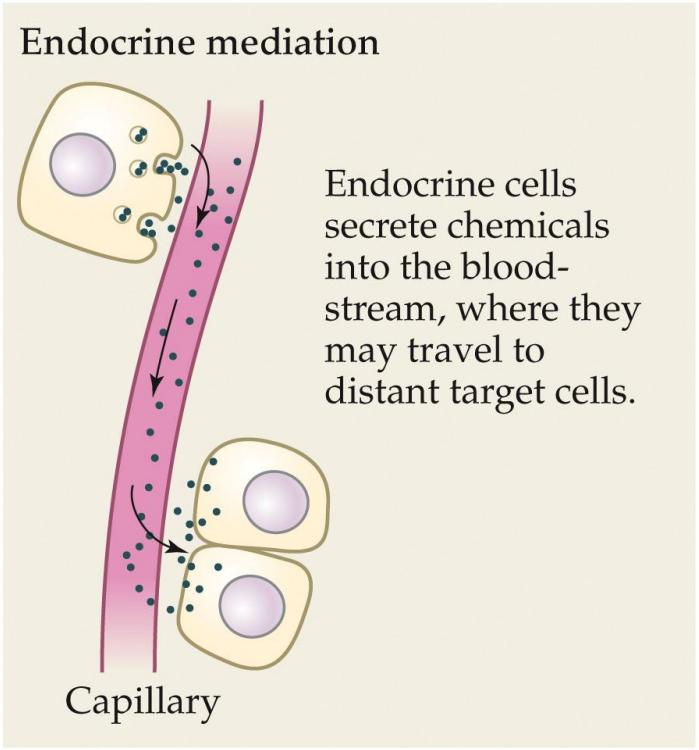
ΨΥΧΟΝΕΥΡΟΕΝΔΟΚΡΙΝΟΛΟΓΙΑ

Χριστίνα Δάλλα, Επ. Καθ. Φαρμακολογίας-Ψυχοφαρμακολογίας, Ιατρική Σχολή, ΕΚΠΑ

Ορμόνες

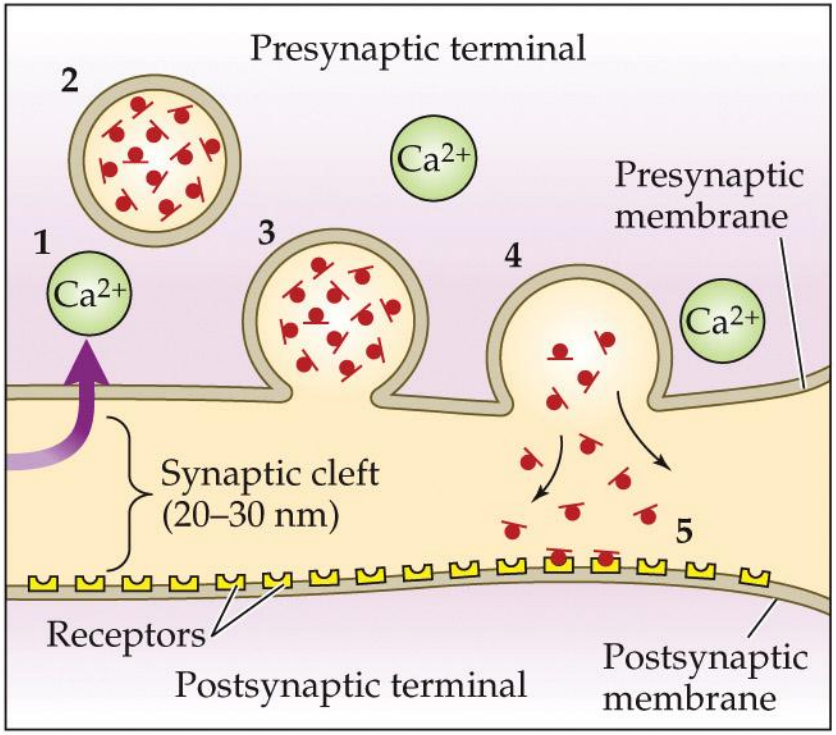
Συμπεριφορά



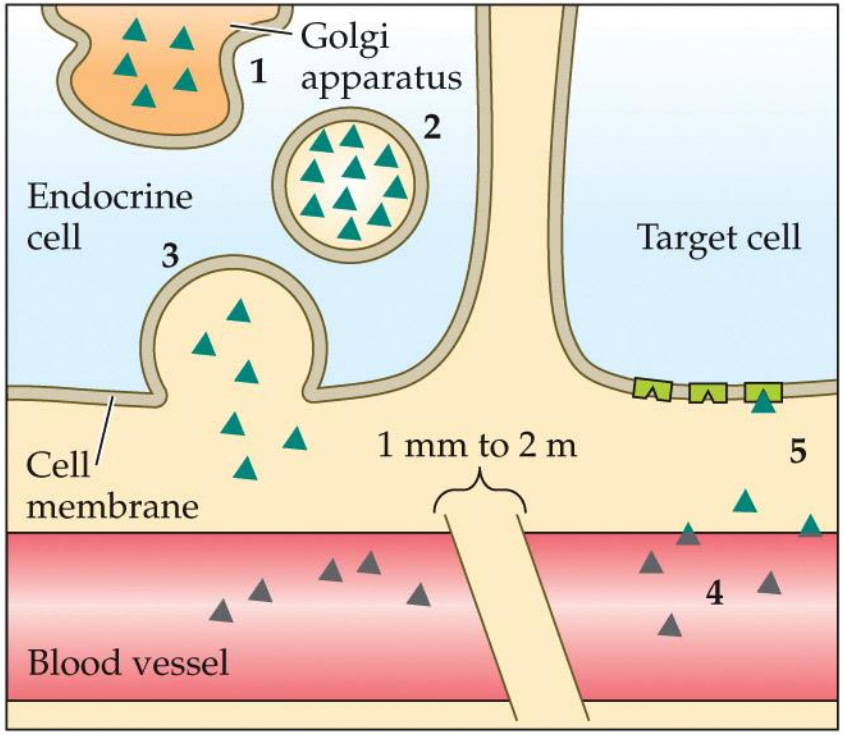
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.1 (Part 4)

Νευροδιαβιβαστές και ορμόνες

(A) Neural transmission

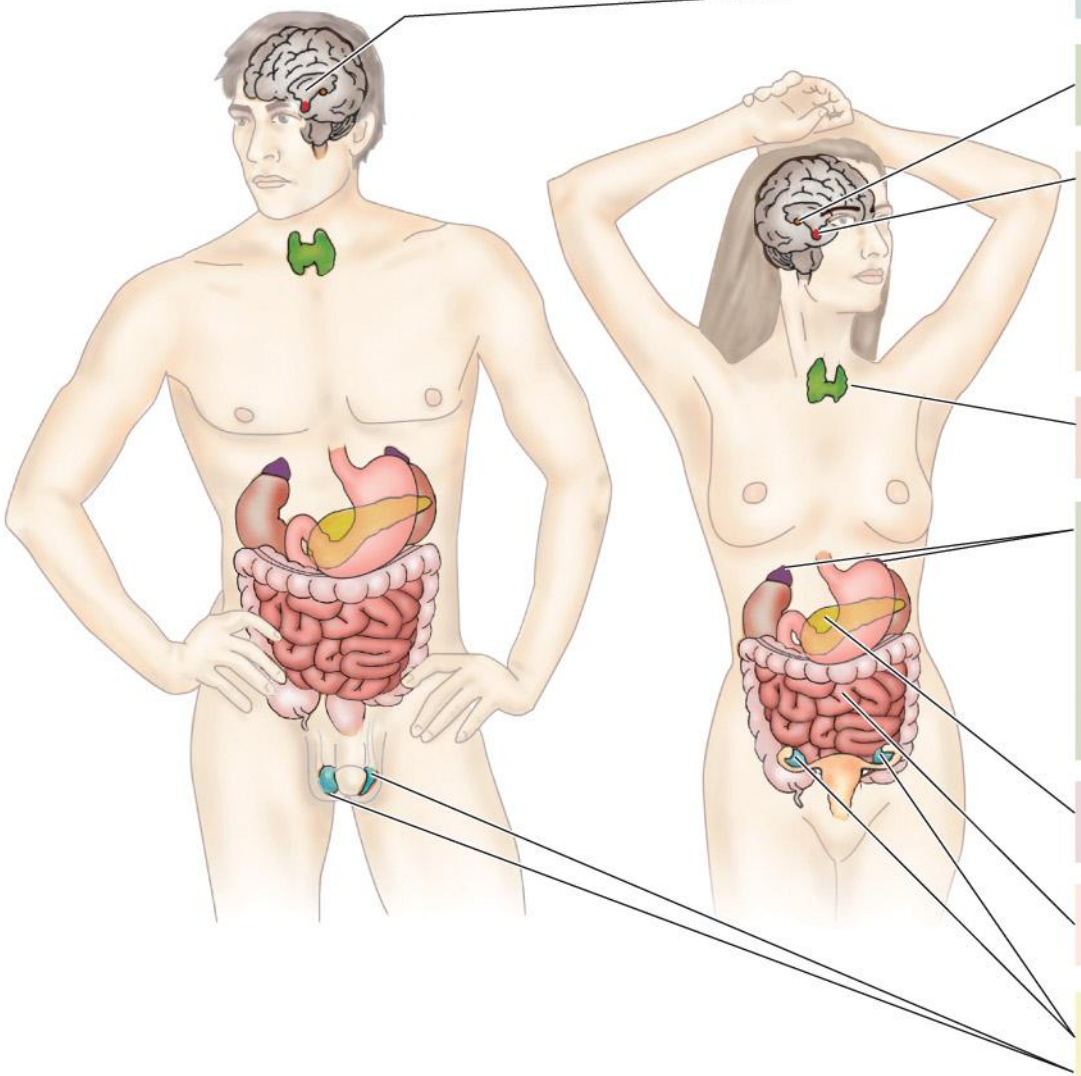


(B) Hormonal communication



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Box 1.2

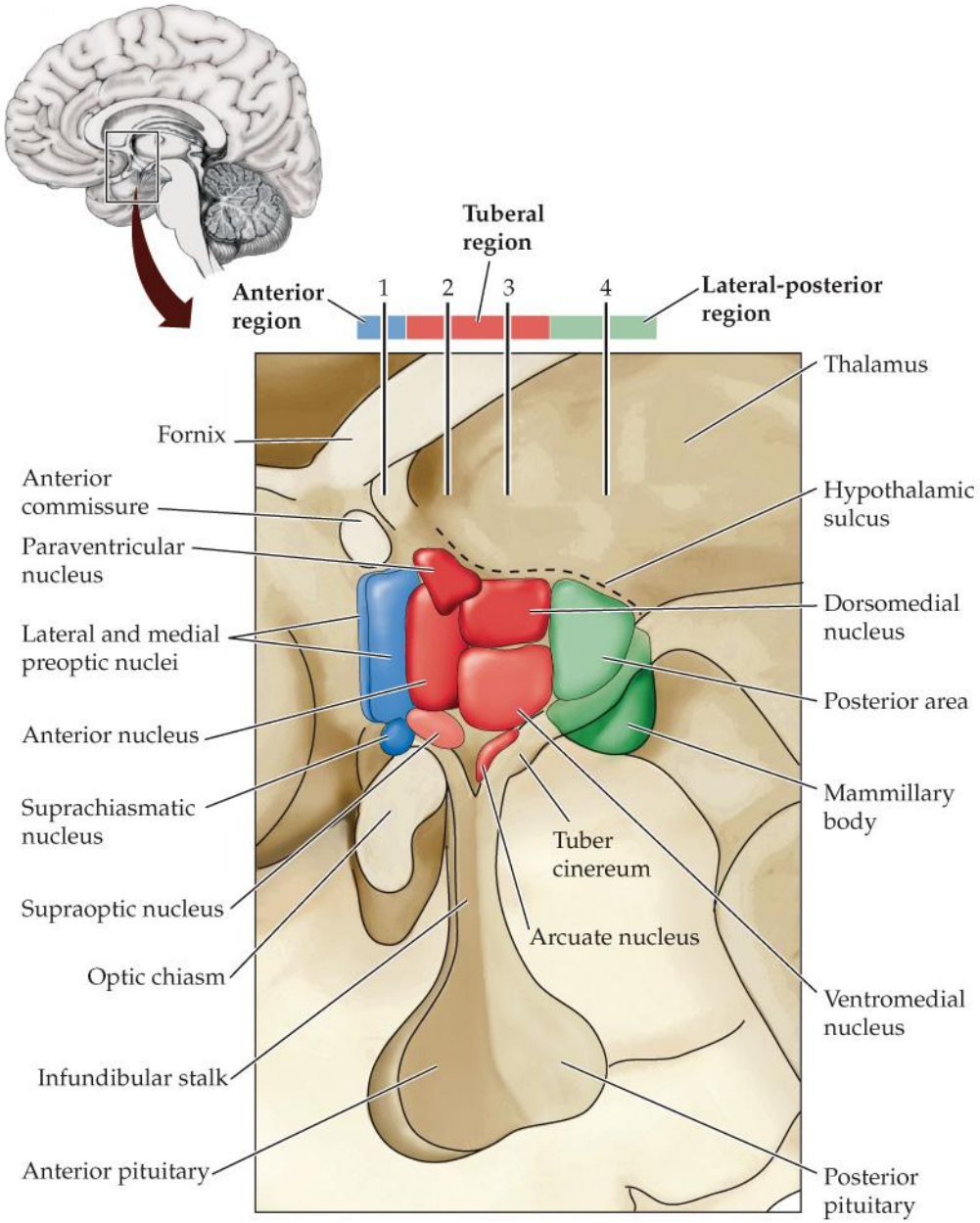
Ενδοκρινείς αδένες



Major endocrine structures	Some main functions regulated by secretion
Hypothalamus	Control of hormone secretions
Pineal gland	Reproductive maturation; body rhythms
Pituitary gland:	
Anterior pituitary	Hormone secretion by thyroid, adrenal cortex, and gonads; growth
Posterior pituitary	Water balance; salt balance
Thyroid	Growth and development; metabolic rate
Adrenal glands:	
Adrenal cortex (outer bark)	Salt and carbohydrate metabolism; inflammatory reactions
Adrenal medulla (inner core)	Emotional arousal
Pancreas (islets of Langerhans)	Sugar metabolism
Gut	Digestion and appetite control
Gonads (testes/ovaries)	Body development; maintenance of reproductive organs in adults

