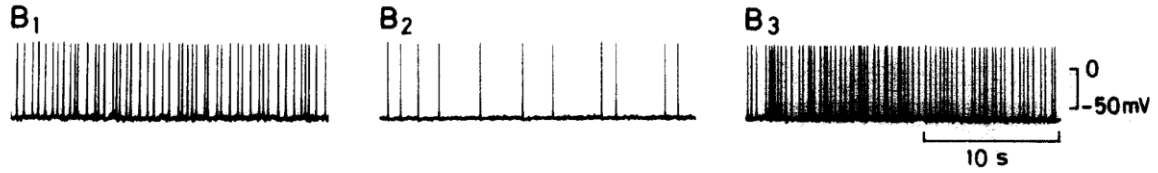
(Left side: Oxytocin administration) **(Right side: Saline administration)**

OW: owner
UF: unfamiliar person

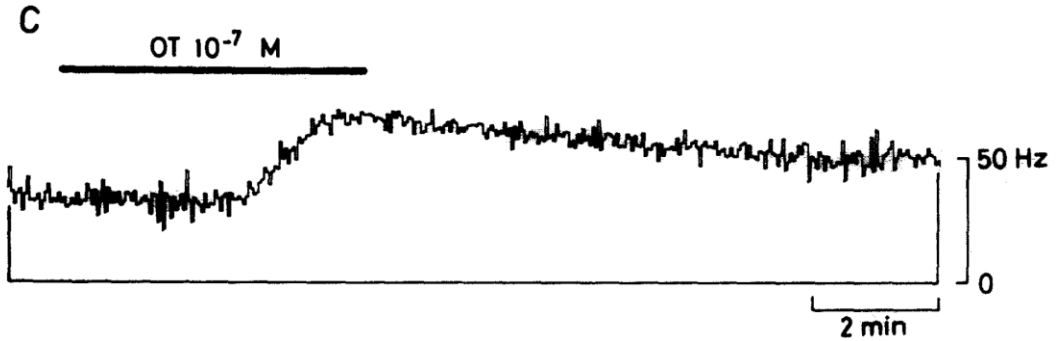
Oxytocin Modulation of Neural Circuits



