UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of report (date of earliest event reported): January 31, 2023

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

Nevada	**001-36019**	**26-1434750**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

26 Main Street, Chatham, New Jersey 07928
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (862) 904-8182

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
□ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
□ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TNXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company □

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. □

Item 7.01 Regulation FD Disclosure.

On January 31, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that David C. Yeomans, Ph.D., presented data from clinical and nonclinical studies in an oral presentation at the 16th Annual Headache Cooperative of the Pacific Winter Conference on January 27, 2023 (the "Presentation"). A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference. The Presentation, which may contain nonpublic information, is filed as Exhibit 99.02 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.01 and 99.02 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

On January 31, 2023, the Company announced that Dr. Yeomans presented data from the Presentation, entitled "*Primary vs Secondary Sex Hormones and Migraine*," which includes research sponsored by the Company and demonstrates that magnesium (Mg^{++}) potentiates the analgesic effects of oxytocin, and includes new preliminary data from a Positron Emission Tomography ("PET") study in human volunteers dosed with a proprietary nitrogen-13 (^{13}N) radioisotope of oxytocin formulated with Mg^{++}. A signal was observed in the trigeminal ganglia, indicating that intranasal oxytocin plus Mg^{++} delivers oxytocin to the trigeminal ganglia, which have known roles in migraine headache. These studies were a collaboration with Aarhus University and the principal investigator, Michael Winterdahl, PhD.

In addition to the PET study, the presentation includes data collected from isolated human trigeminal ganglia neurons *in vitro*, which demonstrates oxytocin receptor co-expressed with calcitonin gene-related peptide ("CGRP"). The results of these studies, which were performed by Vimala Bharadwaj, PhD, are believed to represent the first observation of oxytocin receptors in human tissue rather than in an animal model. The cytokine IL-6 functionally upregulated expression of human trigeminal oxytocin receptors *in vitro*, similar to what has been shown previously in rats, in which oxytocin has been shown to functionally inhibit electrically evoked activity of trigeminal neurons. The Presentation highlights data which suggest a sex difference in oxytocin potency, and indicates that oxytocin is more potent in inhibiting trigeminal ganglion neuronal excitability in female rats compared to males. The data demonstrates that treating male rats with estrogen for four days increased the responsiveness of their isolated trigeminal ganglia to oxytocin *in vitro* such that they showed a similar level of responsiveness to oxytocin as female trigeminal ganglia. The Company believes these findings have potential dosing implications in humans who suffer from chronic migraine.

Forward- Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press release of the Company, dated January 31, 2023
99.02	Primary vs Secondary Sex Hormones and Migraine
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirement of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TONIX PHARMACEUTICALS HOLDING CORP.

Date: January 31, 2023

By: /s/ Bradley Saenger
Bradley Saenger
Chief Financial Officer

Exhibit 99.01

Tonix Pharmaceuticals Announces Presentation of Clinical and Non-Clinical TNX-1900 Data at the Annual Headache Cooperative of the Pacific (HCOP) Winter Conference

Preliminary Results from Human PET Study Show that Intranasal Application of a Radioisotope of Magnesium-Potentiated Oxytocin is Delivered to the Trigeminal Ganglia

Preliminary Results on Human Cadaveric Trigeminal Ganglia Show Co-expression of Oxytocin Receptors and CGRP

Preliminary Results Show Sex Differences in Oxytocin Potency in an Animal Model

CHATHAM, N.J., January 31, 2023 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that David C. Yeomans, Ph.D., presented data from clinical and nonclinical studies in an oral presentation at the 16th Annual Headache Cooperative of the Pacific (HCOP) Winter Conference on January 27, 2023. The oral presentation titled, "***Primary vs Secondary Sex Hormones and Migraine***," includes research sponsored by and licensed to Tonix Pharmaceuticals. Professor Yeomans was a founder of Trigemina, which Tonix acquired, and he remains a consultant to Tonix. A copy of the presentation is available under the Scientific Presentations tab of the Tonix Pharmaceuticals corporate website at www.tonixpharma.com.

"In addition to data showing that magnesium (Mg^{++}) potentiates the analgesic effects of oxytocin, the presentation includes new preliminary data from a Positron Emission Tomography (PET) study in human volunteers dosed with a proprietary nitrogen-13 (^{13}N) radioisotope of oxytocin formulated with Mg^{++}," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "A signal was observed in the trigeminal ganglia, indicating that intranasal oxytocin plus Mg^{++} delivers oxytocin to the trigeminal ganglia which have known roles in migraine headache. These studies were a collaboration with Aarhus University and the principal investigator, Michael Winterdahl, PhD."

In addition to the PET study, the presentation includes data collected from isolated human trigeminal ganglia neurons *in vitro* which show oxytocin receptor co-expressed with calcitonin gene-related peptide (CGRP). The results of these studies, which were performed by postdoctoral fellow Vimala Bharadwaj, PhD, are believed to represent the first observation of oxytocin receptors in human tissue rather than in an animal model. Previously, it has been shown that oxytocin receptors and CGRP co-localize in rat trigeminal ganglia neurons. The cytokine IL-6 functionally upregulated expression of human trigeminal oxytocin receptors *in vitro*, similar to what has been shown previously in rats, in which oxytocin has been shown to functionally inhibit electrically evoked activity of trigeminal neurons.

Finally, the presentation highlights data which suggest a sex difference in oxytocin potency. "The results indicate that oxytocin is more potent in inhibiting trigeminal ganglion neuronal excitability in female rats compared to males," said Professor David C. Yeomans. "Moreover, treating male rats with estrogen for four days increased the responsiveness of their isolated trigeminal ganglia to oxytocin *in vitro* such that they show a similar level of responsiveness to oxytocin as female trigeminal ganglia. The Company believes that together, these findings have potential dosing implications in humans who suffer from chronic migraine."

In late 2021, Tonix received Investigational New Drug clearance from the U.S. Food and Drug Administration to support the initiation of a Phase 2 study of TNX-1900 (intranasal magnesium potentiated oxytocin) for the prevention of migraine headache in chronic migraineurs. The Company expects to begin enrollment in the Phase 2 study during the first quarter of 2023.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study launched in the second quarter of 2022 and interim data expected in the second quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix initiated a Phase 2 study in Long COVID in the third quarter of 2022 and expects interim data in the third quarter of 2023. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the first quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is expected to enter the clinic with a Phase 2 study in the first quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily formulation of tianeptine being developed as a potential treatment for major depressive disorder (MDD) with a Phase 2 study expected to be initiated in the first quarter of 2023. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the first half of 2023. Tonix's infectious disease pipeline includes a vaccine in development to prevent smallpox and monkeypox, TNX-801, a next-generation vaccine to prevent COVID-19, TNX-1850, a platform to make fully human monoclonal antibodies to treat COVID-19, TNX-3600, and humanized anti-SARS-CoV-2 monoclonal antibodies, TNX-3800, recently licensed from Curia. TNX-801, Tonix's vaccine in development to prevent smallpox and monkeypox, also serves as the live virus vaccine platform or recombinant pox vaccine (RPV) platform for other infectious diseases. A Phase 1 study of TNX-801 is expected to be initiated in Kenya in the second half of 2023.

**All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*

This press release and further information about Tonix can be found at www.tonixpharma.com.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those

indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the "SEC") on March 14, 2022, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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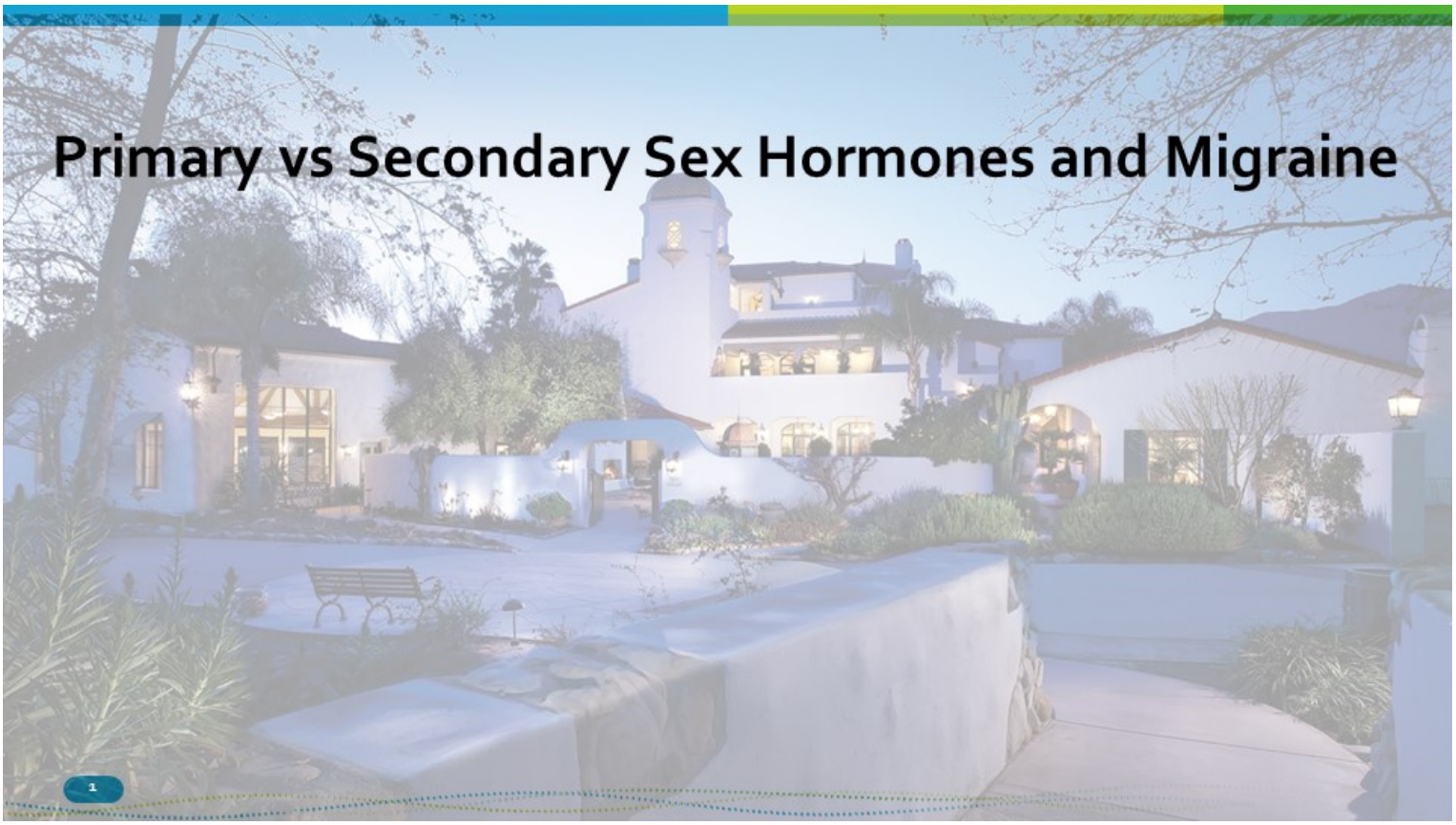
Exhibit 99.02