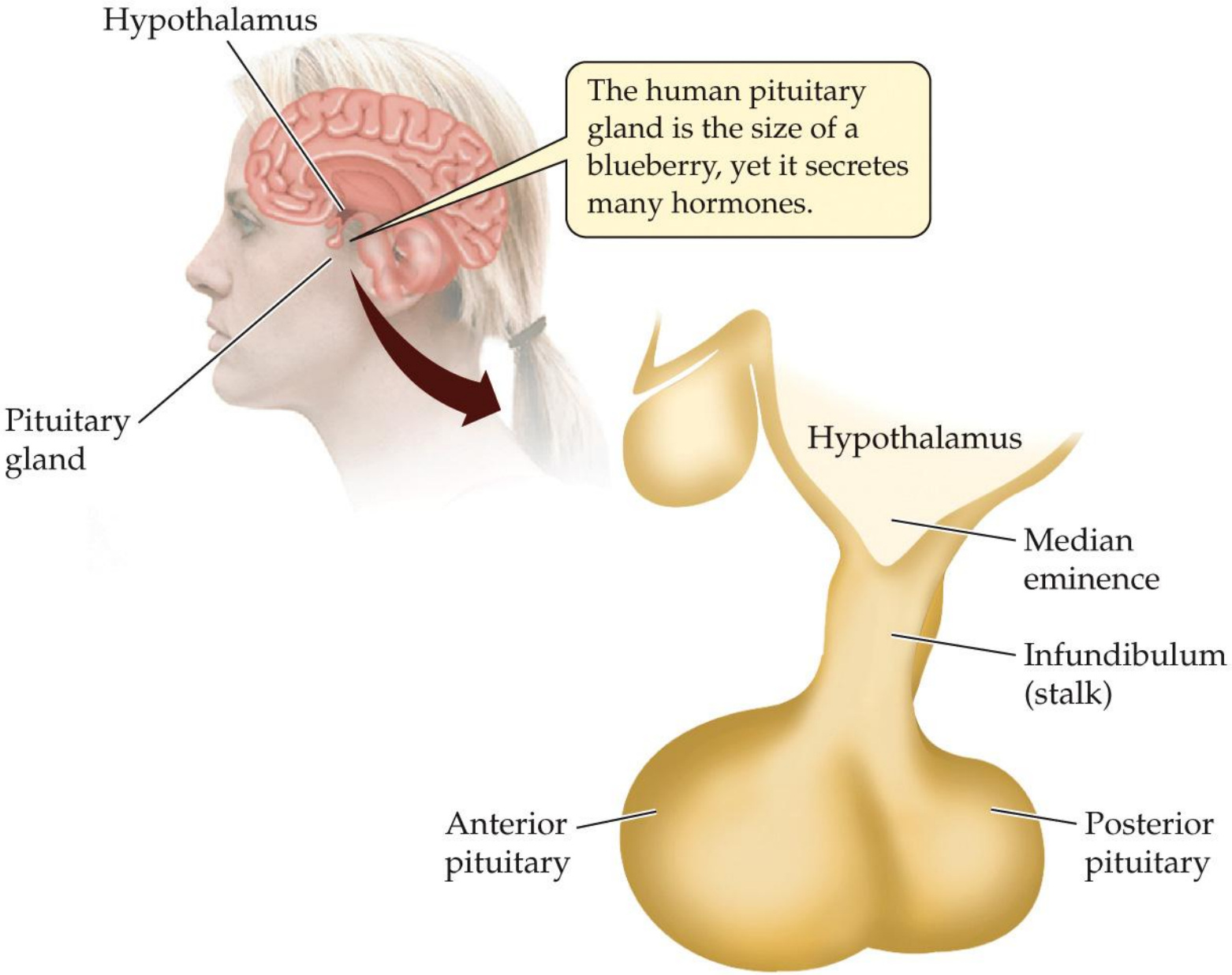
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.3

Υποθάλαμος

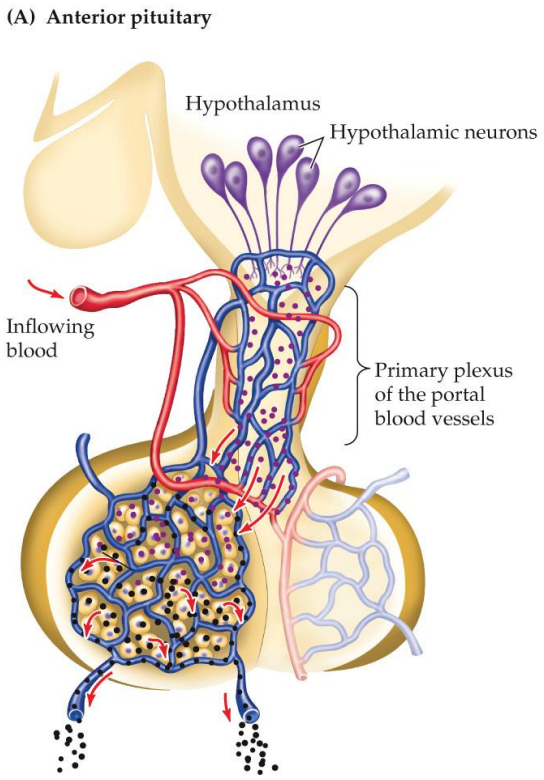


AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.5

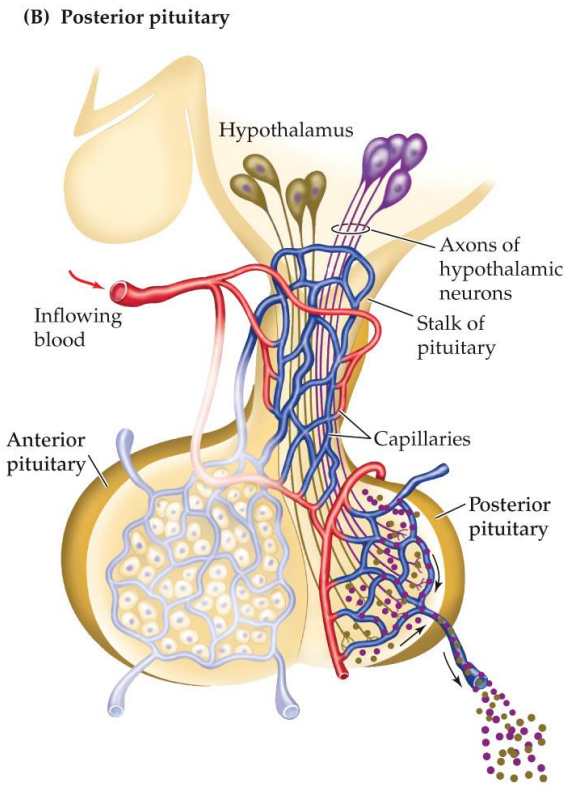
Η υπόφυση



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.9



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.10 (Part 1)



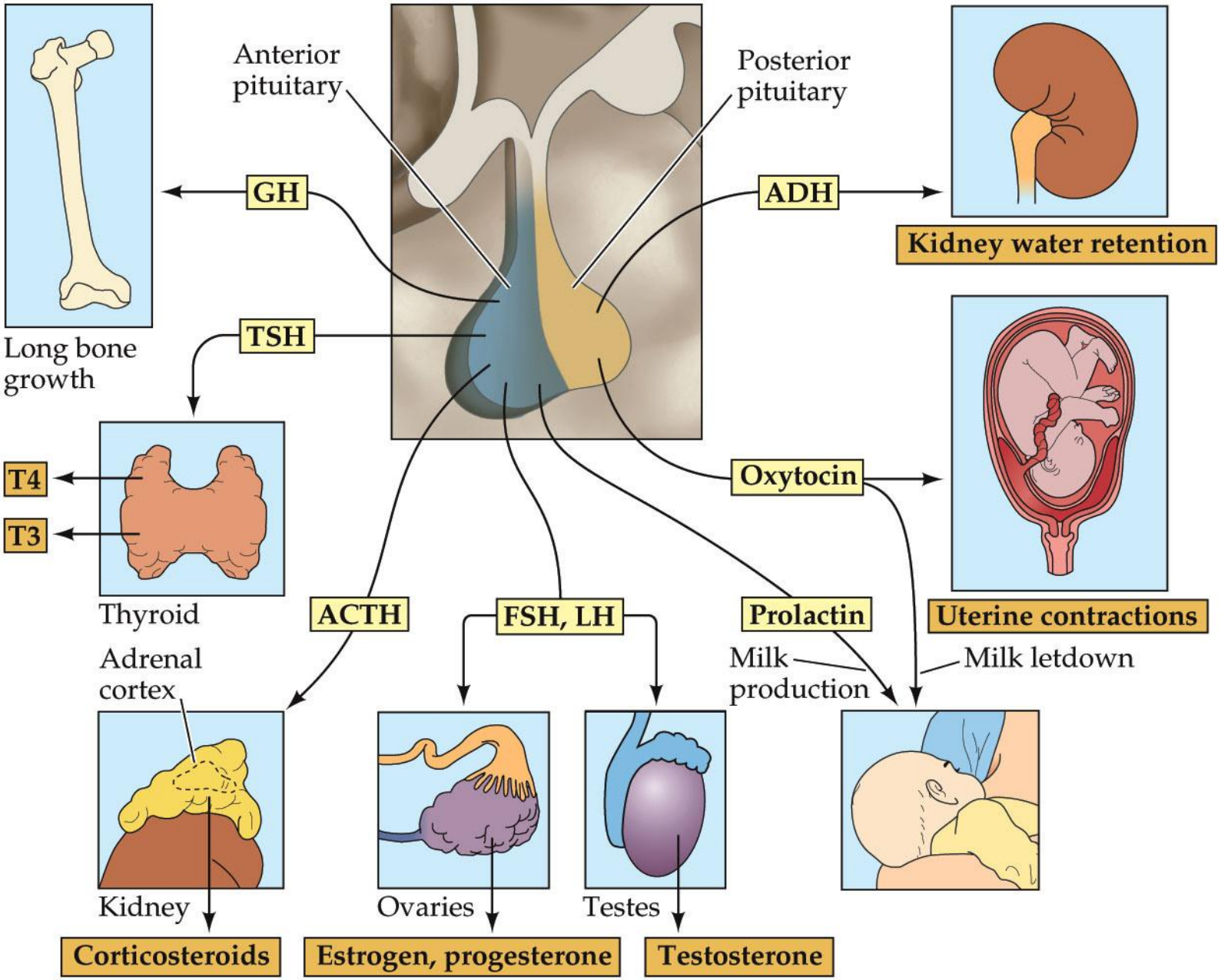
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.10 (Part 2)

Σύνδεση υποθαλάμου με υπόφυση

TABLE 17.2 Anterior Pituitary Hormones and Hypothalamic Releasing and Inhibitory Factors