CA1 pyramidal neuron

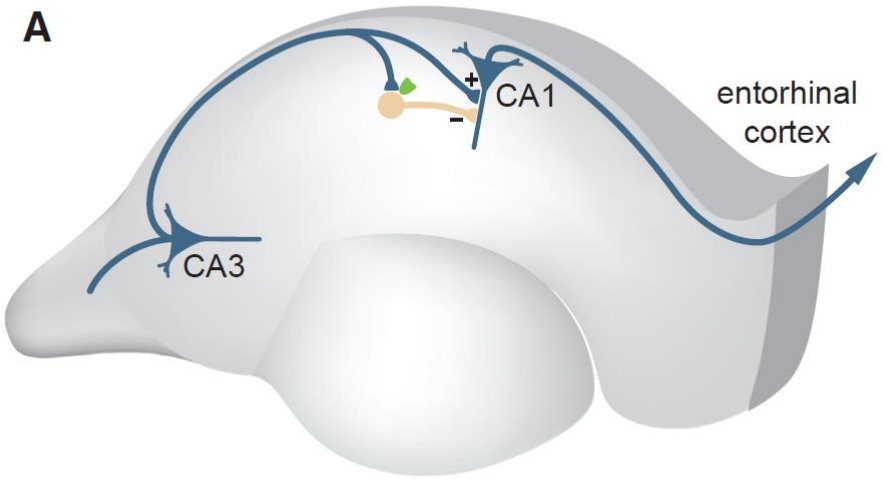


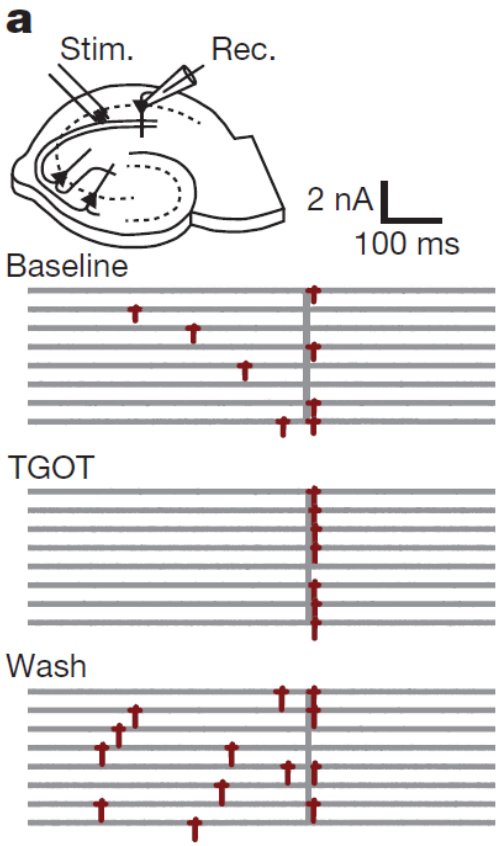
Non-pyramidal neuron



Muhlethaler et al 1984

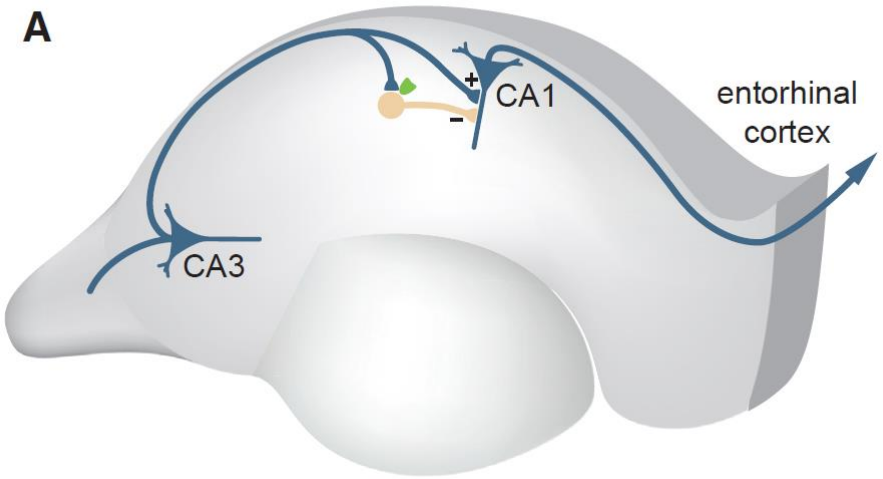
Oxytocin Modulation of Neural Circuits