Disclosures

Professor David C Yeomans, Director of Pain Research, Stanford Medical School

- SiteOne Therapeutics – Founder
- NewBio – Founder
- Tonix Pharmaceuticals - Consultant
- Nalu Medical – SAB chair
- Cytonics – SAB chair
- Circuit Therapeutics – Consultant
- Endo Pharmaceuticals - Consultant

Sex Hormones

Sex hormones are critical regulators of sex-related characteristics and behaviors

Primary:

- Progesterone
- Estrogens
- Androgens

Secondary:

- Prolactin
- Oxytocin

Estrogens and Migraine

The "Estrogen withdrawal hypothesis", developed by Somerville and colleagues in 1972, postulates that attacks of menstrual migraine are triggered by the decrease in estrogen levels preceding menstruation.

Hypothesized pathology:

- A drop in estrogen may cause an increased sensitivity to prostaglandins and a release of neuropeptides such as CGRP, substance P and neurokinins which could result in neurogenic inflammation.
- This physiological response provokes alterations in the microvasculature of the dura mater, changes in calcium and magnesium concentrations, and an imbalance in serotonin and dopamine concentrations

However, estrogens are generally ineffective in in migraine prevention RCTs

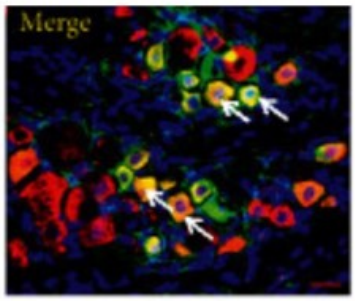
RCT (35 pts): Percutaneous Estradiol reduced migraine frequency by 22% compared to placebo but increased migraines as soon as drug stopped (MacGregor et al., 2006)

RCT (27 pts): Percutaneous Estradiol no significant effect vs. placebo (Almén-Christensson et al. 2011).

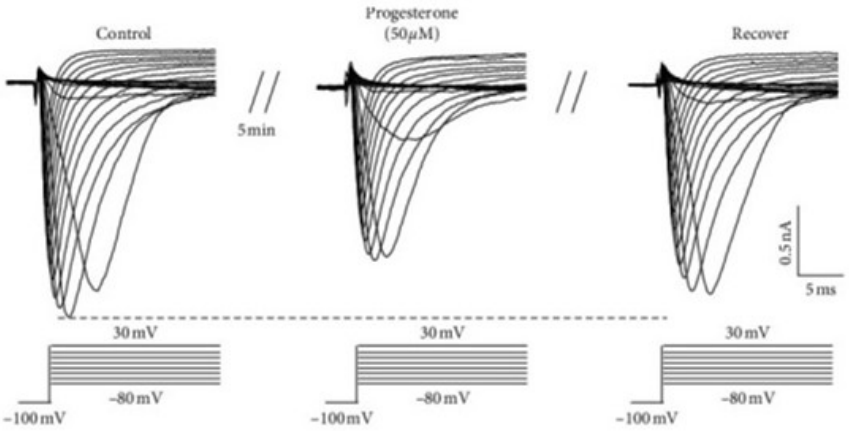
RCT (50 pts) Percutaneous Estradiol and progesterone or oral estradiol plus progesterone: significantly worsened migraine with aura (Nappi et al, 2001).

RCT (22 pts) Percutaneous estradiol significantly v placebo, reduced frequency of menstrual migraine (Dennerstein et al., 1988).

Progesterone is analgesic in the trigeminal system



Progesterone Receptors are co-Expressed with Nav1.7 in trigeminal ganglia neurons



Progesterone decreases sodium currents in mouse trigeminal ganglia neurons

Bi et al., 2020

However, Progesterone is minimally effective NO RCTs

Clinical implications Warhurst et al., 2017

- The desogestrel 75 mcg/day POP is associated with modest reductions in migraine frequency and duration as well as reduced use of analgesics and triptans after 180 days' use in most women.
- Evidence is observational and future prospective, randomised trials will assist in determining the true clinical effects of the desogestrel POP and other progestin-only contraceptives in migraine treatment.
- The desogestrel POP should be considered in women with migraine, particularly those with common contra-indications to COC pill use such as migrainous aura and hypertension.

PROGESTERONE IN THE TREATMENT OF MIGRAINE

INDER SINGH
M.B. Rangoon, M.R.C.P.E., F.R.F.P.S.
LIEUT.-COLONEL I.M.S.

INDERJIT SINGH
M.B. Rangoon, Ph.D. Camb., M.R.C.S., F.A.Sc.
CAPTAIN I.M.S.

DEVINDER SINGH
L.S.M.F. Punjab

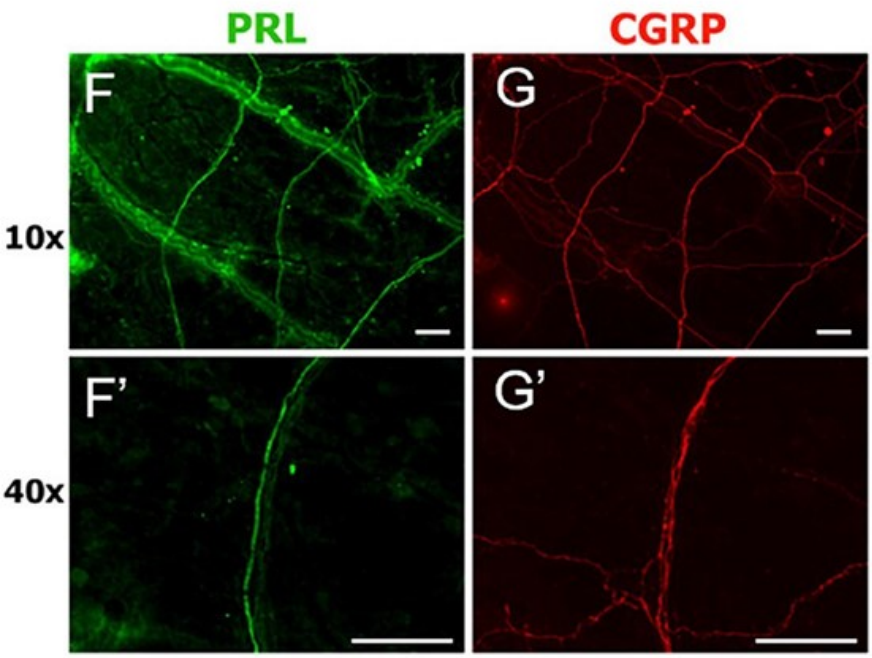
the amount of progesterone required to alleviate an induced attack of migraine was inversely proportional to the amount of œstradiol used to induce it. To prevent spontaneous attacks the amount of progesterone required was generally directly proportional to the severity of the symptoms of œstrogen hyperactivity.

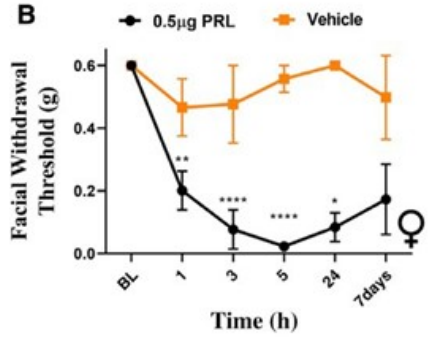
In no case did we inform the patient of the nature and action of the drugs used, and the relief from migraine was associated with disappearance of symptoms of œstrogen hyperactivity. Accordingly, it is unlikely that the success of treatment was due to suggestion

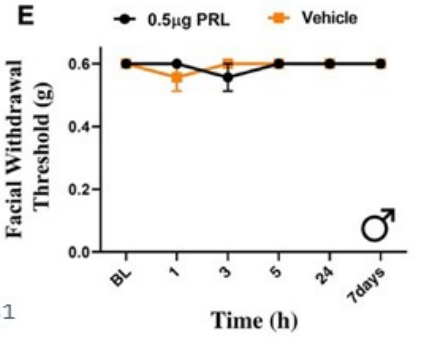
Testosterone

No RCT but pilot study showing strong effects of testosterone implant on 27 female migraineurs with symptoms of androgen insufficiency. Compared to pre-treatment, testosterone produced a significant decrease in migraine severity with 74% reporting severity scores of zero (Glaser et al., 2012).