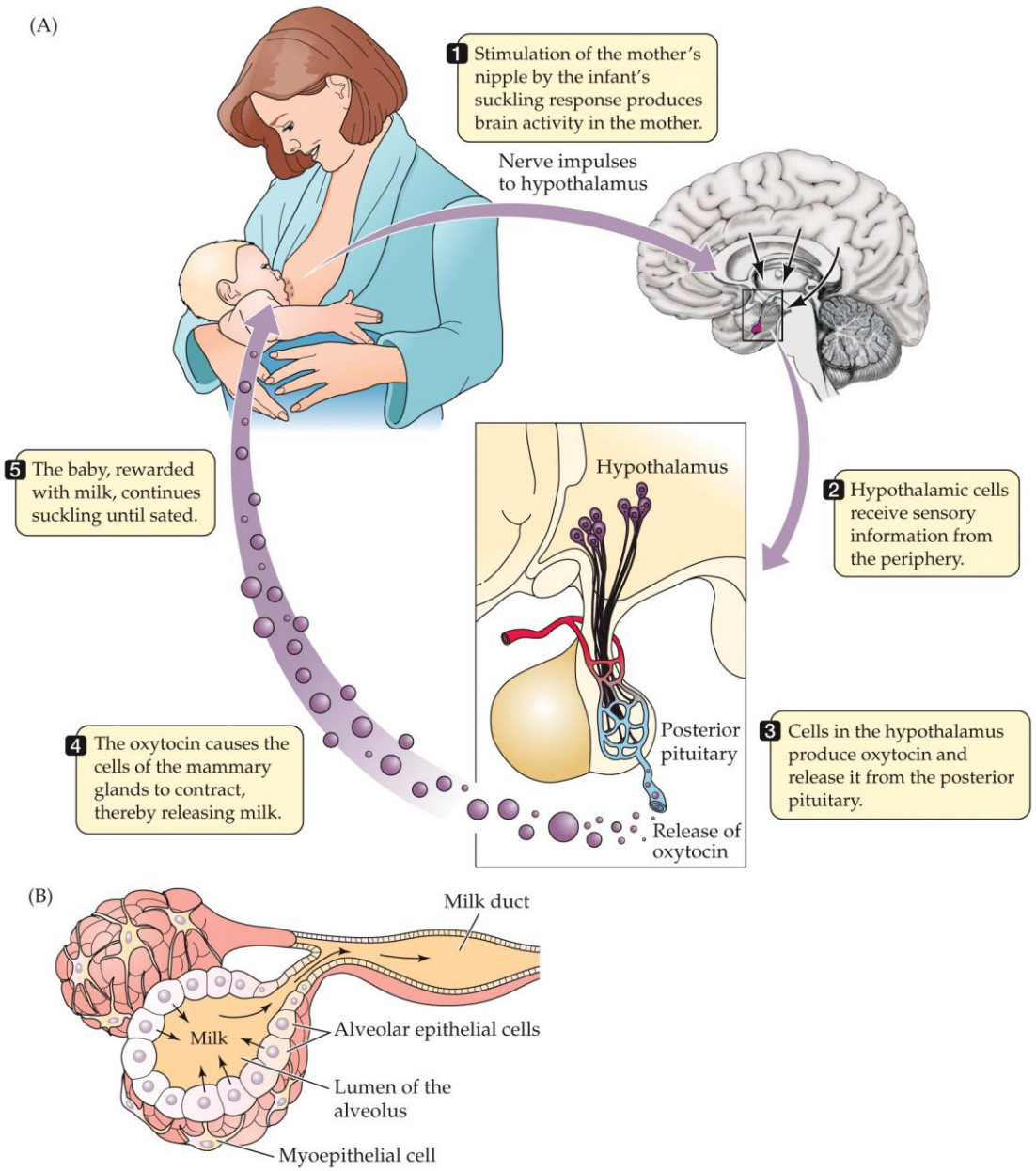
PITUITARY HORMONE	HYPOTHALAMIC RELEASING FACTORS	HYPOTHALAMIC INHIBITORY FACTORS
Adrenocorticotropic hormone (ACTH)	Corticotropin-releasing hormone (CRH), vasopressin, and other peptides	—
Thyroid-stimulating hormone (TSH)	Thyrotropin-releasing hormone (TRH)	Growth hormone–inhibiting hormone (GIH, somatostatin)
Growth hormone (GH)	Growth hormone–releasing hormone (GHRH)	Growth hormone–inhibiting hormone (GIH, somatostatin)
Prolactin	Prolactin-releasing factor (PRF) and thyrotropin-releasing hormone (TRH)	Prolactin release–inhibiting factor (PIF, dopamine)
Luteinizing hormone (LH)	Luteinizing hormone–releasing hormone (LHRH)	—
Follicle-stimulating hormone (FSH)	Luteinizing hormone–releasing hormone (LHRH)	—

Οι δράσεις της υπόφυσης



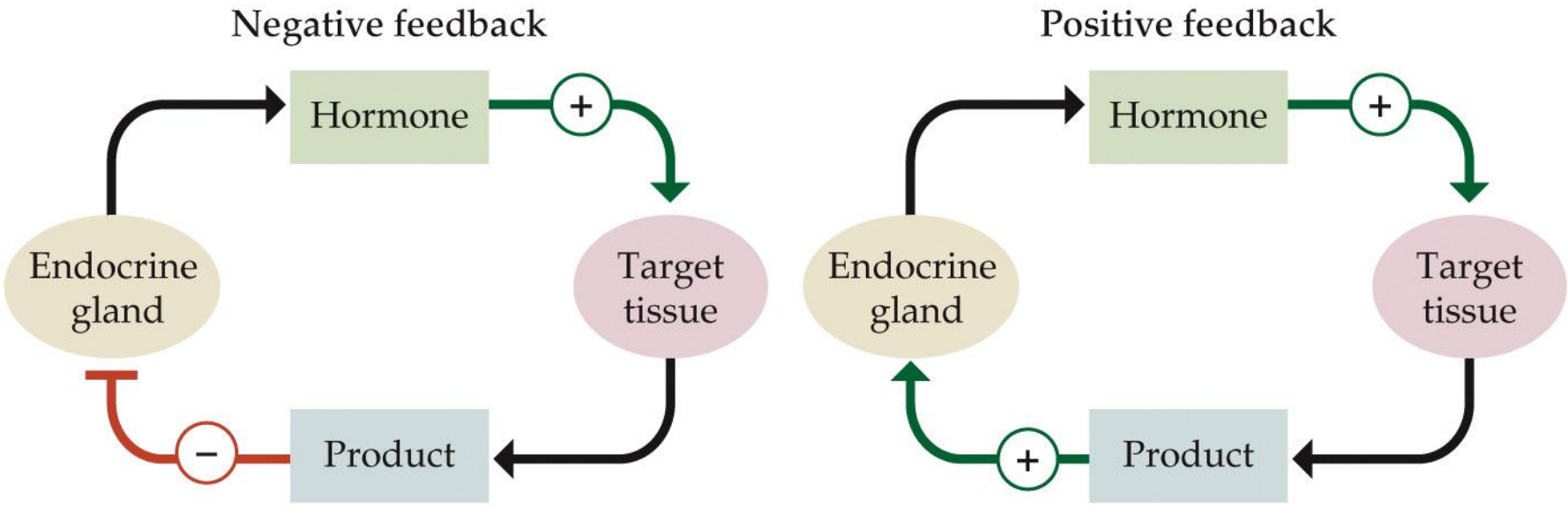
NEUROANATOMY 2e, Figure 17.6

Γαλακτόρροια και θηλασμός



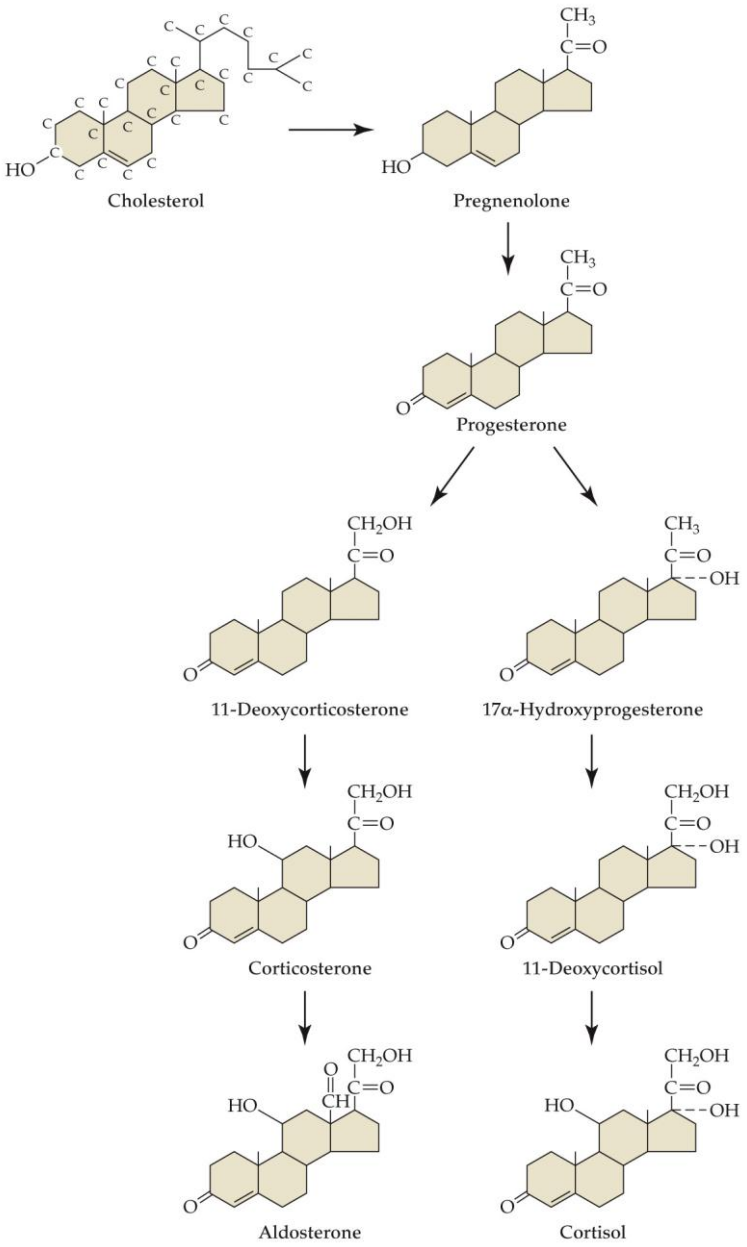
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.13