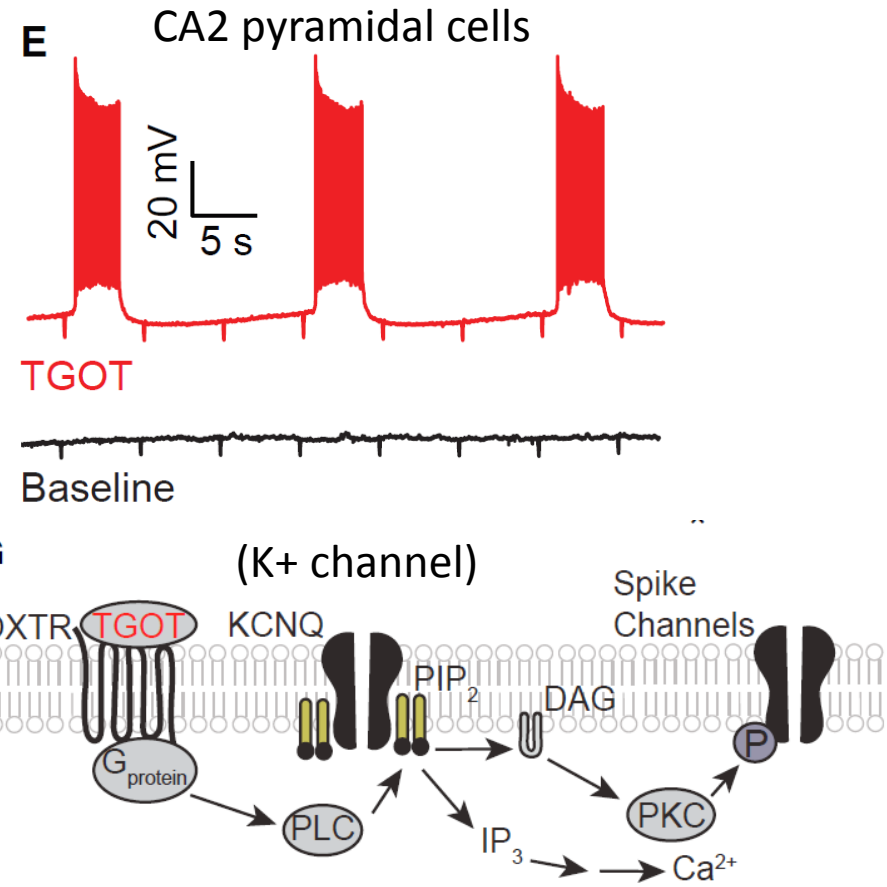




Owen et al 2013

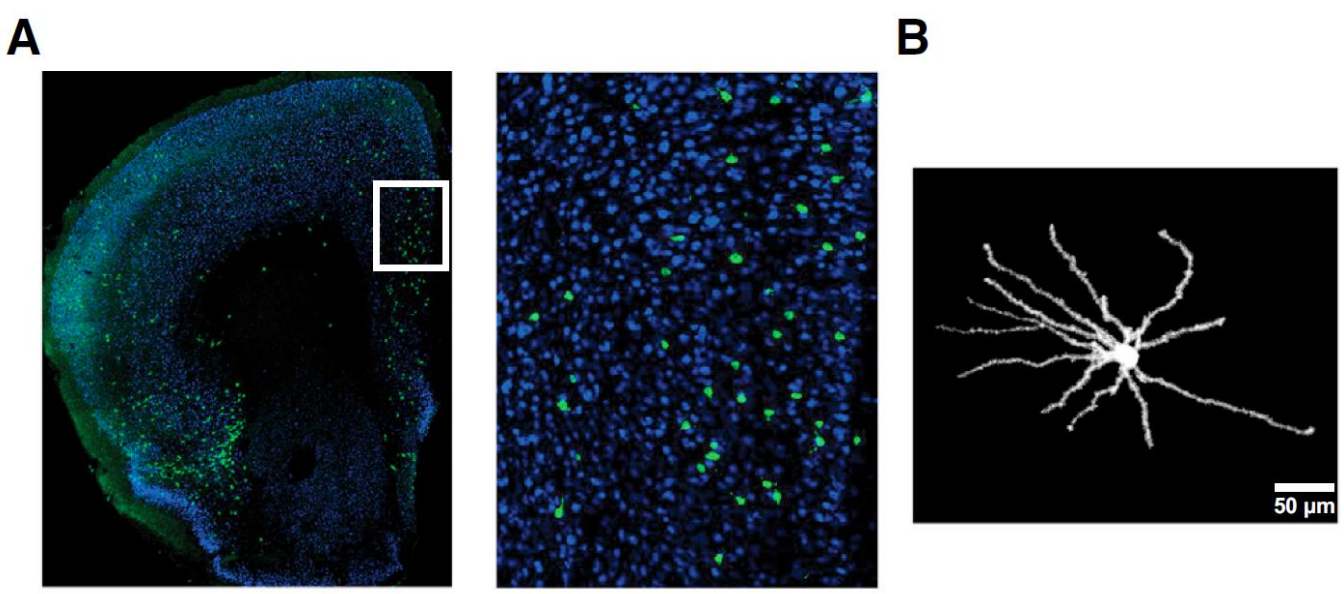
Oxytocin Modulation of Neural Circuits

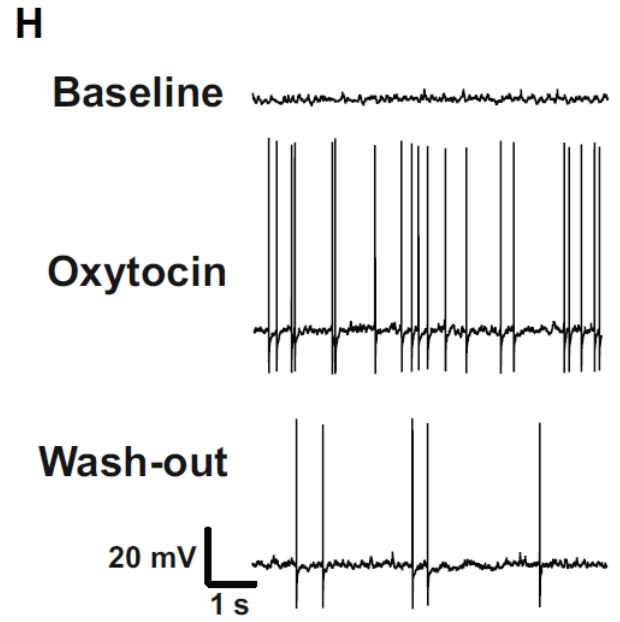




Tirko et al 2018

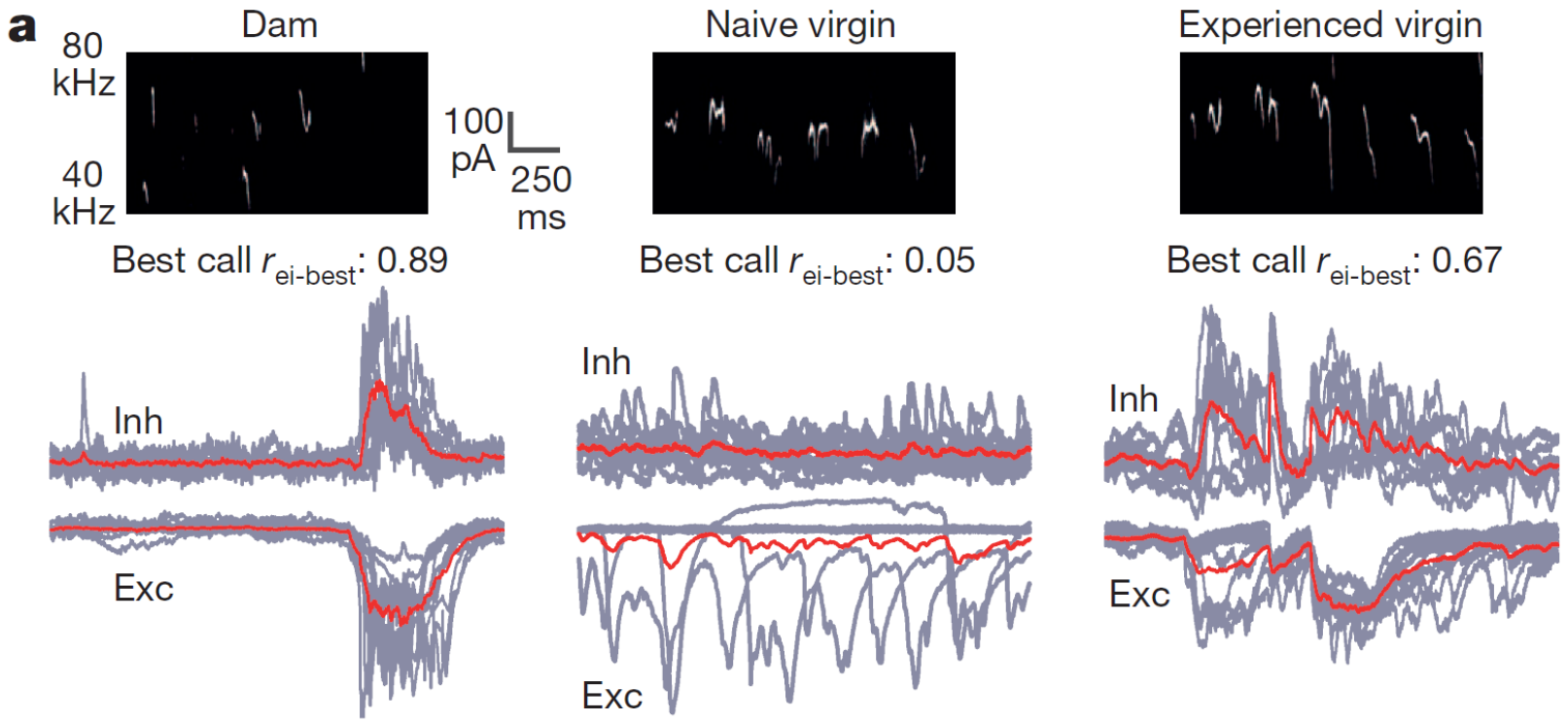