Prolactin receptors on female, but not male mouse dural afferents

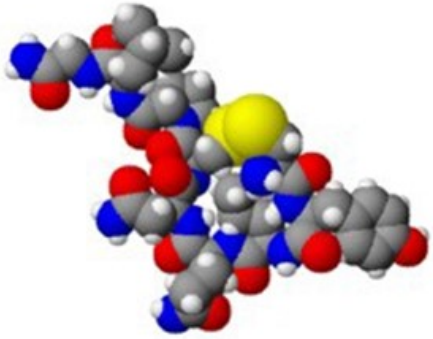


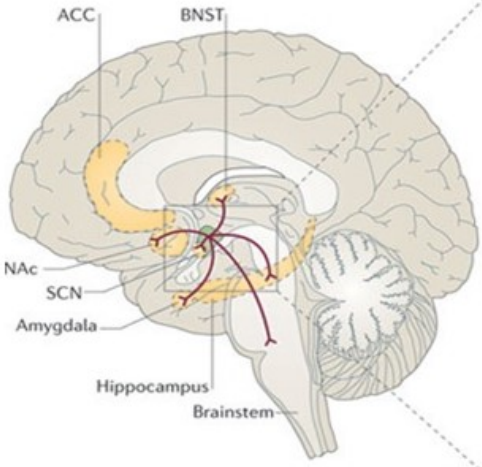


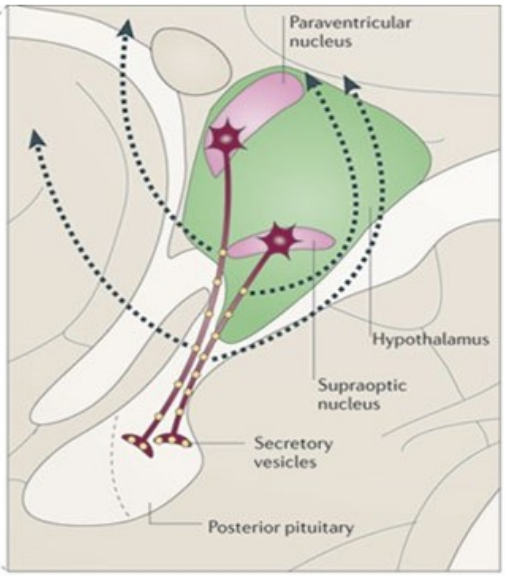


Avona et al., 2021

Oxytocin is a 9 amino acid polypeptide hormone/neurotransmitter which is made in the hypothalamus and secreted both into the systemic circulation and into certain CNS sites