Αρνητική και θετική παλίνδρομη ρύθμιση

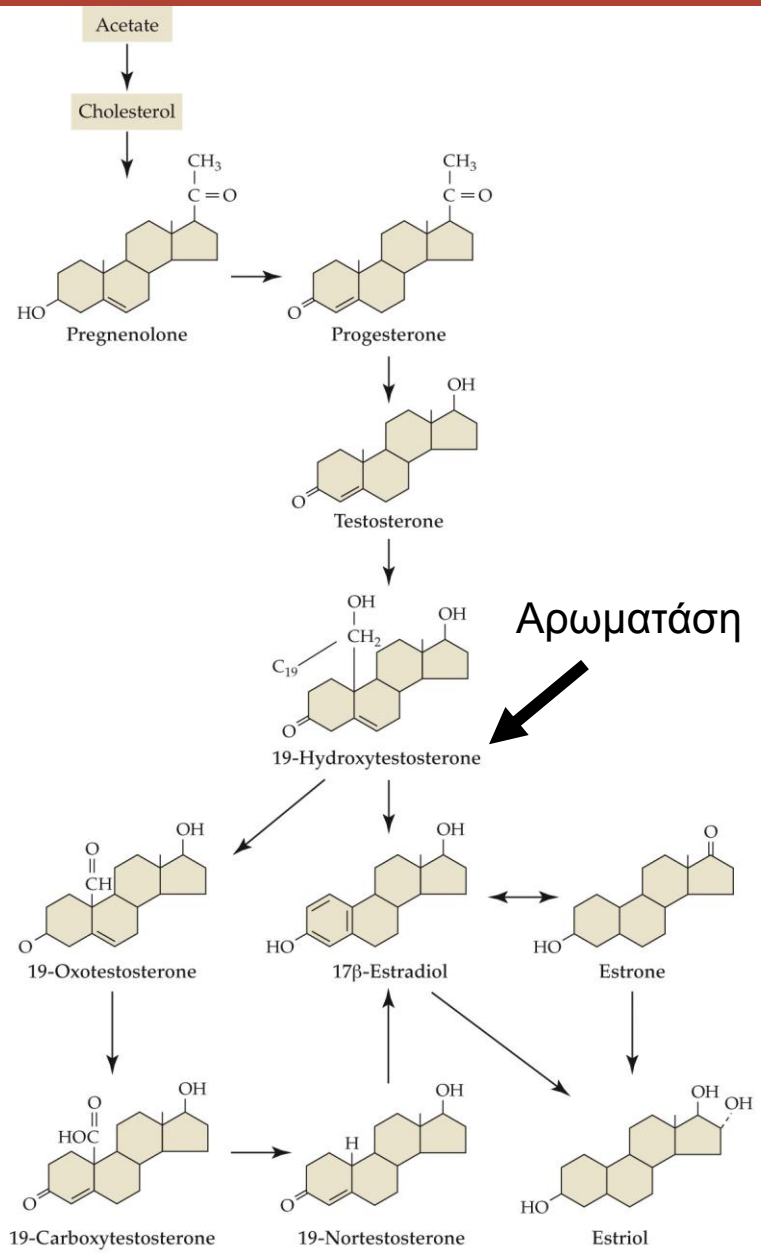


AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.29

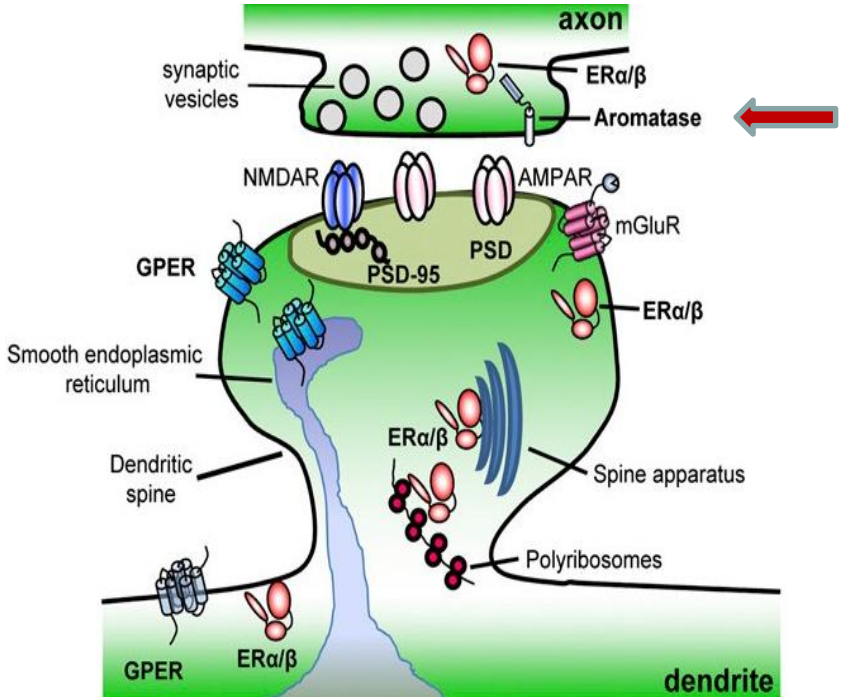
Στερεοειδογένεση



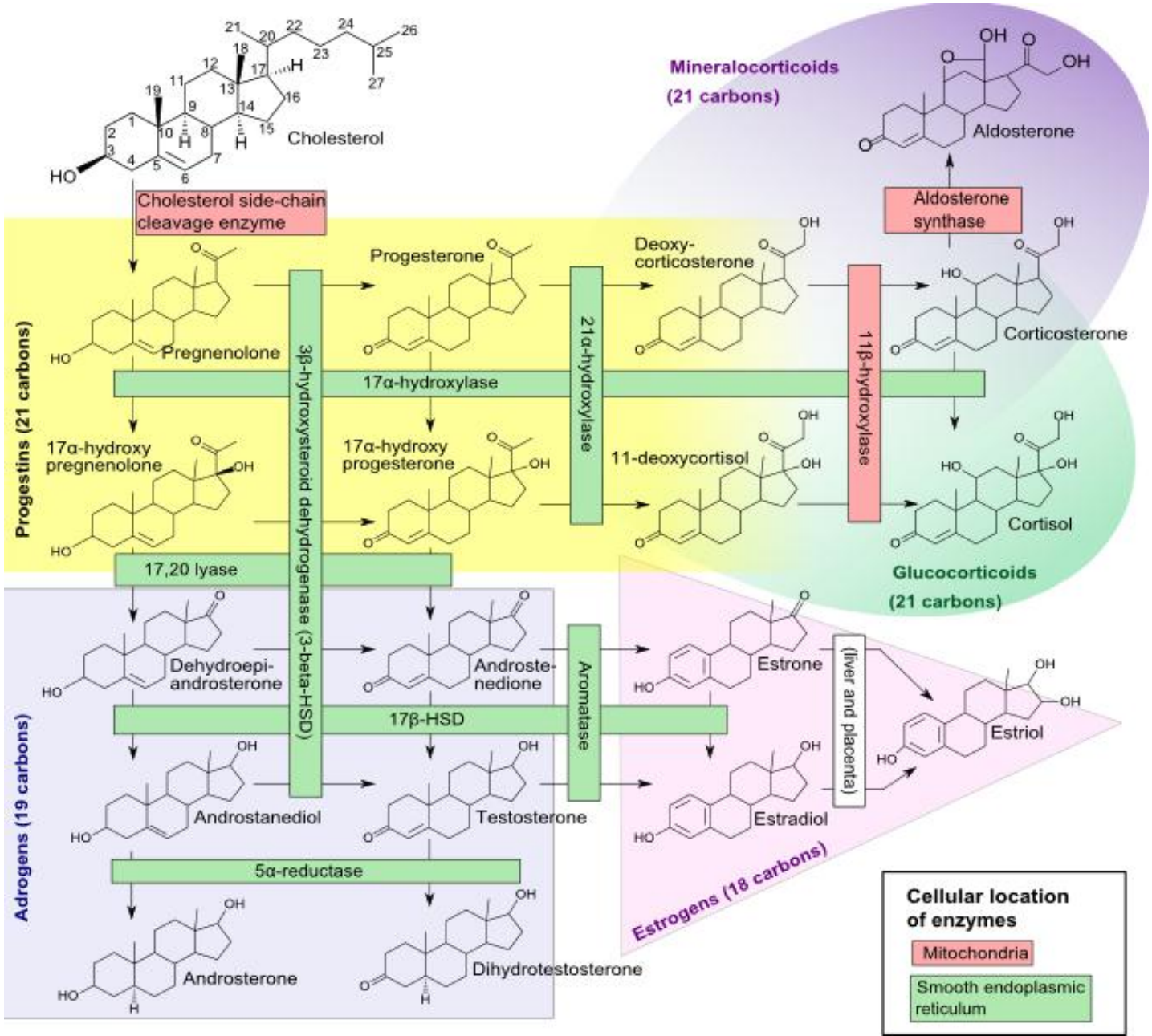
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.24



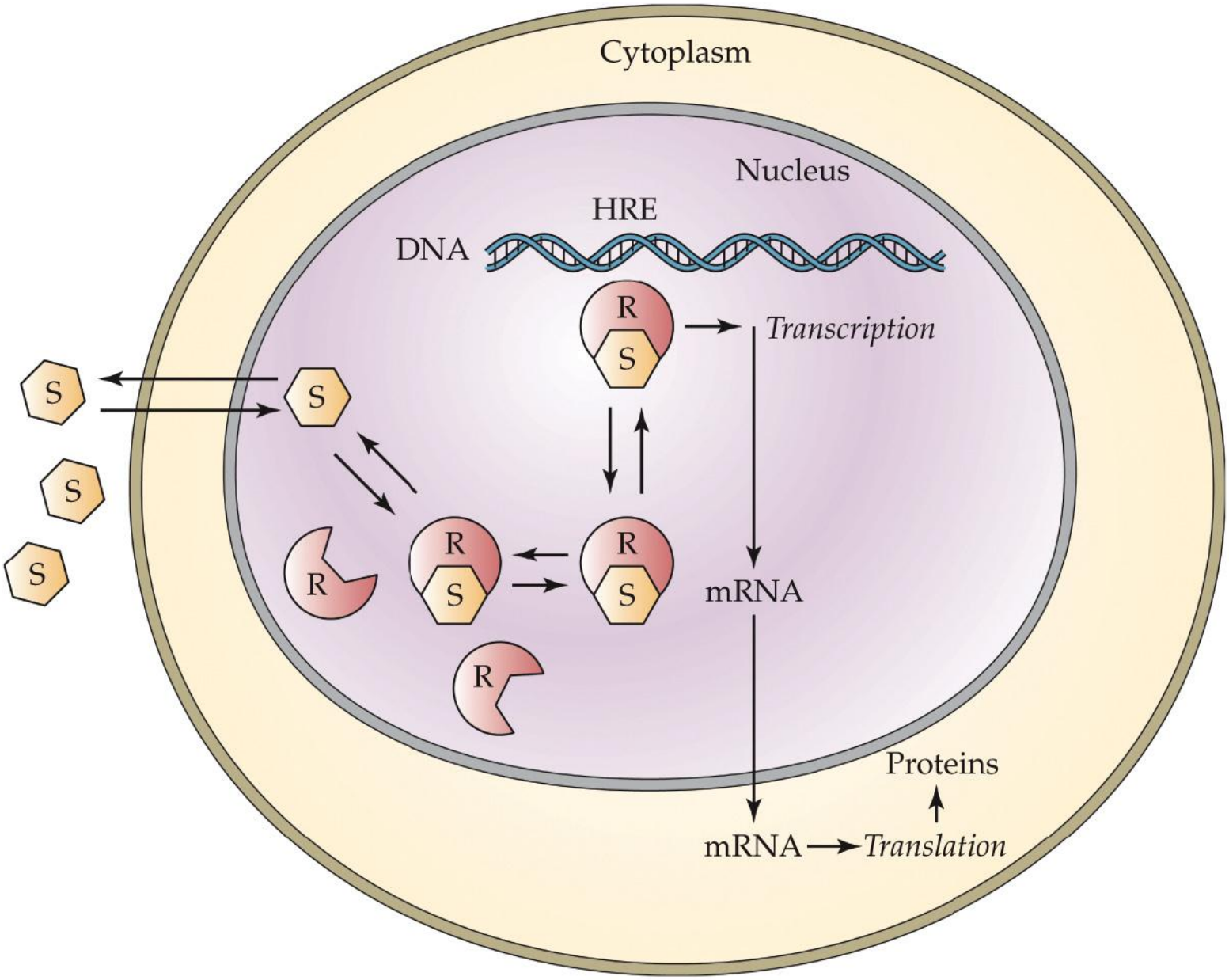
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.26