Oxytocin Modulation of Neural Circuits





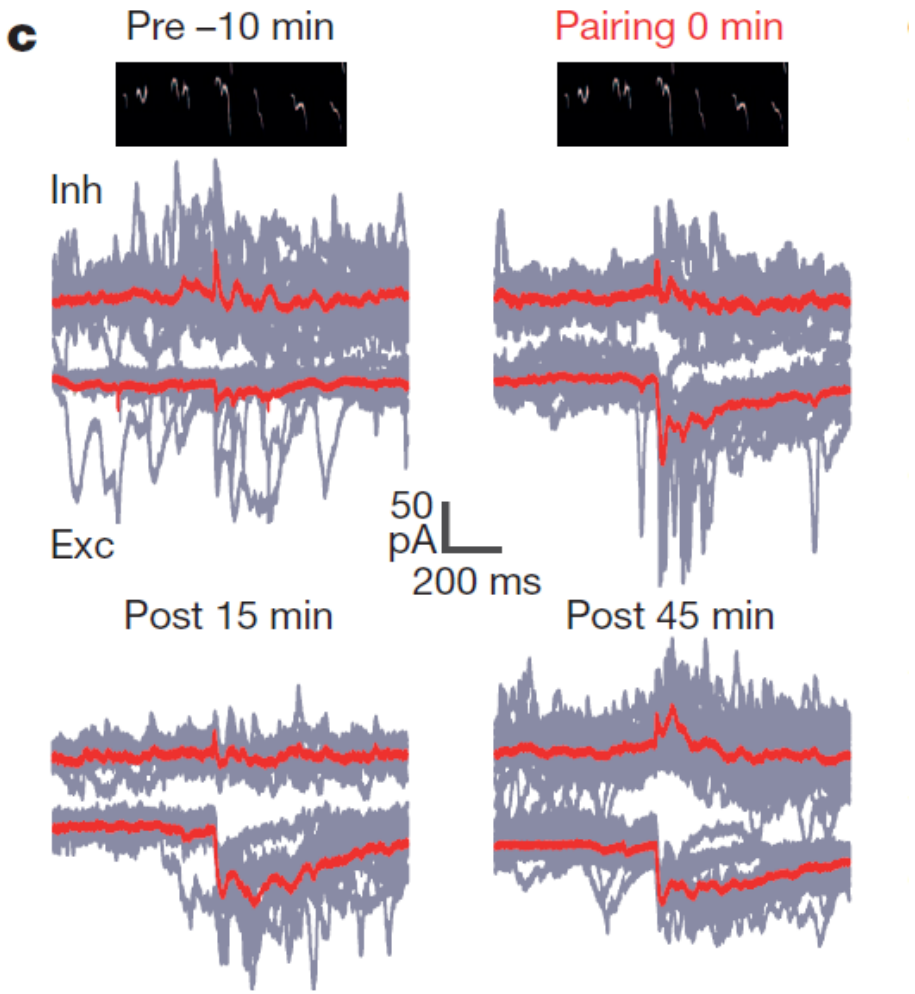
Nakajima et al 2014

Oxytocin Modulation of Sensory Circuits



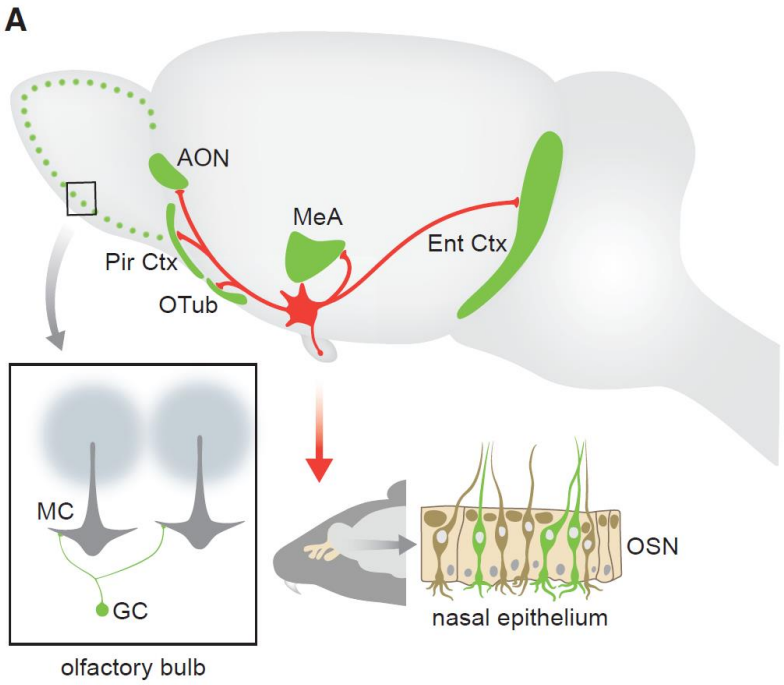
Marlin et al 2015