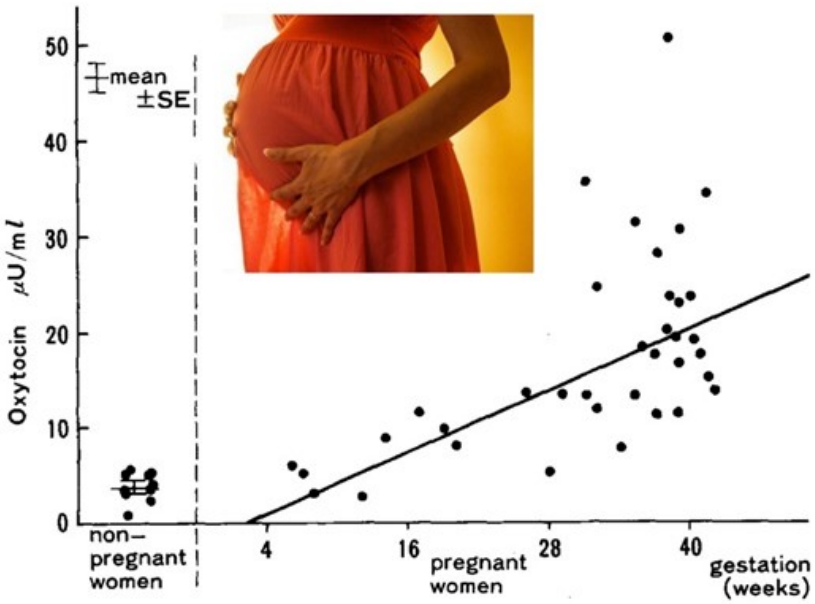




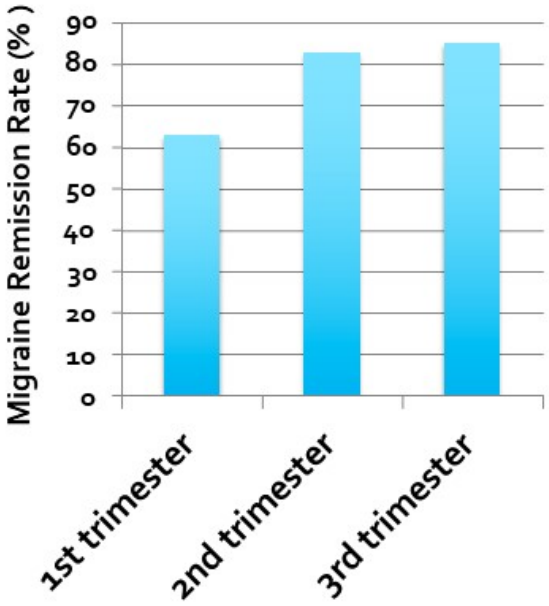


Nature Reviews | Neuroscience

Pregnancy increases oxytocin and decreases migraine frequency

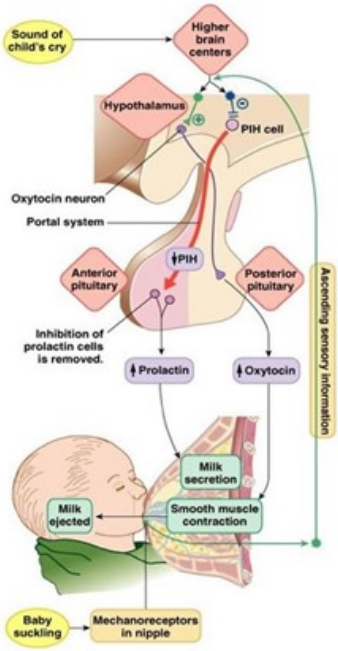


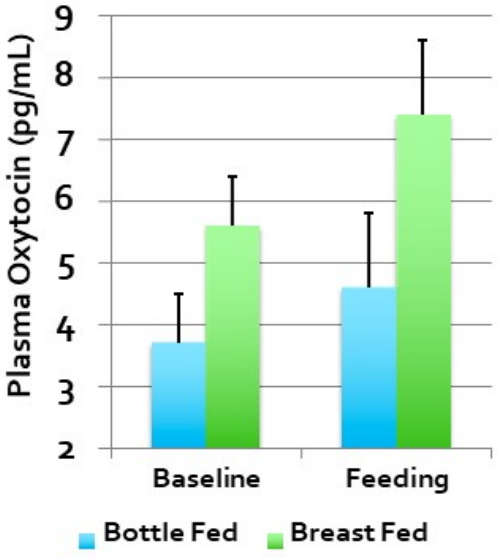
Kuwabara et al., 1987



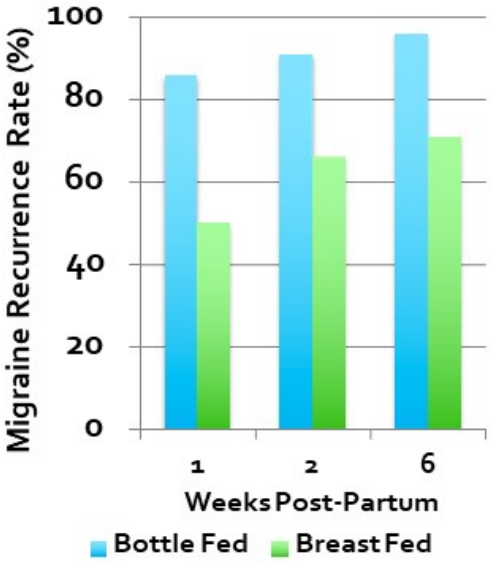
Adapted from Hoshiyama, 2012

Breast feeding releases oxytocin and prevents migraines



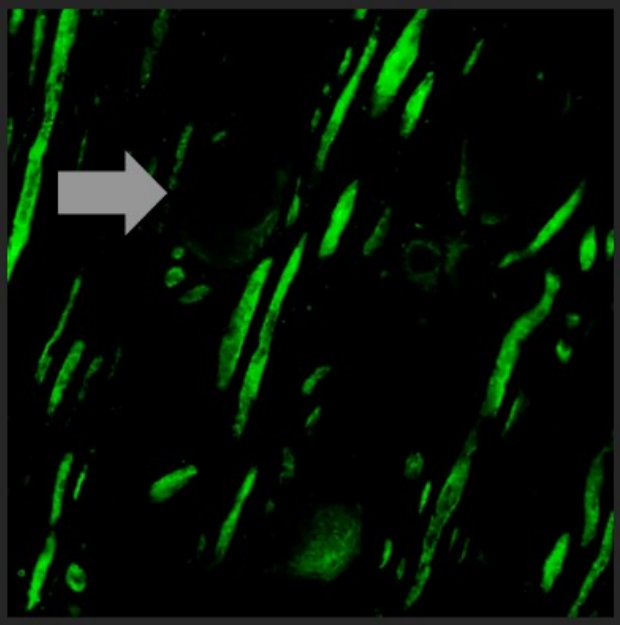


Grewen et al, 2010

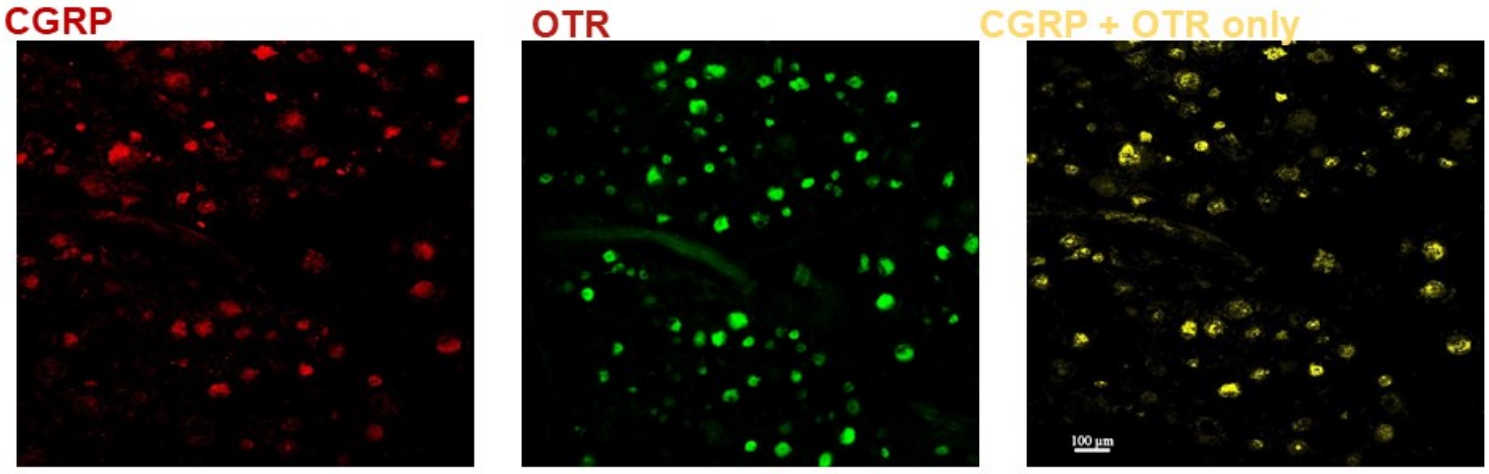


Hoshiyama, 2012

Oxytocin receptor expression on trigeminal ganglia neurons

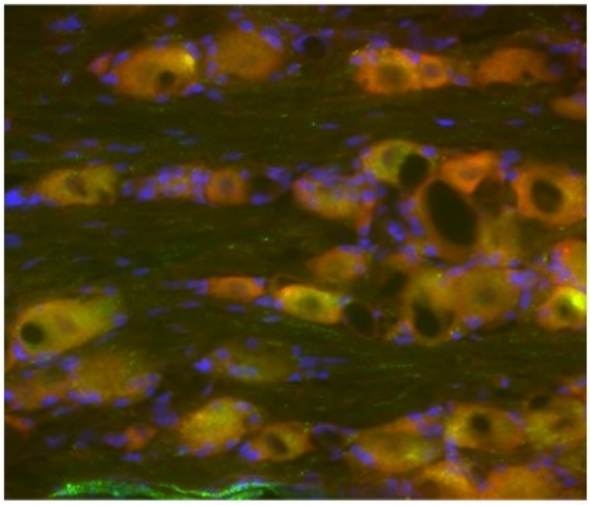


Oxytocin receptors co-express CGRP in human trigeminal ganglia neurons



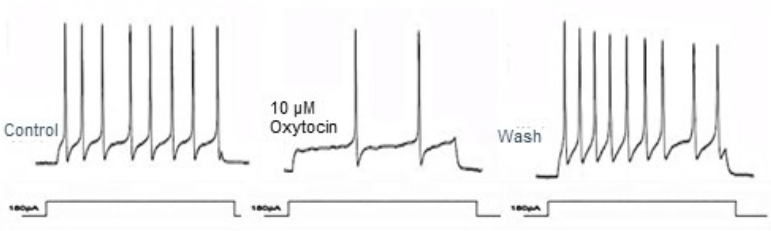
Oxytocin Inhibits Firing of Rat Trigeminal (TG) CGRP Neurons

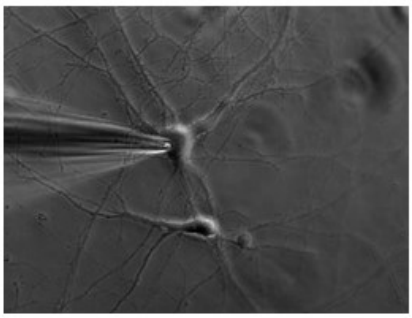
Oxytocin Receptors Co-Localize with CGRP in Trigeminal Ganglia Neurons



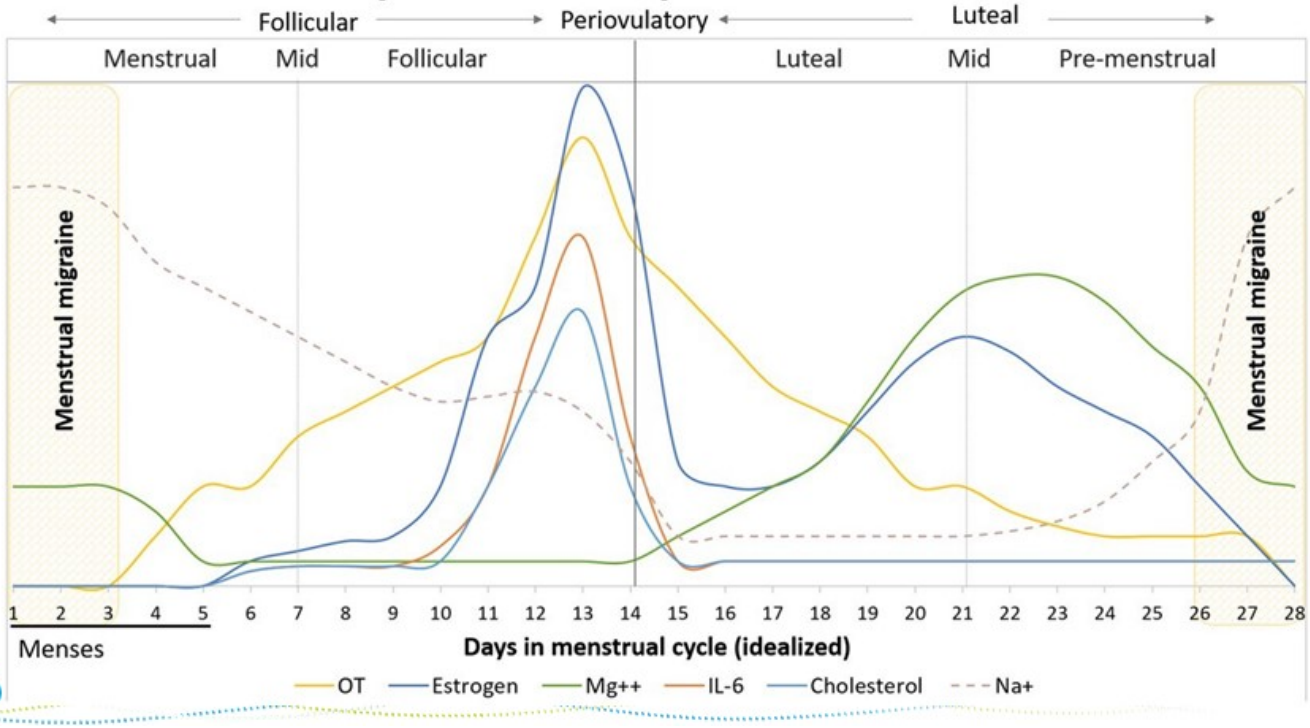
Oxytocin Receptors = red
CGRP = green

Oxytocin Inhibits Electrically Evoked Activity of Trigeminal Ganglia Neurons

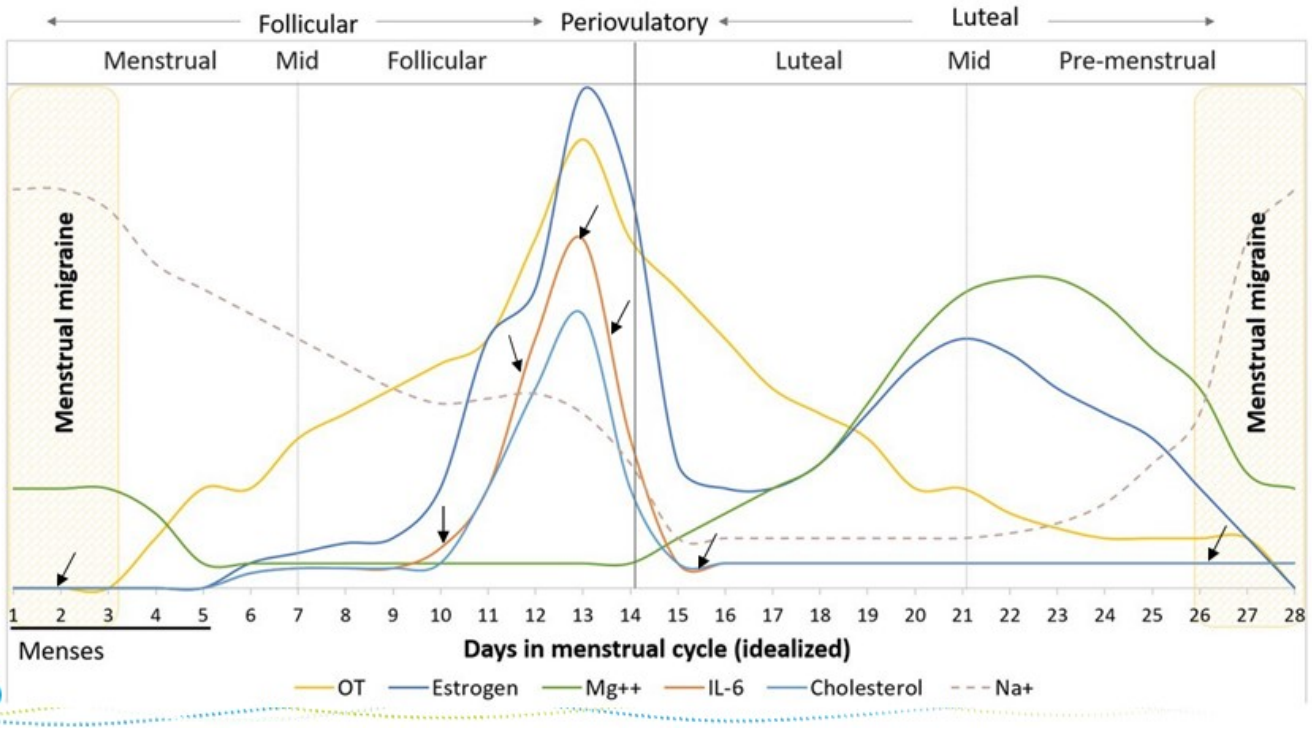




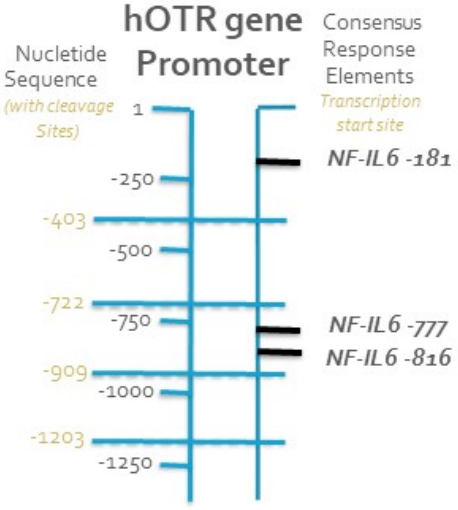
Multiple factors that vary over the menstrual cycle have been shown to control oxytocin activity



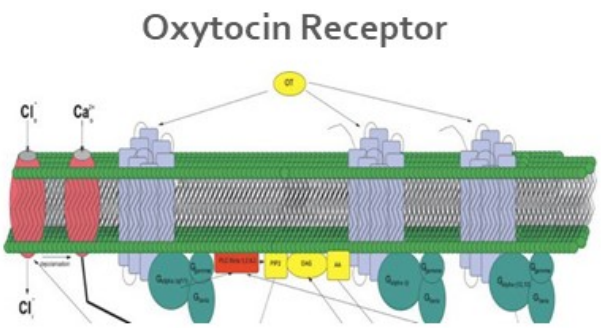
1. IL-6 is low during menstrual migraine