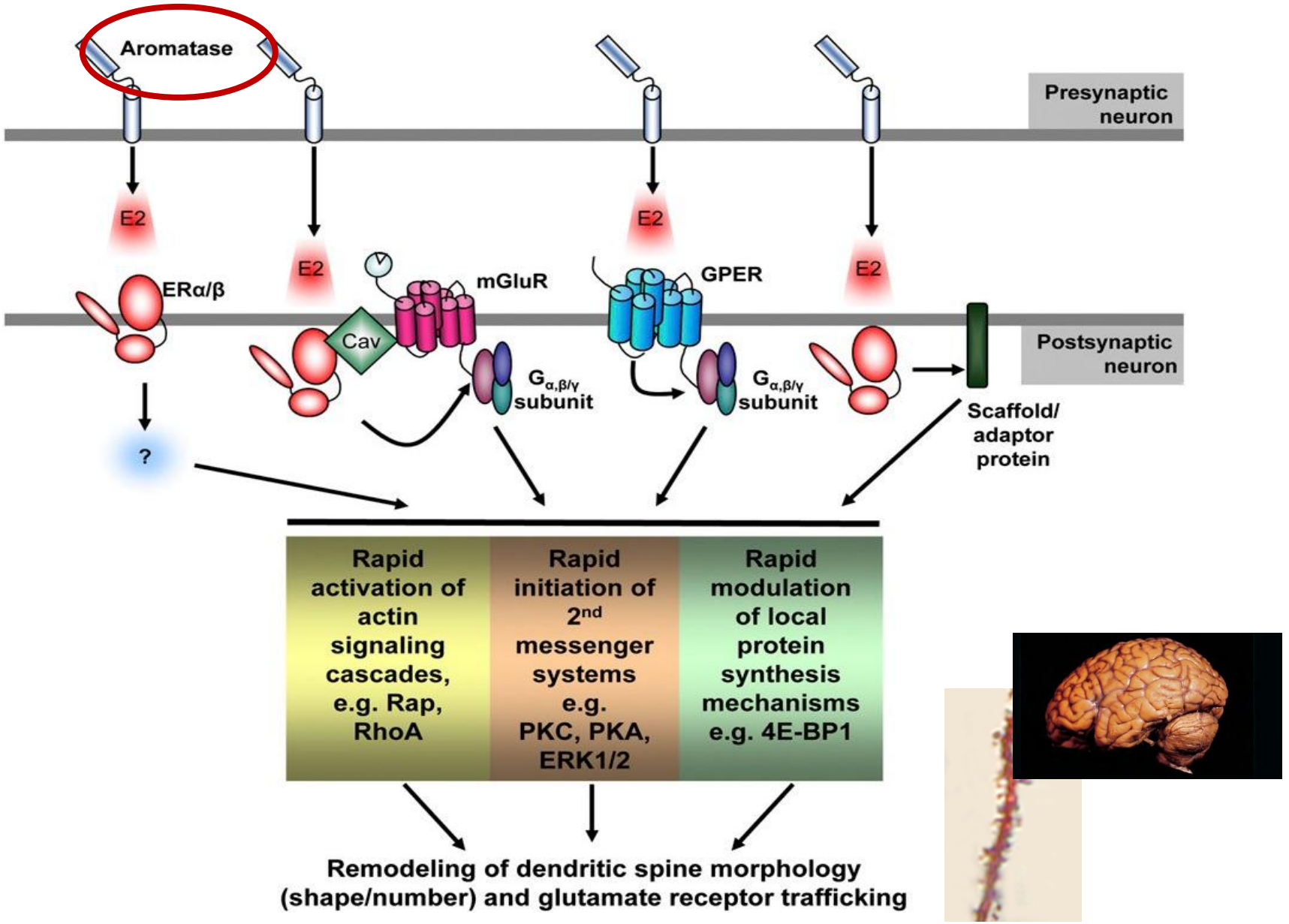
Στεροειδή


Cholesterol
Cholesterol side-chain cleavage enzyme
Mineralocorticoids
(21 carbons)
Aldosterone
Aldosterone synthase
Progestins (21 carbons)
Pregnenolone
Progesterone
Deoxy-corticosterone
Corticosterone
3β-hydroxysteroid dehydrogenase (3-beta-HSD)
17α-hydroxylase
21α-hydroxylase
11β-hydroxylase
17α-hydroxy pregnenolone
17α-hydroxy progesterone
11-deoxycortisol
Cortisol
17,20 lyase
Glucocorticoids
(21 carbons)
Dehydroepi-androsterone
Androste-nedione
17β-HSD
Aromatase
Estrone
(liver and placenta)
Estriol
Androstanediol
Testosterone
Estradiol
5α-reductase
Androsterone
Dihydrotestosterone
Adrogens (19 carbons)
Estrogens (18 carbons)
Cellular location of enzymes
Mitochondria
Smooth endoplasmic reticulum

Κλασσικοί υποδοχείς στεροειδών



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 2.23



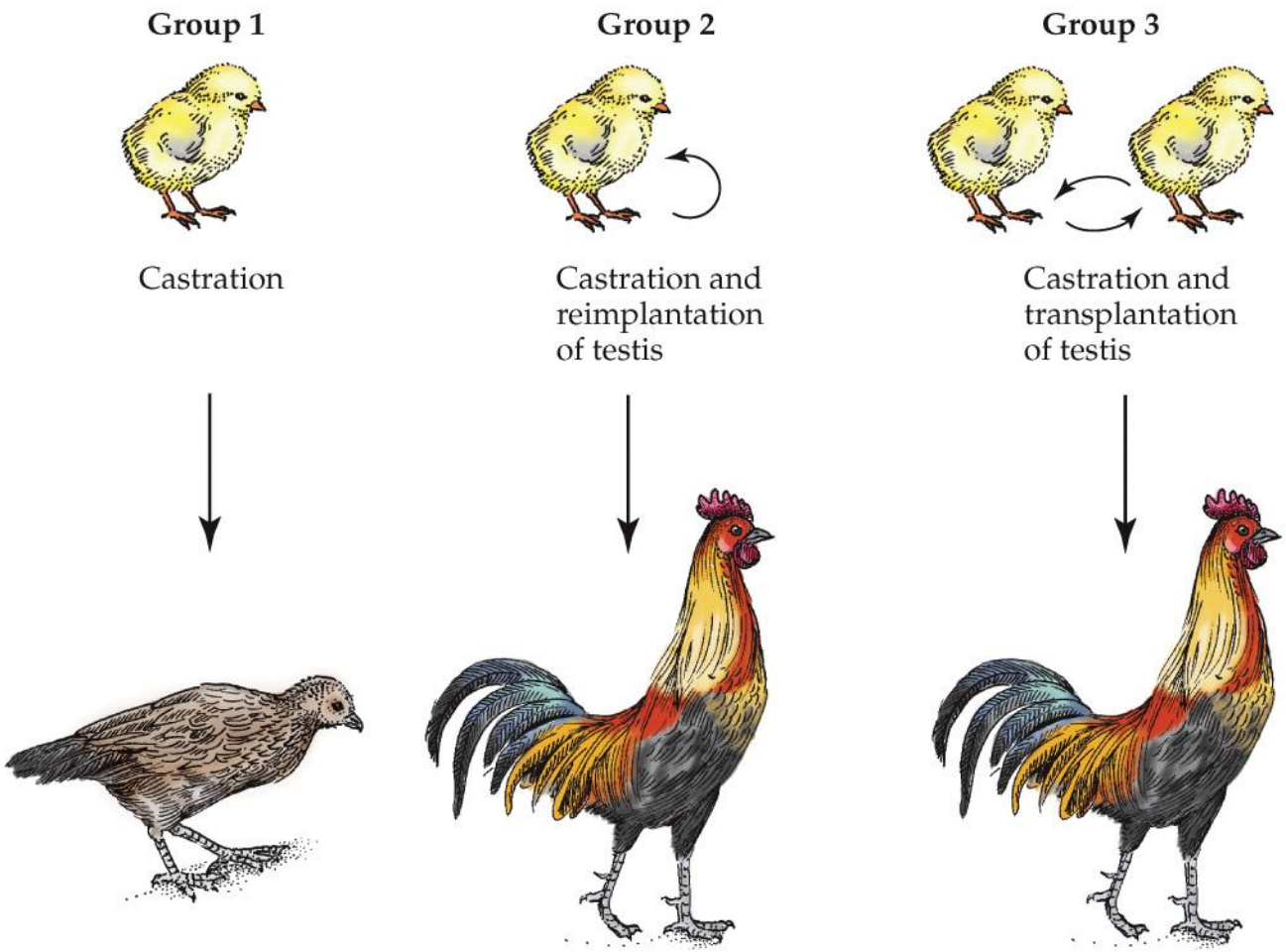
Srivastava D.P. et al 2013, Pharmacological Reviews

Ιστορική Αναδρομή

AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 1.2

Το πρώτο πείραμα: Berthold's Experiment

AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 1.4
© 2017 Sinauer Associates, Inc.

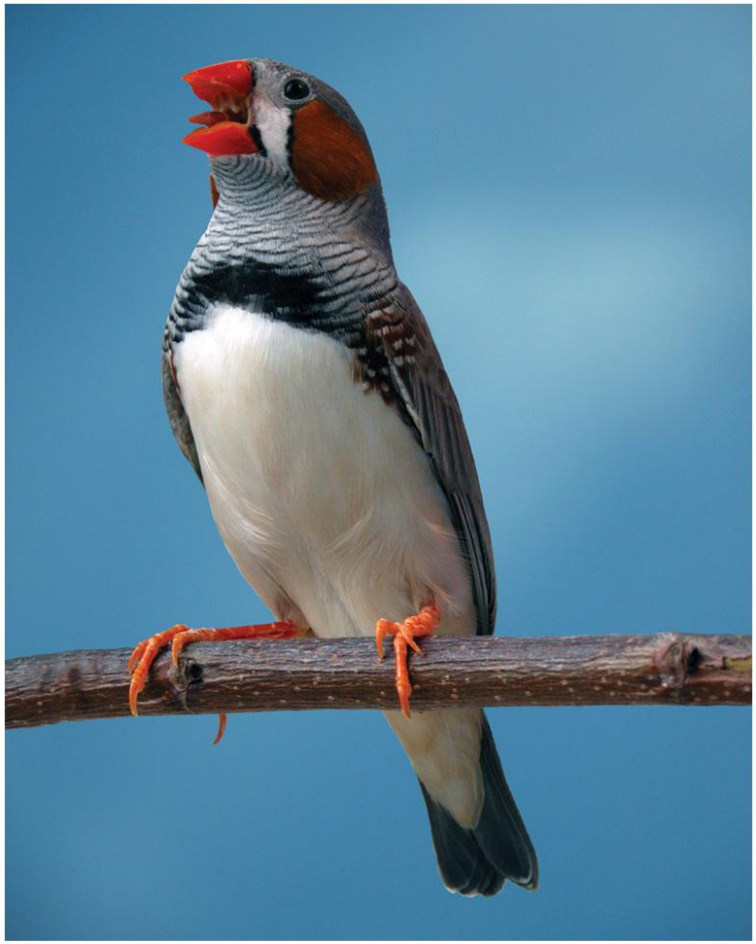


AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 1.5
© 2017 Sinauer Associates, Inc.

Frank A. Beach and the Origins of the Modern Era of Behavioral Endocrinology (1948)

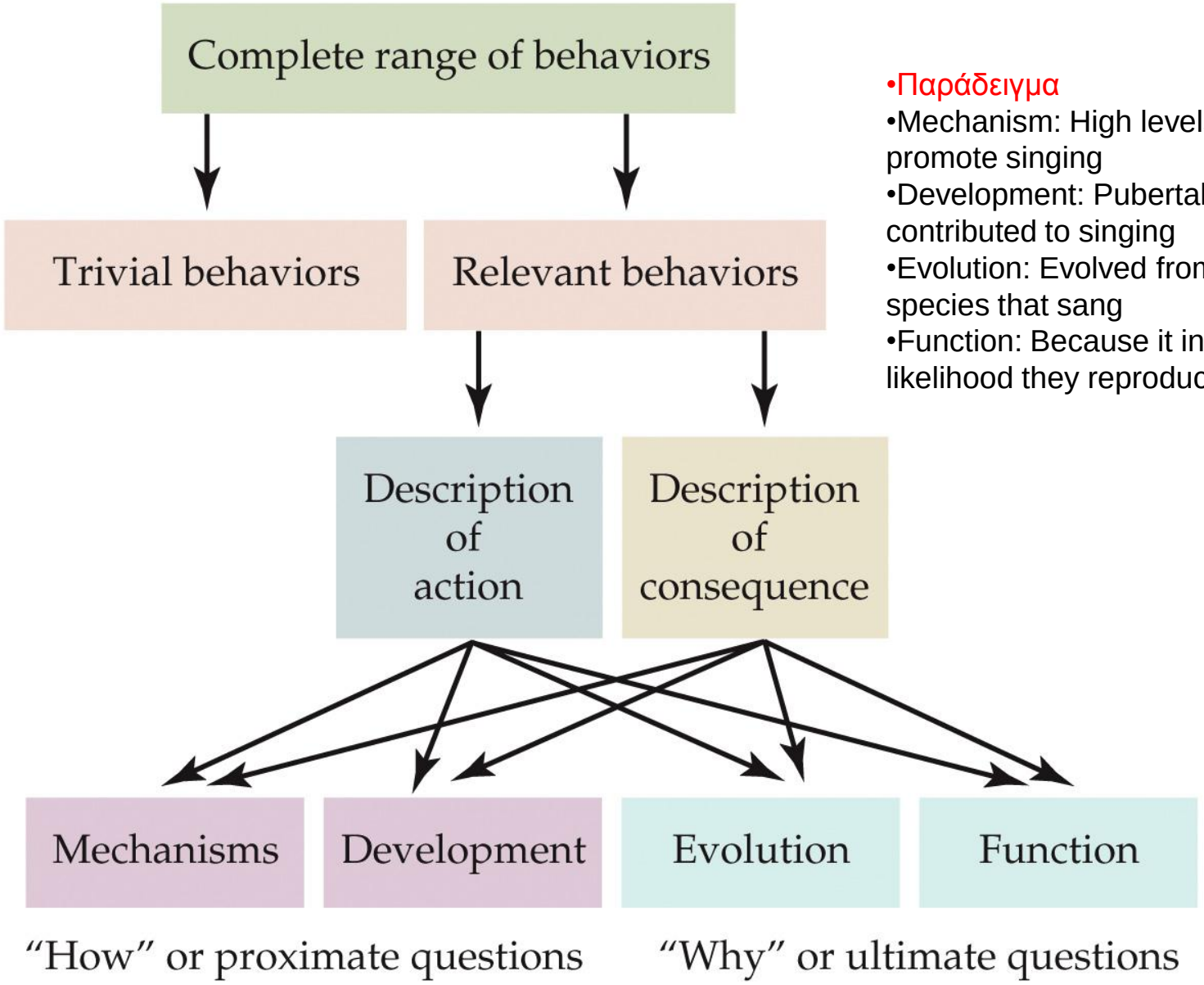
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Box 1.1