Oxytocin Modulation of Sensory Circuits

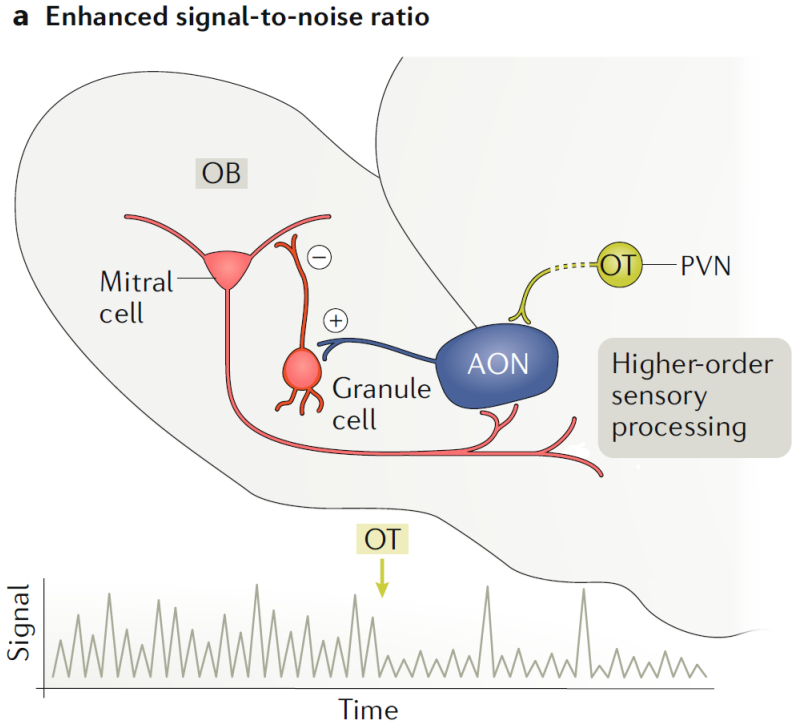


Marlin et al 2015

Oxytocin Modulation of Sensory Circuits

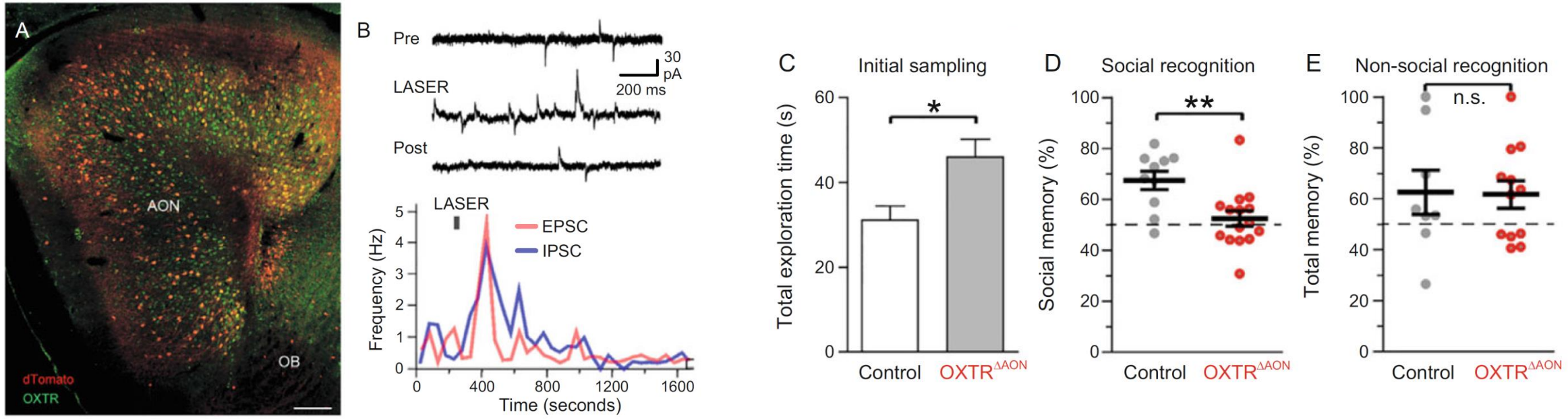


Grinevich & Stoop 2018



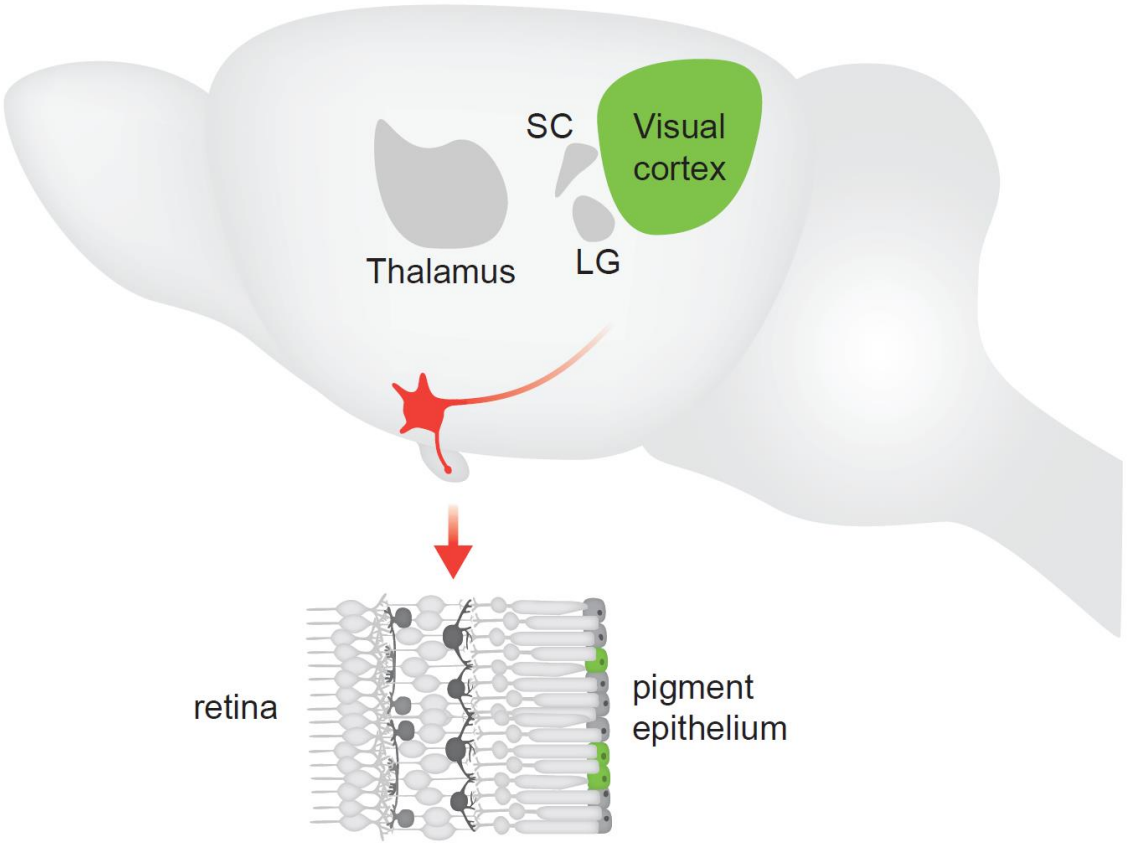