The OTR gene promoter has multiple response elements for the inflammatory cytokine IL-6



Schmid *et al.*, 2001



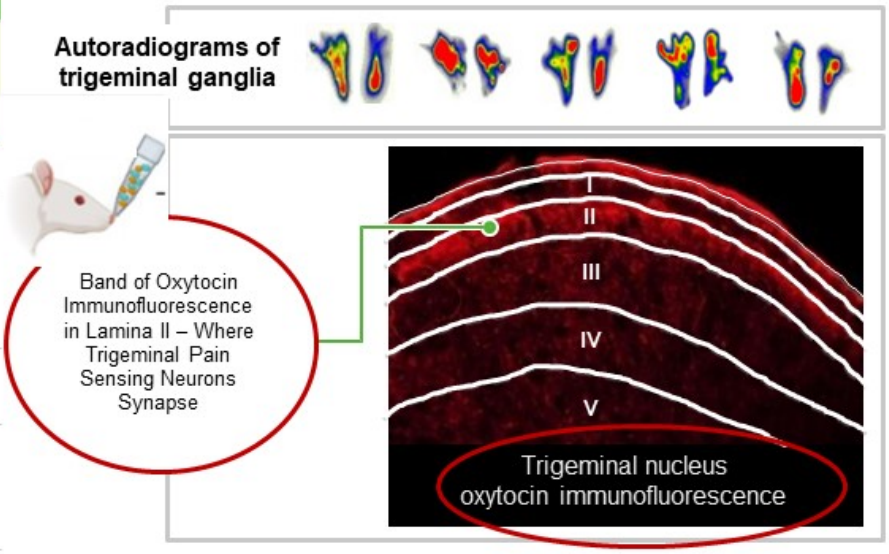
Gould and Zingg, 2003

Oxytocin Is Preferentially Transported Throughout the Trigeminal System After Nasal Delivery (not systemically distributed)

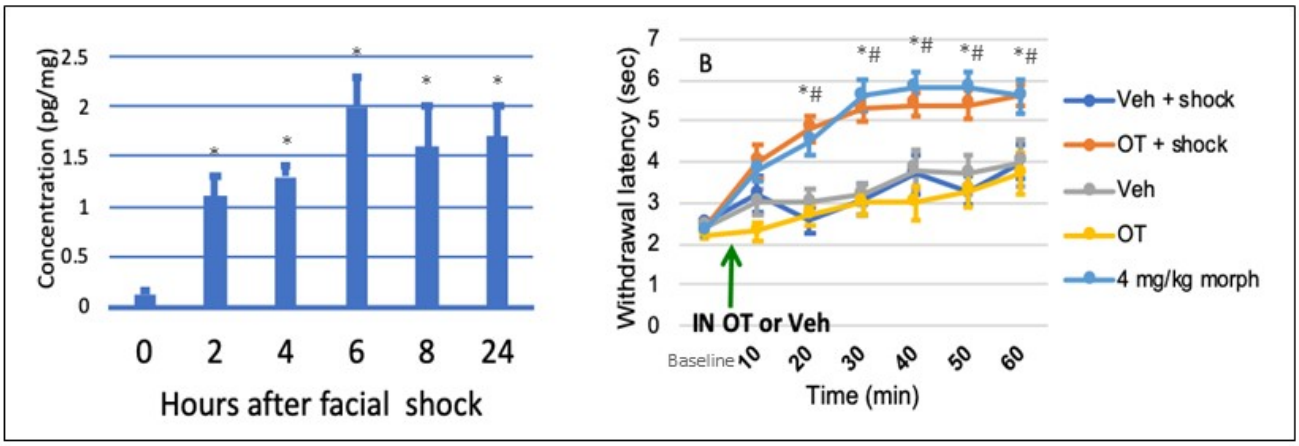
Oxytocin tissue levels (nM) after intranasal administration*			
TRIGEMINAL NERVE	Ganglion	574	±191
	Maxillary branch	471	±117
	Mandibular branch	676	±235
	Ophthalmic branch	423	±143
OLFACTORY NERVE	Nucleus	34	±10
	Bulbs	33	±13
BRAIN	Cortex	29	±8
	Caudate	39	±12
	Thalamus	15	±6
	Midbrain	23	±12
	Cerebellum	20	±8
	Medulla	26	±10
SPINAL CORD	Cervical	34	±9
	Thoracic	5	±1
	Lumbar	5	±1
OTHER TISSUES	Muscle	16	±3
	Liver	16	±2
	Kidney	50	±5
	Lung	25	±4
	Heart	23	±4
BLOOD	Blood	63	±4

*Oxytocin applied to nose of rats, tissue levels assessed by gamma counts

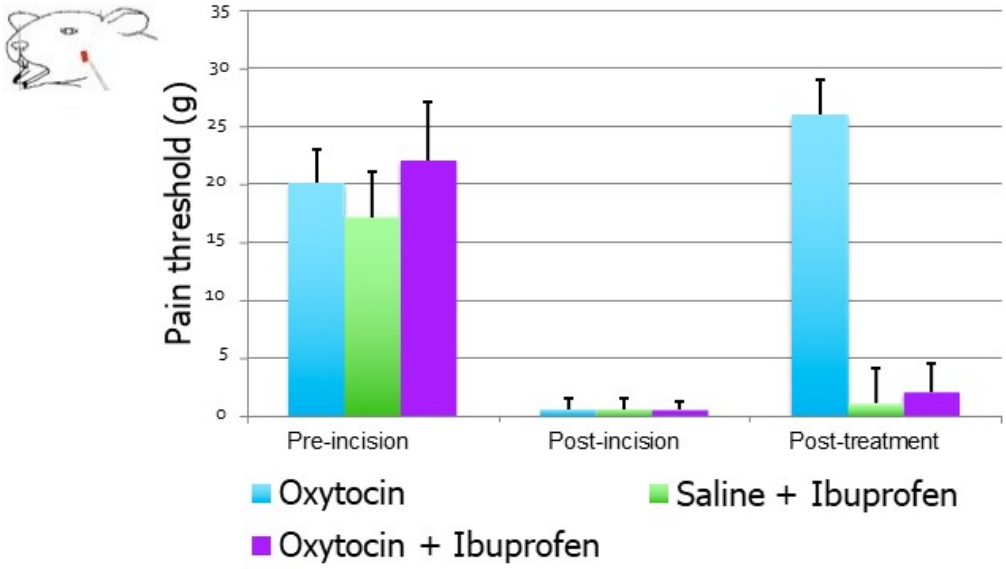
Broad Distribution of ^{125}I-oxytocin in Trigeminal Ganglia After Nasal Application



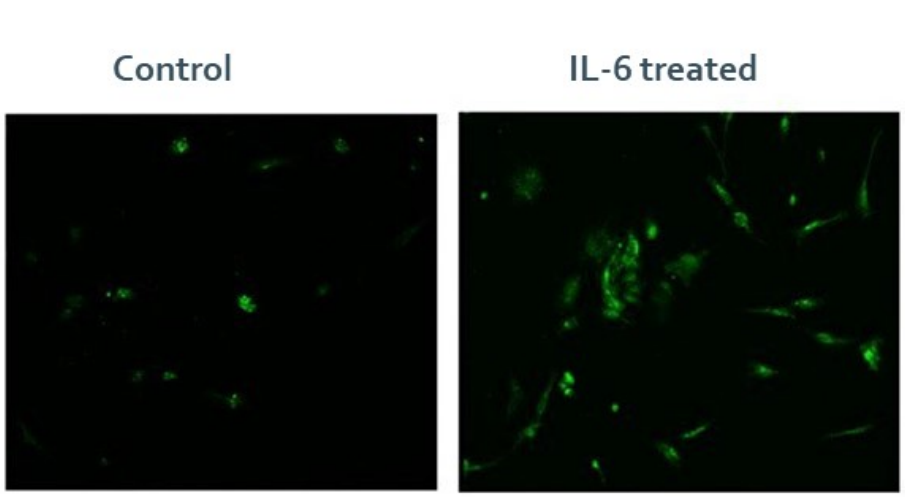
Inflammation increases trigeminal Oxytocin receptor expression

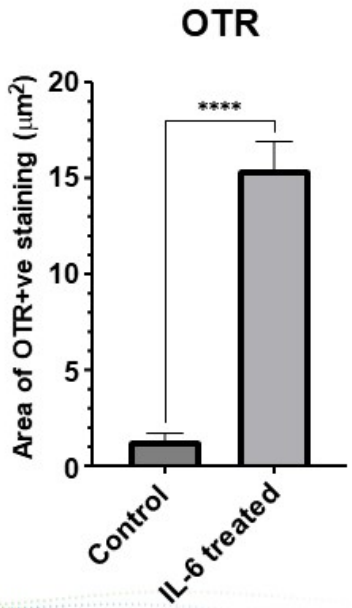


After incision, the analgesic efficacy of nasal oxytocin is blocked by ibuprofen – which blocks IL-6 production

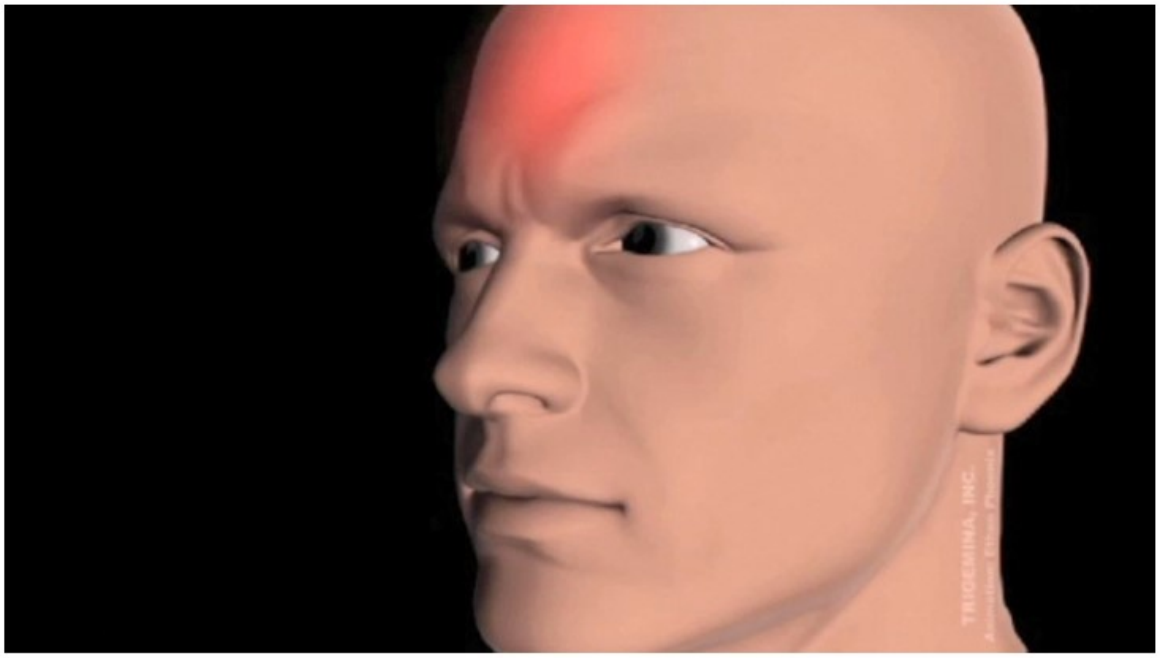


In vitro treatment of human ganglia with IL-6 induces upregulation of oxytocin receptors