Μελέτη διαφορετικών ζωικών μοντέλων



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 1.7

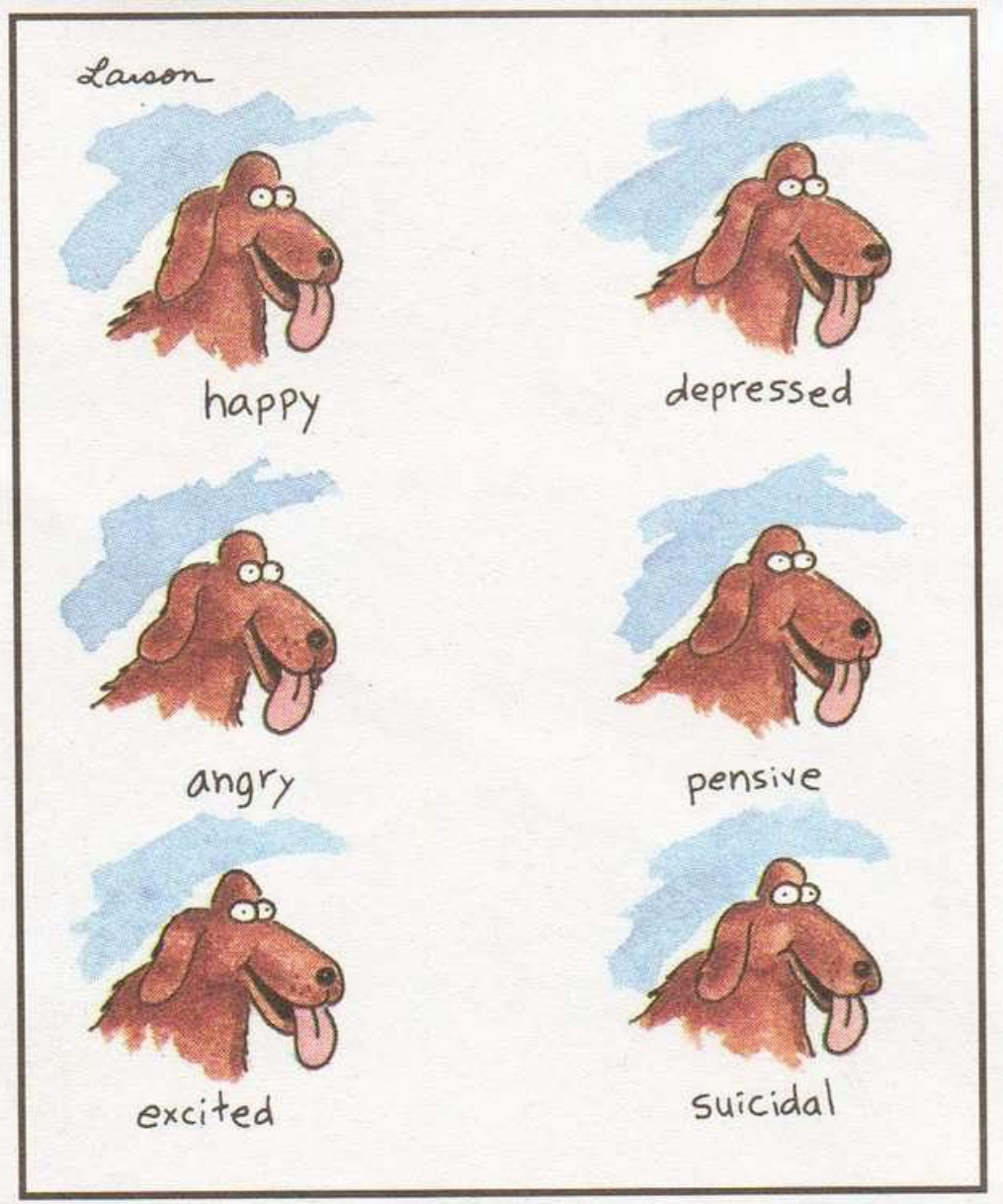
Stages of Behavioral Research



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 1.8

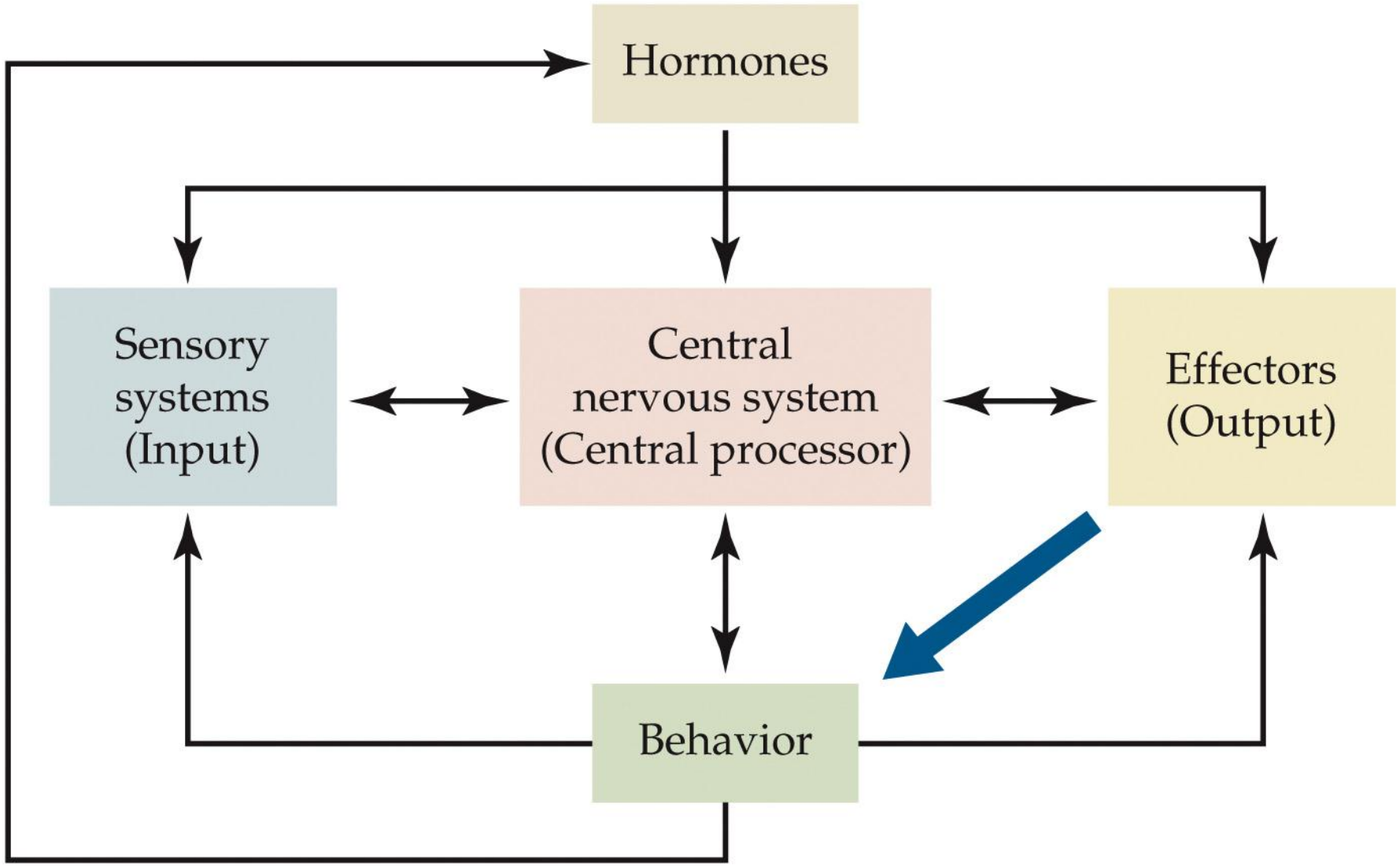
- Παράδειγμα
- Mechanism: High levels of estrogens promote singing
- Development: Pubertal hormone surge contributed to singing
- Evolution: Evolved from a common species that sang
- Function: Because it increases the likelihood they reproduce

Αναγνώριση της συμπεριφοράς



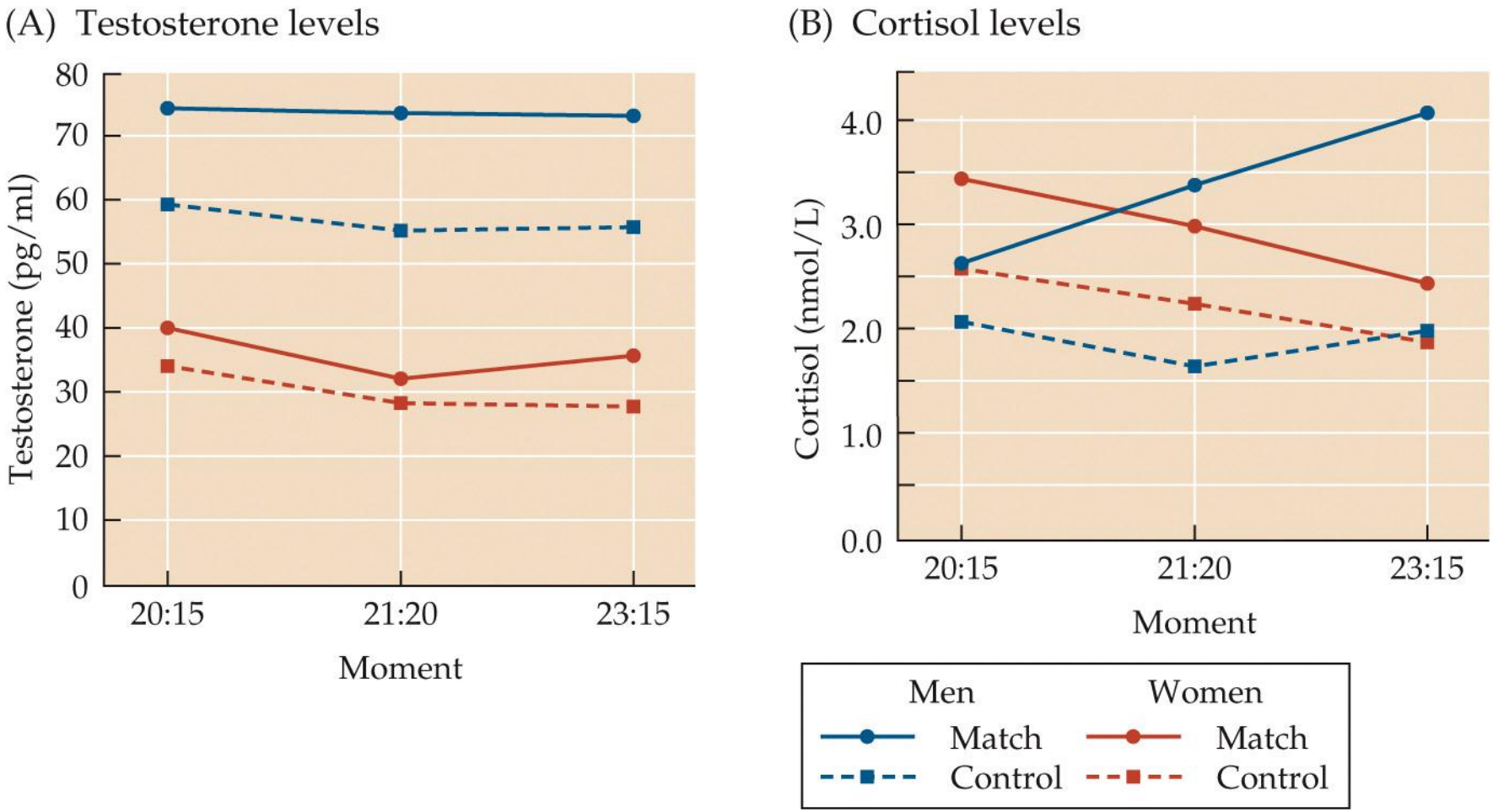
How to recognize the moods of an Irish setter

Οι ορμόνες επηρεάζουν τη συμπεριφορά



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 1.9

Ορμονικές αποκρίσεις κατά την παρακολούθηση ποδοσφαίρου!