Walum & Young 2018
Oettl et al 2016

Oxytocin Modulation of Sensory Circuits

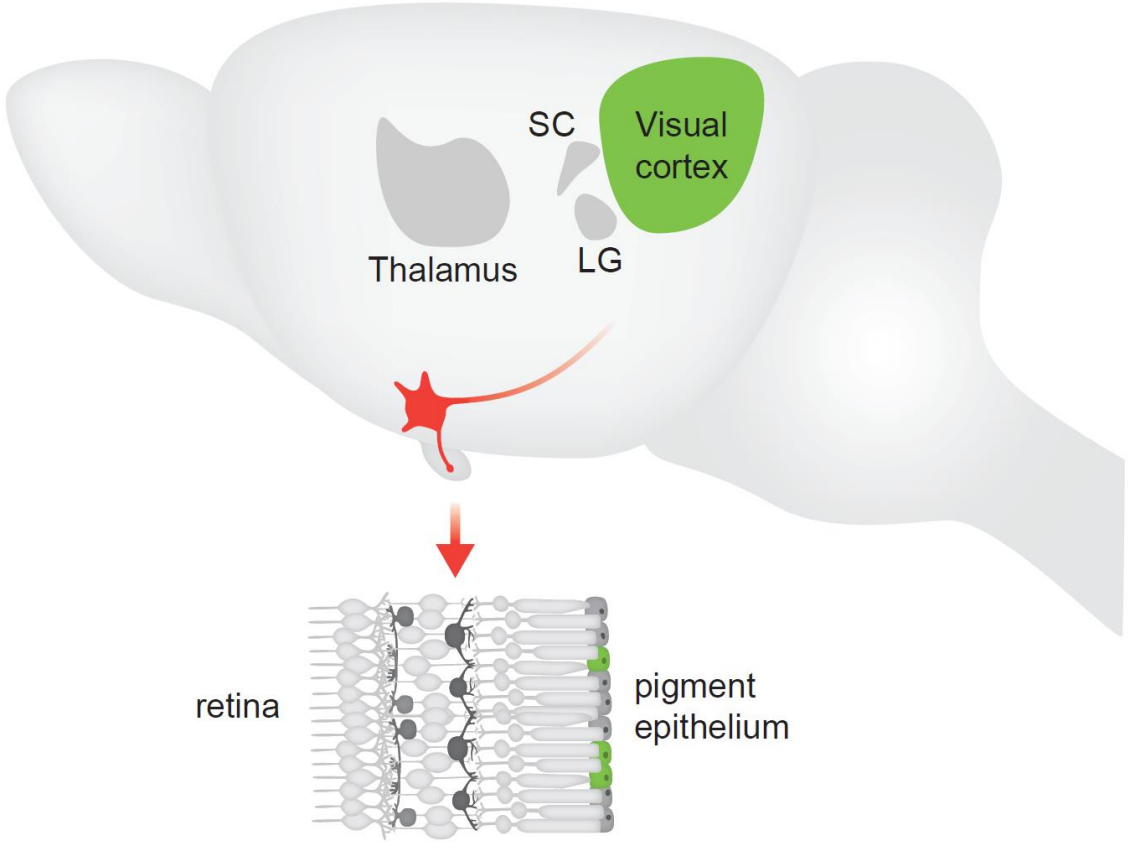


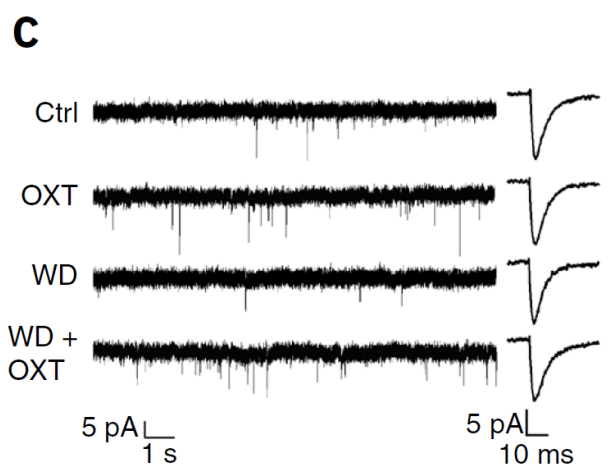
Oettl et al 2016

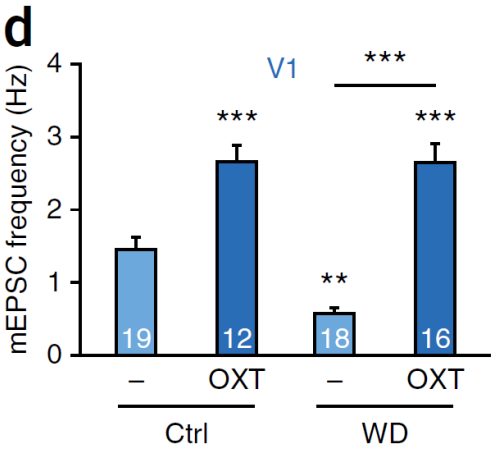