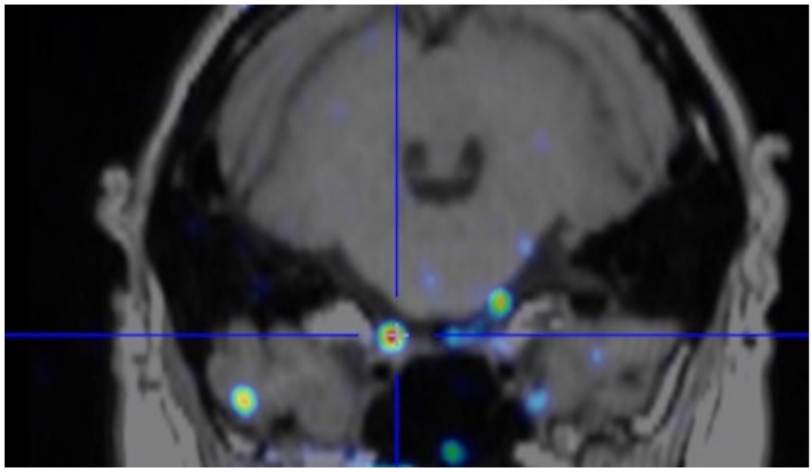




Nasal delivery of oxytocin to the trigeminal system of humans

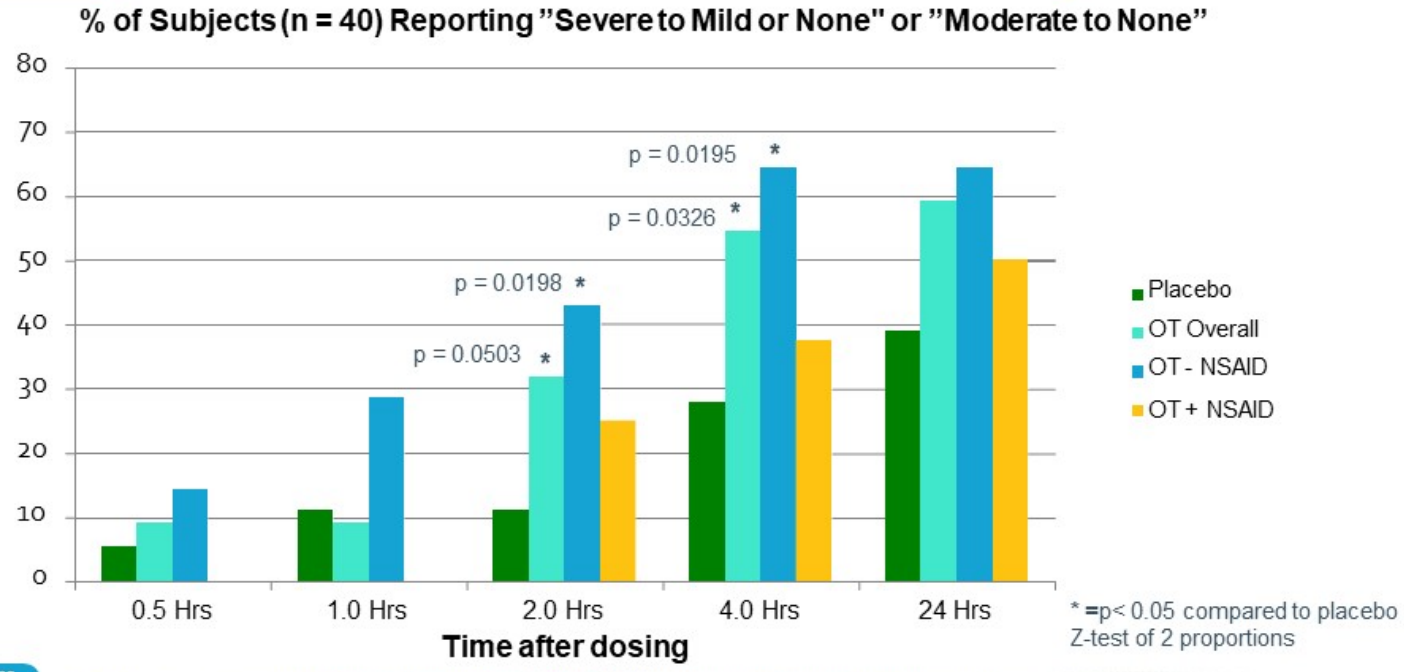


^{13}N-Oxytocin in human TG after nasal application

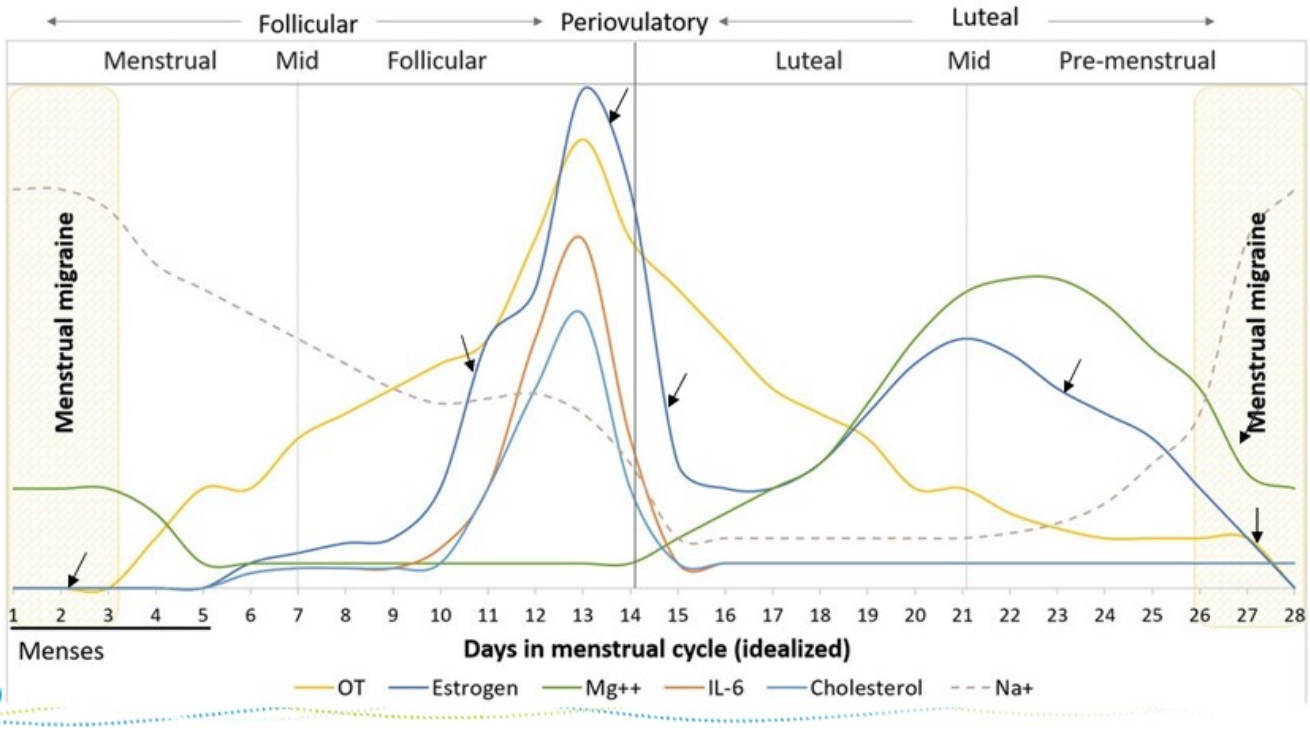


Pilot Clinical Study: Nasal Oxytocin Reduces Pain In Chronic Migraineurs

Excluding patients who took NSAIDs within 24 hours increases efficacy

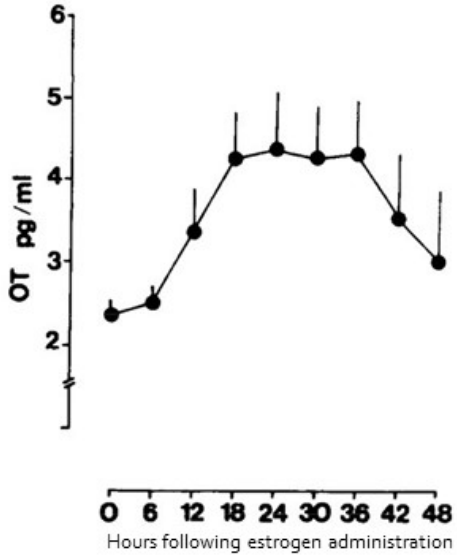


2. Estrogen is low during menstrual migraine



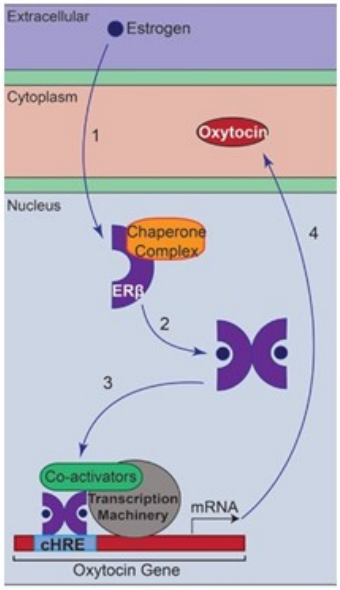
Plasma OT level is modulated by exogenous estrogen