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 1.10

Προκλινικές μελέτες

BJP British Journal of Pharmacology

Themed Section: Animal Models in Psychiatry Research

REVIEW

Sex differences in animal models of psychiatric disorders

N Kokras[1,2] and C Dalla[1]

[1]Department of Pharmacology, Medical School, University of Athens, Greece, and [2]First Department of Psychiatry, Eginition Hospital, Medical School, University of Athens, Greece

Psychoneuroendocrinology 87 (2018) 93–107

Contents lists available at ScienceDirect

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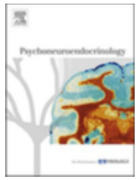
journal homepage: www.elsevier.com/locate/psyneuen

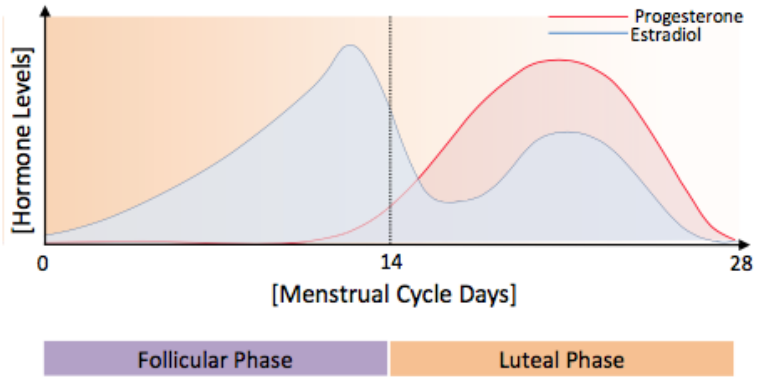


Sex differences in behavioral and neurochemical effects of gonadectomy and aromatase inhibition in rats

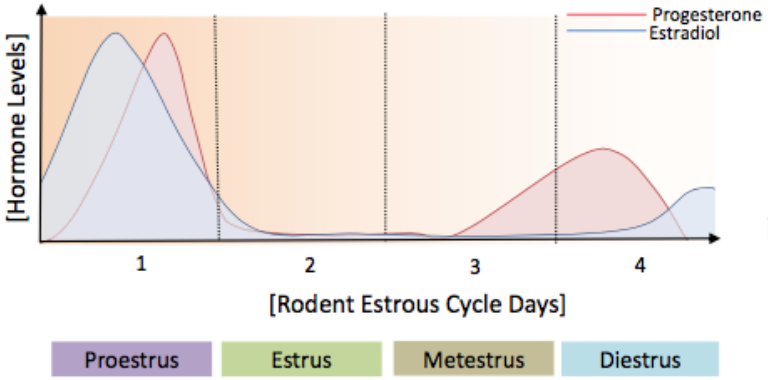
N. Kokras[a,b,1], N. Pastromas[a,1], D. Papasava[a], C. de Bournonville[c,2], C.A. Cornil[c], C. Dalla[a,*]

[a] Department of Pharmacology, Medical School, National and Kapodistrian University of Athens, Greece
[b] First Department of Psychiatry, Eginition Hospital, Medical School, National and Kapodistrian University of Athens, Greece
[c] Behavioral Neuroendocrinology Research Group, GIGA Neurosciences, University of Liège, Belgium

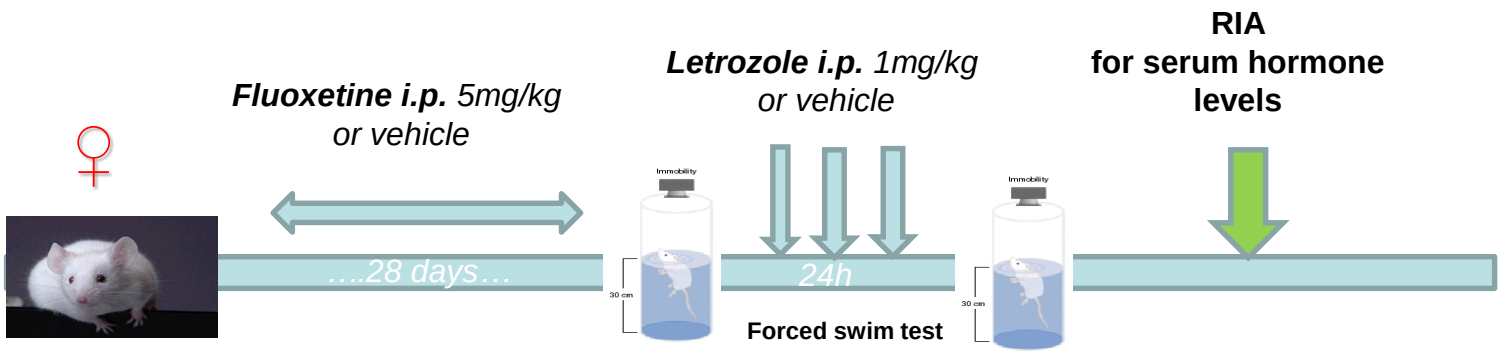
Human


Progesterone
Estradiol
[Hormone Levels]
0
14
28
[Menstrual Cycle Days]
Follicular Phase
Luteal Phase

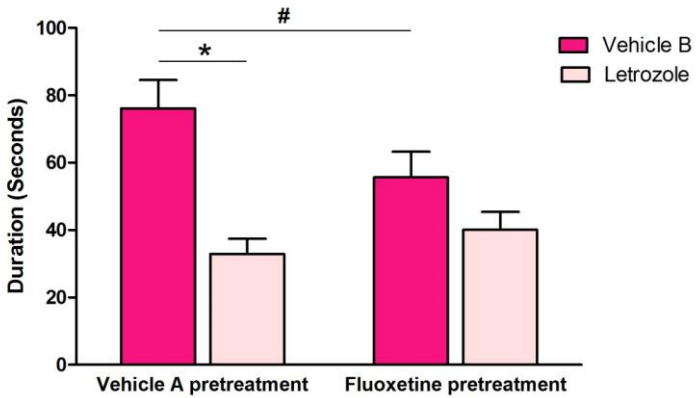
Rat


Progesterone
Estradiol
[Hormone Levels]
1
2
3
4
[Rodent Estrous Cycle Days]
Proestrus
Estrus
Metestrus
Diestrus

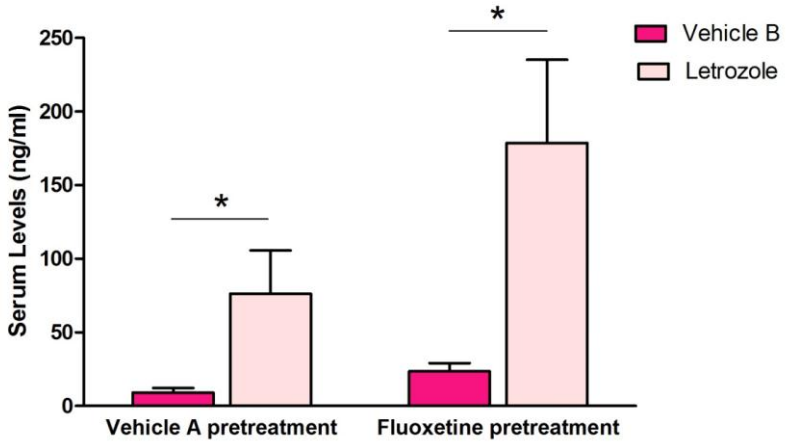
Πώς επηρεάζουν οι αναστολείς αρωματάσης τη διάθεση?



Η λετροζόλη εμφανίζει παρόμοιο αποτέλεσμα με την φλουοξετίνη



Η λετροζόλη αυξάνει την τεστοστερόνη



Kokras … and Dalla, Int. J. Neuropsychopharm, 2014

Χρόνια χορήγηση αναστολέα αρωματάσης

Gonadectomy or sham-operation

Adult male & female Wistar rats

…3 weeks…

Aromatase Inhibition
(Letrozole i.p.)

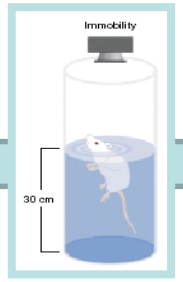
1 week

1mg/kg or vehicle

Open Field 10 min

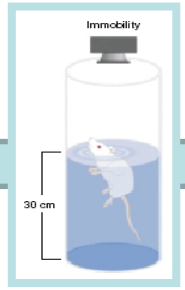
24h

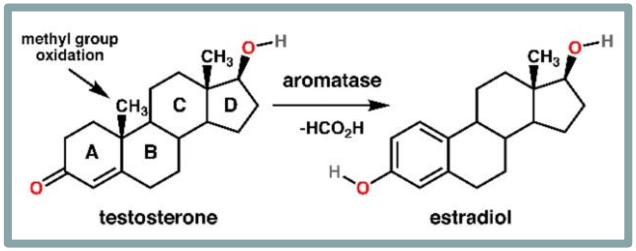
FST Pretest



24h

FST Test





AROMATASE INHIBITON

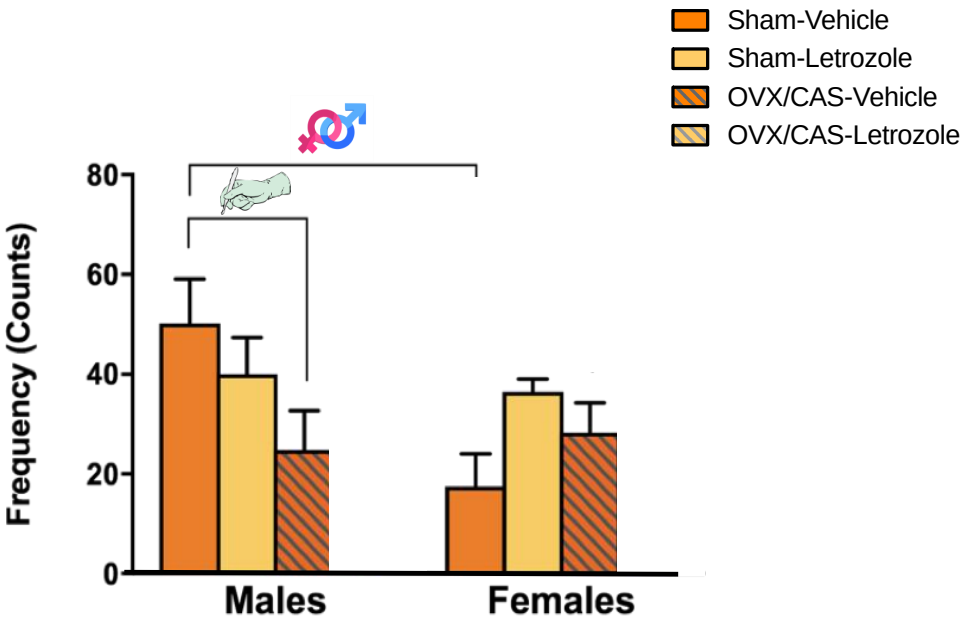
RIA

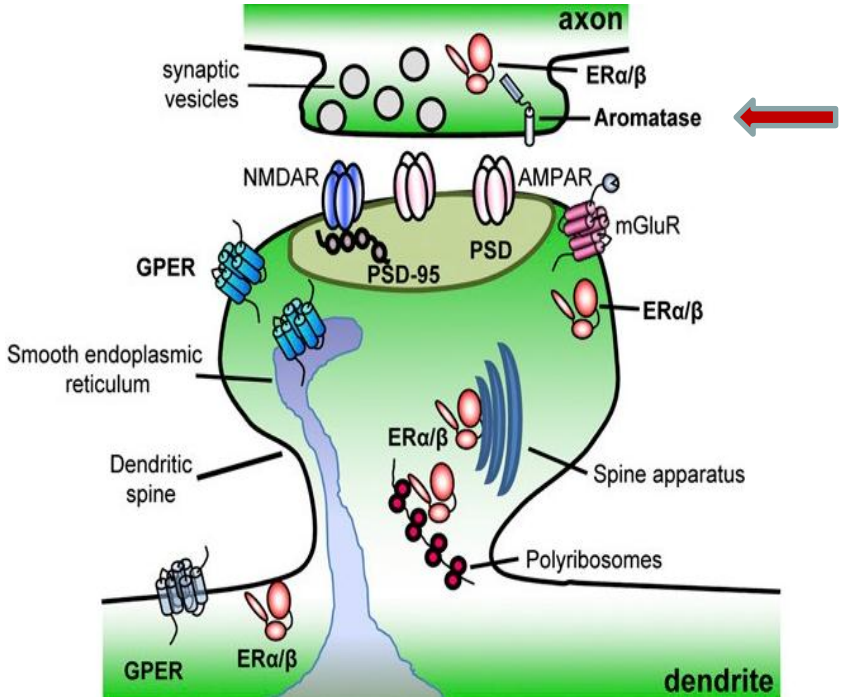
HPLC-ED

Sacrifice

Kokras … and Dalla, Psychoneuroendocrinology, 2018

Η συμπεριφορά των πειραματοζώων επηρεάζεται από τη μείωση της τεστοστερόνης, αλλά και από τη λετροζόλη