Oxytocin Modulation of Sensory Circuits



Oxytocin Modulation of Sensory Circuits



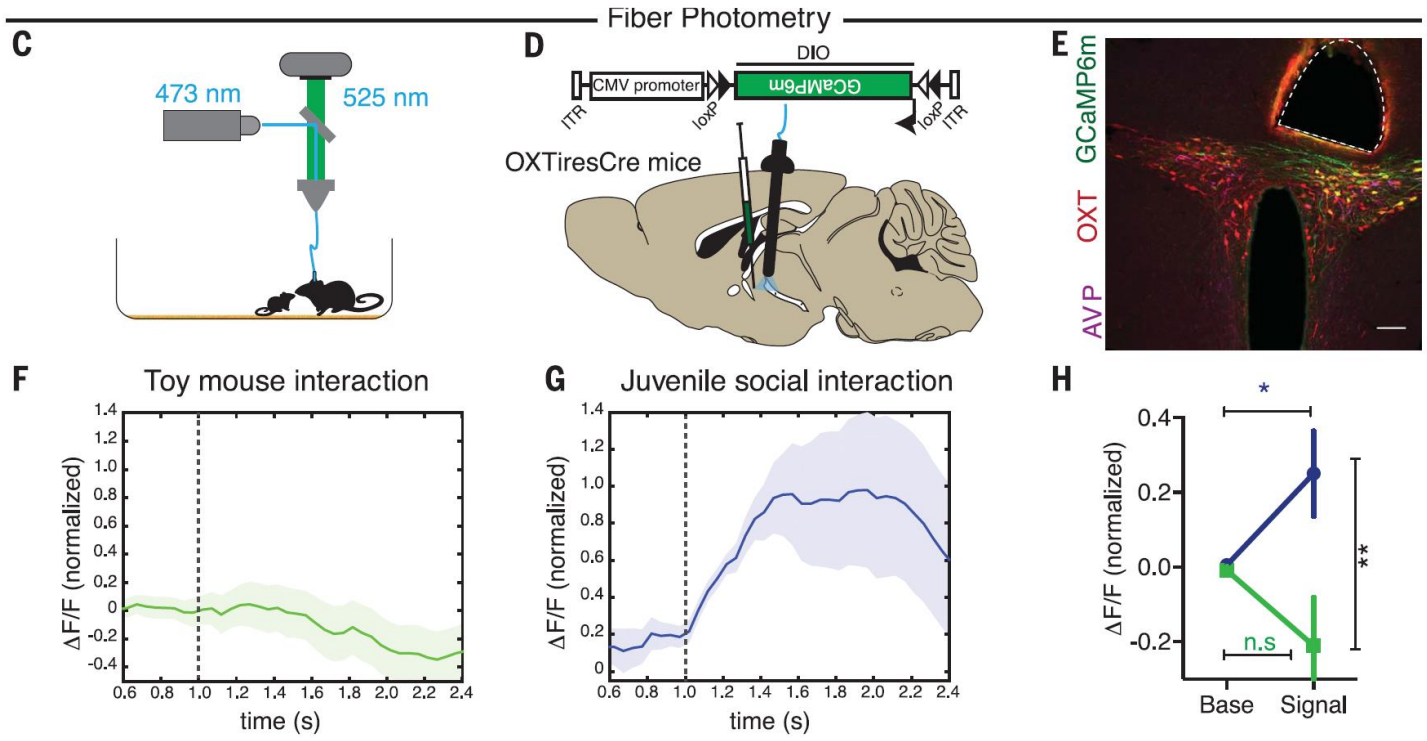




Zheng et al 2014

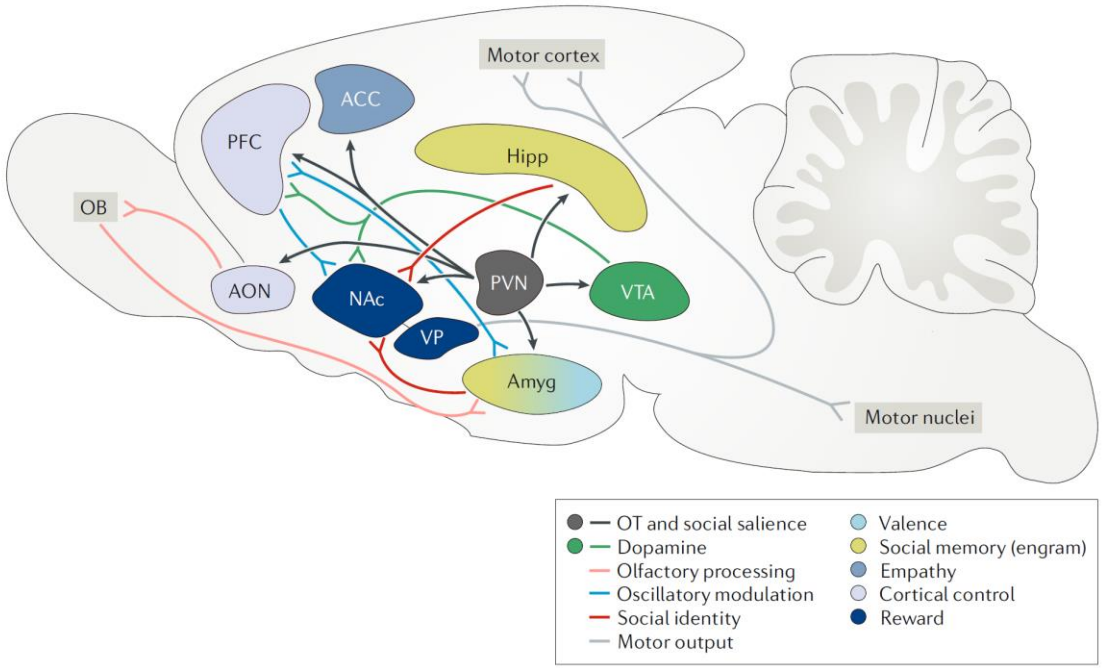
Outstanding questions

- Not much is known about the natural release of oxytocin in response to natural stimuli



Hung et al 2017

Conclusion



Walum & Young 2018

- Oxytocin might play a general role in facilitating the flow of social information across multiple brain regions
- (E-I balance, SNR)