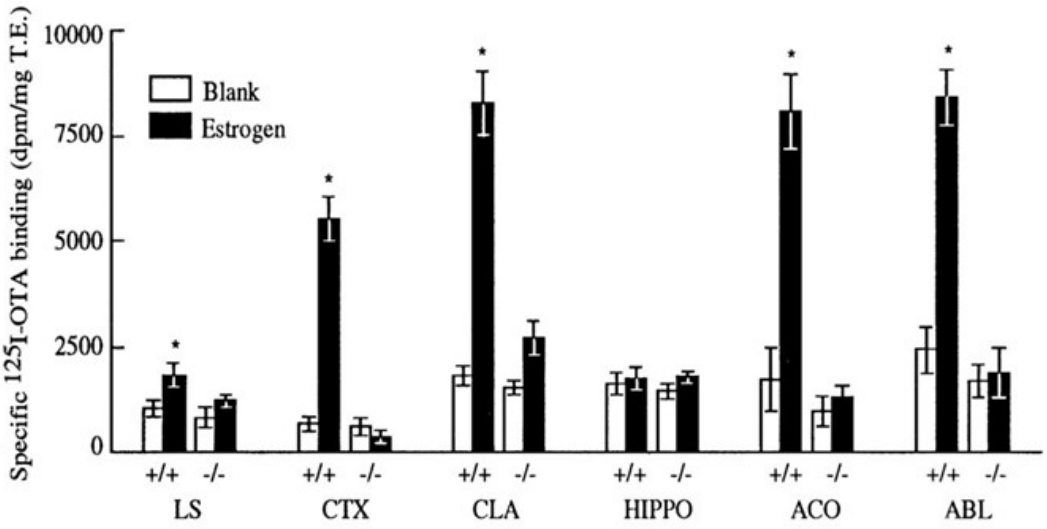
Plasma oxytocin levels following oral estrogen (1 mg)



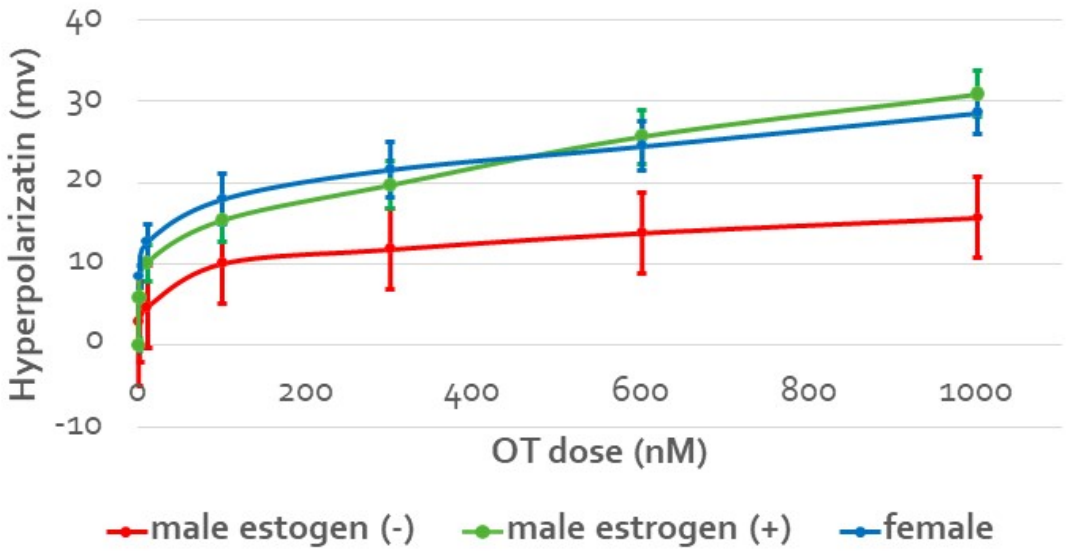
Chiodera et al., 1991

Increase in brain OXTR induced by estrogen

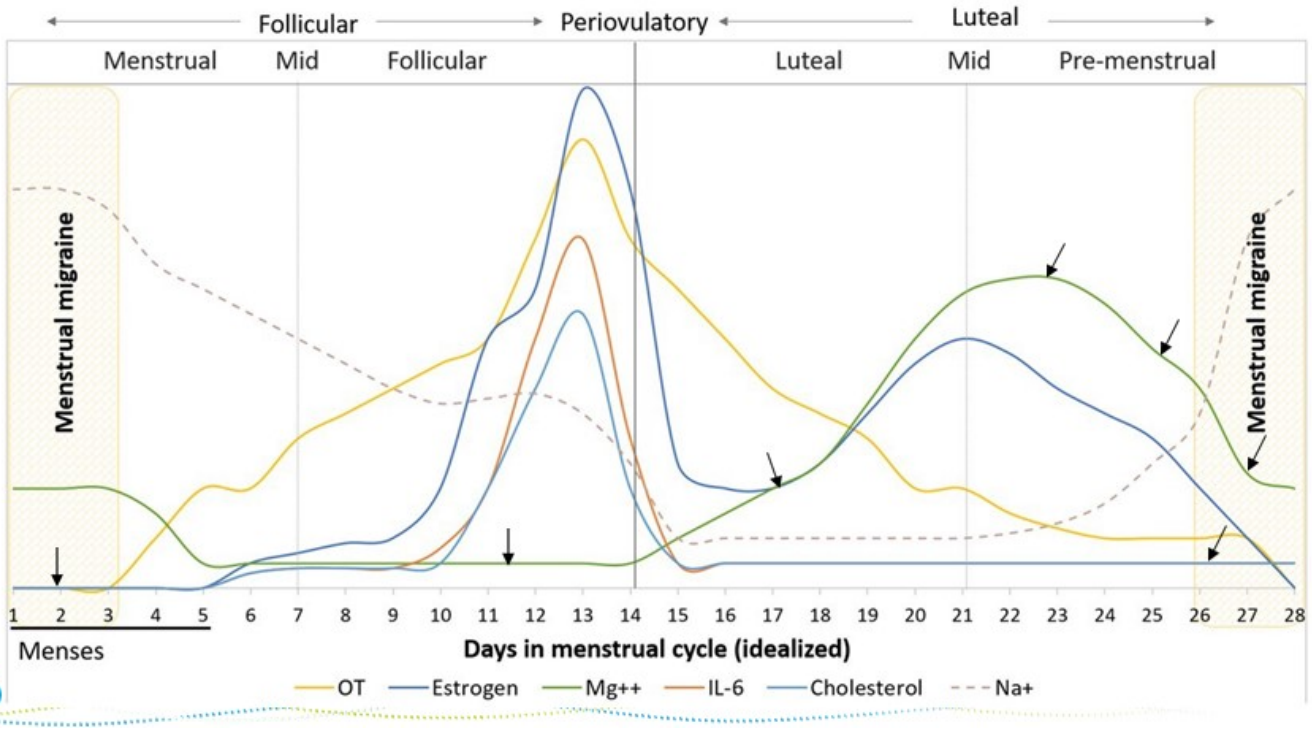




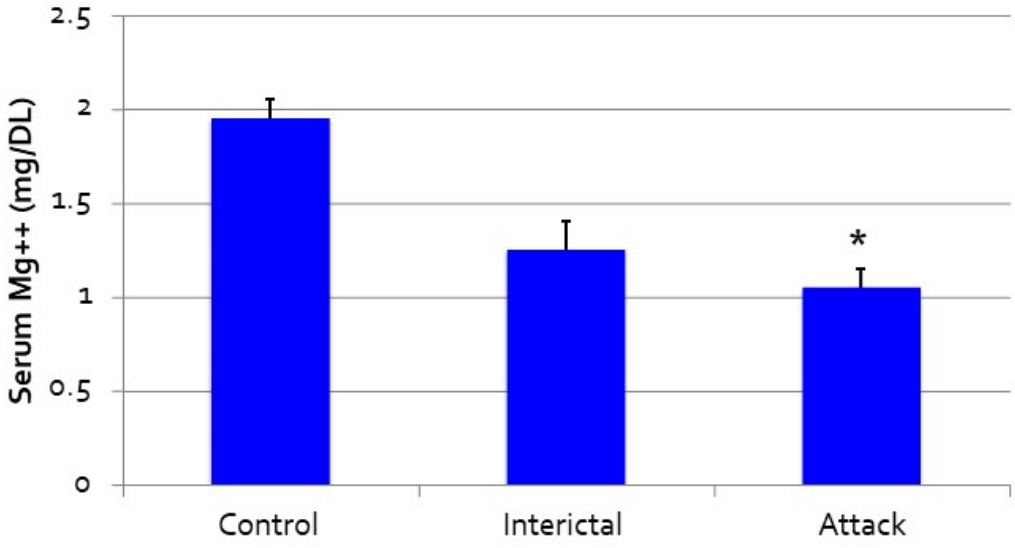
OT is more potent in inhibiting TG excitability in females, but with estrogen pretreatment, male potency is similar to female



3. Magnesium ion plasma level is low during menstrual migraine



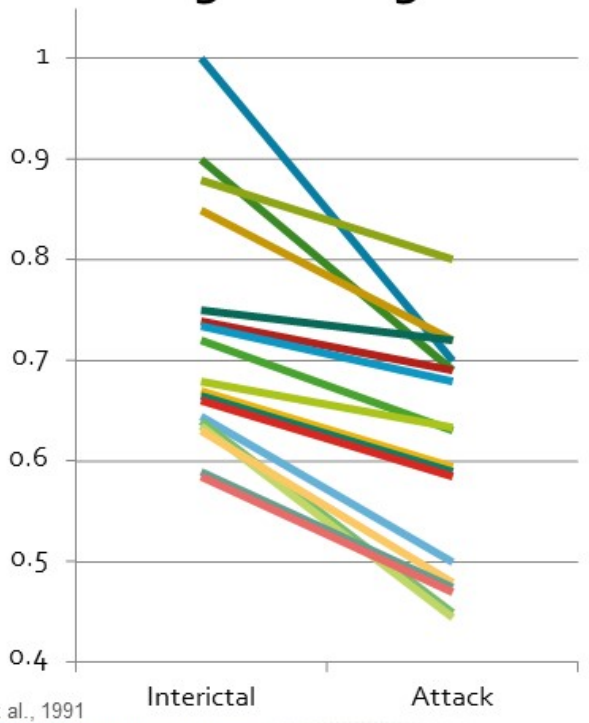
Serum Mg++ is lower in migraineurs



Assarzadegan et al., 2016

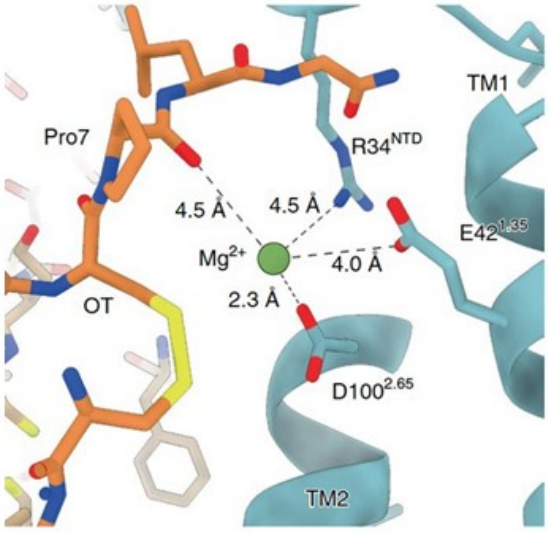
Reduced basal and attack-dependent serum Mg++ in migraineurs

- Odds of migraine is increased 35.3 times when serum levels of magnesium reached below the normal level.