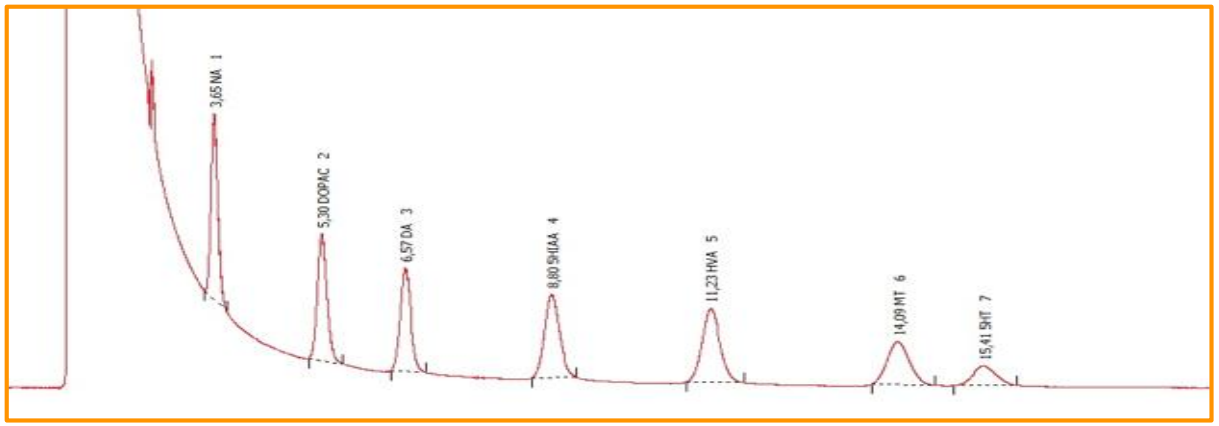




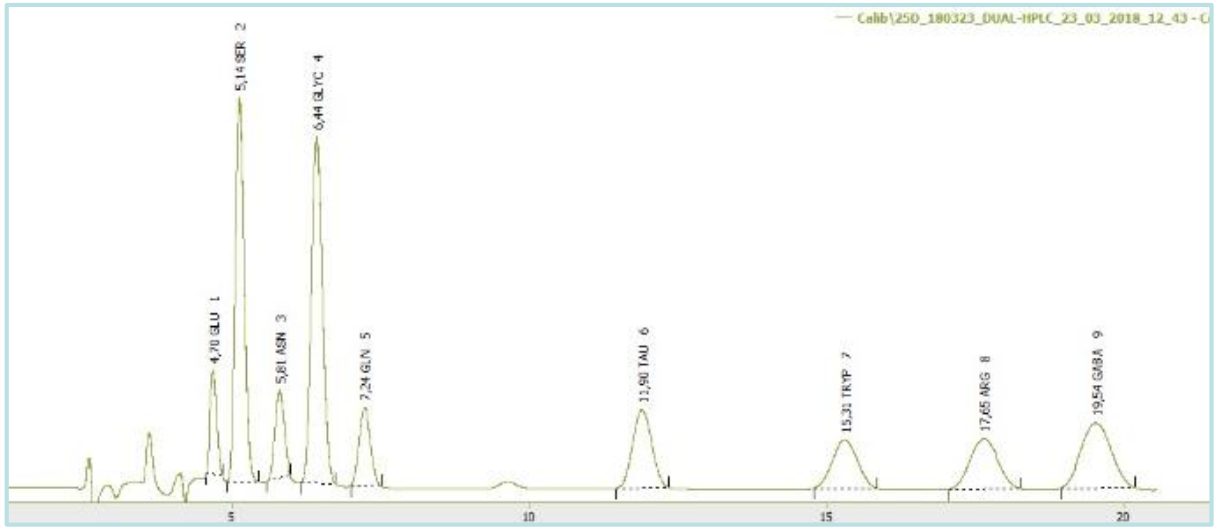
Kokras & Dalla, Pharmacology Biochemistry & Behavior, 2016

Νευροχημική ανάλυση των νευροδιαβιβαστών με HPLC-ED

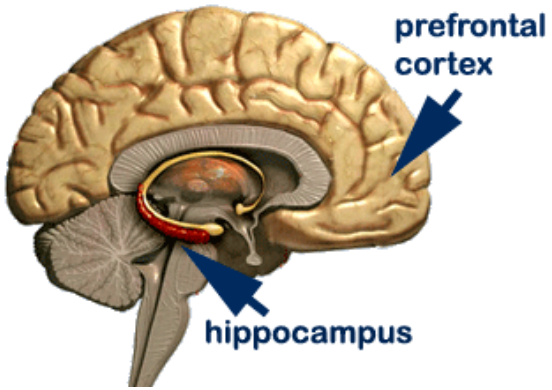
Μονοαμίνες: NA, DA, 5-HT και μεταβολίτες

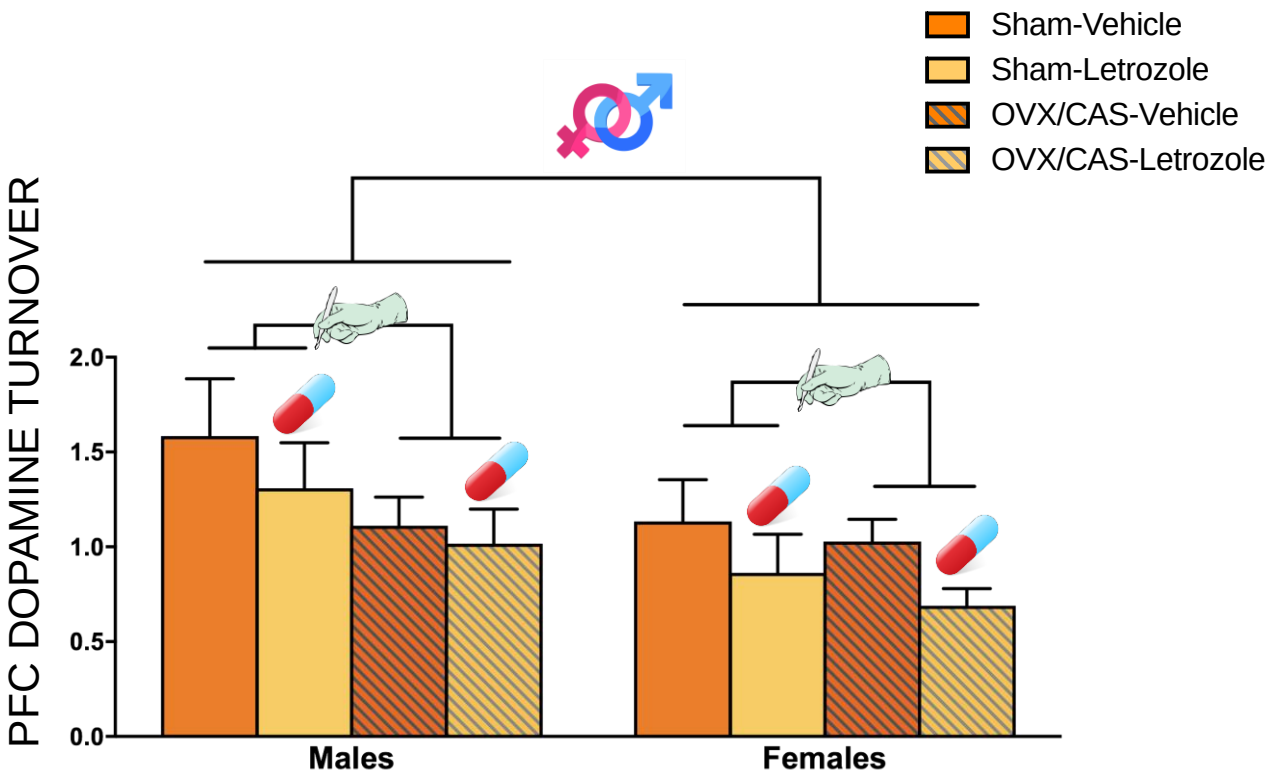


Αμινοξέα: GABA, Glutamate, Glutamine, Glycine, Taurine, Serine…



Η λετροζόλη επηρεάζει την ντοπαμίνη και τη σεροτονίνη στον εγκέφαλο, οι οποίες σχετίζονται με τη συμπεριφορά



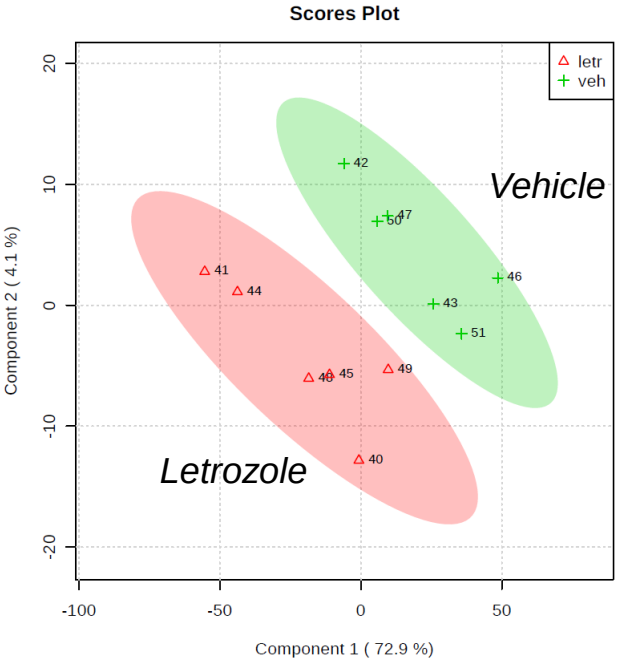


Kokras … and Dalla, Psychoneuroendocrinology, 2018

Η ανάλυση μεταβολομικής έδειξε ότι η λετροζόλη επηρεάζει το μεταβολικό προφίλ στον ιππόκαμπο

Important features identified by SAM

	Peaks(mz/rt)	d.value	stdev	rawp	q.value
1	Phosphorylcholine	4.9169	1.8453	0.00052174	0.073191
2	betaine	4.1665	0.96036	0.0014783	0.090269
3	dimethylglycine	4.0345	0.16966	0.0019565	0.090269
4	histidine	3.7231	1.5654	0.0031304	0.090269
5	nicotinamide	3.7217	4.7186	0.0032174	0.090269
6	D-gluconate	3.5881	0.091968	0.004087	0.095555
7	betaine aldehyde	3.4162	0.13536	0.0054348	0.10892
8	Ng,NG-dimethyl-L-arginine	3.2844	0.33221	0.0064348	0.11284
9	Glycerophosphocholine	3.2077	3.2446	0.0075652	0.11711
10	folate	3.1429	0.12084	0.0083478	0.11711



MAX-PLANCK-GESELLSCHAFT

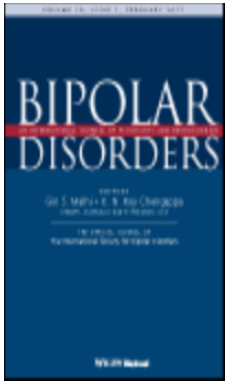
SAM: significance analysis of microarrays

Kokras N, Filiou M and Dalla C., unpublished data

Ερωτήματα που προκύπτουν..

- Τι μπορεί να προκαλέσει η έναρξη αγωγής (π.χ. αναστολείς αρωματάσης - υπερθυμία ή/και ψυχοκινητική ανησυχία);
- Τι μπορεί να προκαλέσει η χρόνια θεραπεία (π.χ. αναστολείς αρωματάσης – κατάθλιψη);
- Με ποιο μηχανισμό δράσης;
- Πώς αντιμετωπίζονται;

Aromatase inhibitors and bipolar mood disorder: a case report



Goodwin G. M. Aromatase inhibitors and bipolar mood disorder: a case report.
Bipolar Disord 2006: 8: 516–518. © Blackwell Munksgaard, 2006

Guy M. Goodwin

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"I had a completely sleepless night and the following night awoke at 3 am in a complete frenzy. I felt angry and aggressive and so wound up that I got dressed and went out for a 3–4 mile walk."

Palliative and Supportive Care (2012), **10**, 225–227.

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CASE REPORT

Aromatase inhibitors and mood disturbances

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