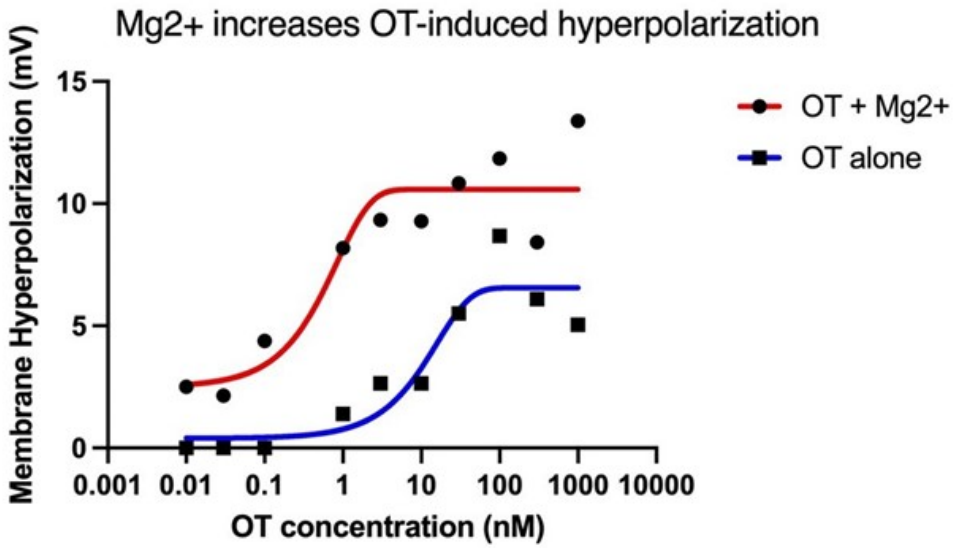


Sarchielli et al., 1991

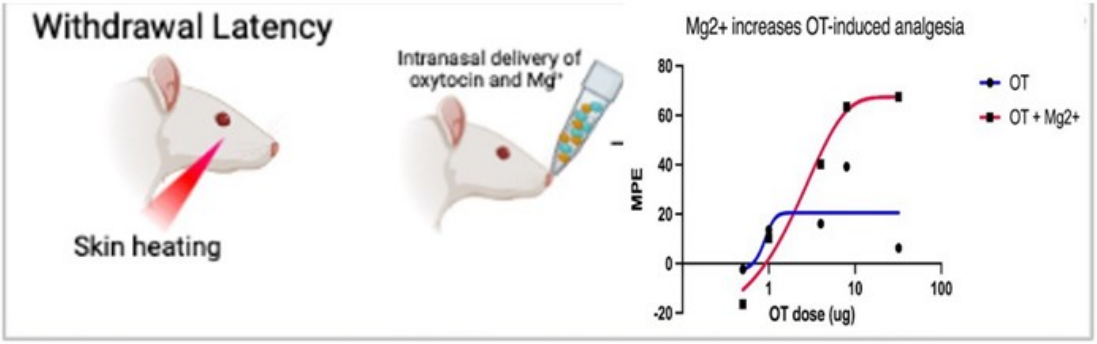
Binding site for Mg^{2+} between OT and OTR



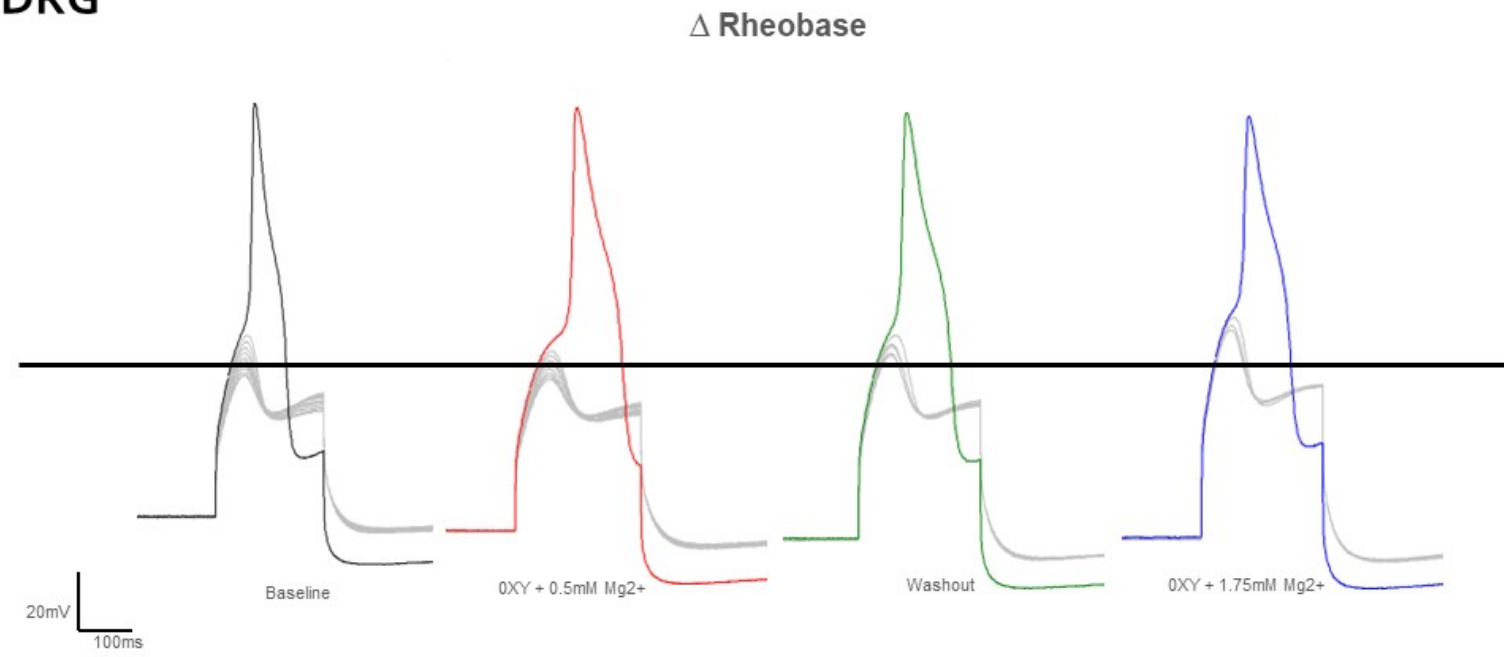
Addition of Mg^{2+} enhanced OT-driven desensitization of rat TG



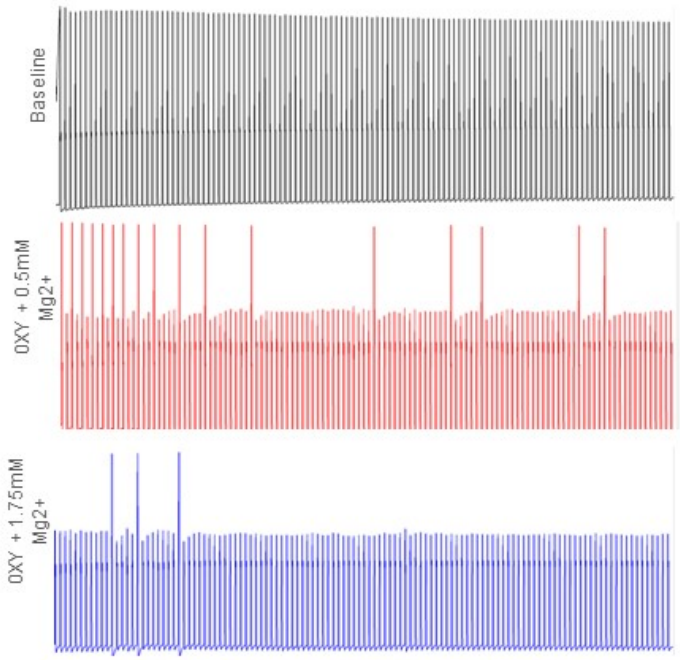
Addition of Mg^{2+} enhanced OT-driven craniofacial analgesia



Addition of Mg^{2+} enhanced OT-driven increase of rheobase of human DRG



Addition of Mg^{2+} enhanced OT-driven decrease in AP following in human DRG



Summary: Sex hormone modulation of migraine

- Evidence for Direct modulation of TG excitability by primary sex hormones in not strong
- Evidence for extended sex hormones (Prolactin, oxytocin) robust
- Oxytocin effects are modulated by several endogenous factors that vary over the menstrual cycle
- IL-6 levels drive OT receptor expression and increases OT analgesic efficacy
- Estrogen drives OT and OT receptor expression and likely enables OT analgesia
- Mg^{2+} is decreased during menstruation and during migraine attacks
- There is a binding site for Mg^{2+} between OT and its receptor
- Mg^{2+} dramatically increases the analgesic efficacy of OT in animal models and human sensory neurons

A Mg^{2+} containing nasal formulation of OT is being used in an ongoing multi-site US study of chronic migraine prophylaxis

Alternatively, hugging, massage, sex, looking at your dog could help prevent migraines

Thank you!