



ΔΙΑΦΟΡΕΣ ΤΟΥ ΦΥΛΟΥ

Χριστίνα Δάλλα, Επ. Καθηγήτρια, Ιατρική
Σχολή, ΕΚΠΑ

(A)



(B)



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 3.1
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- Sex vs. gender

(A)



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(B)



- Βιολογία ή κοινωνία;
- Πώς μπορεί να μελετηθεί;

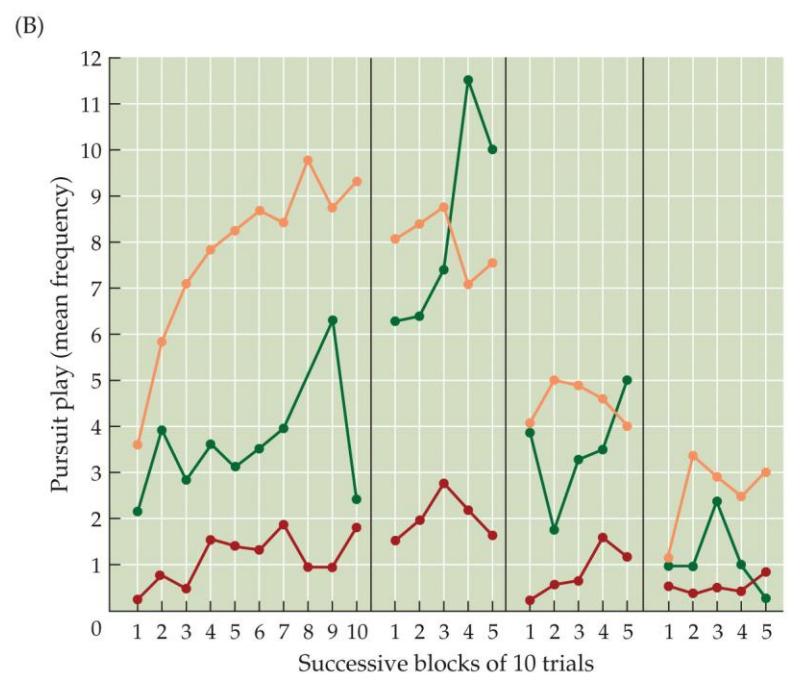
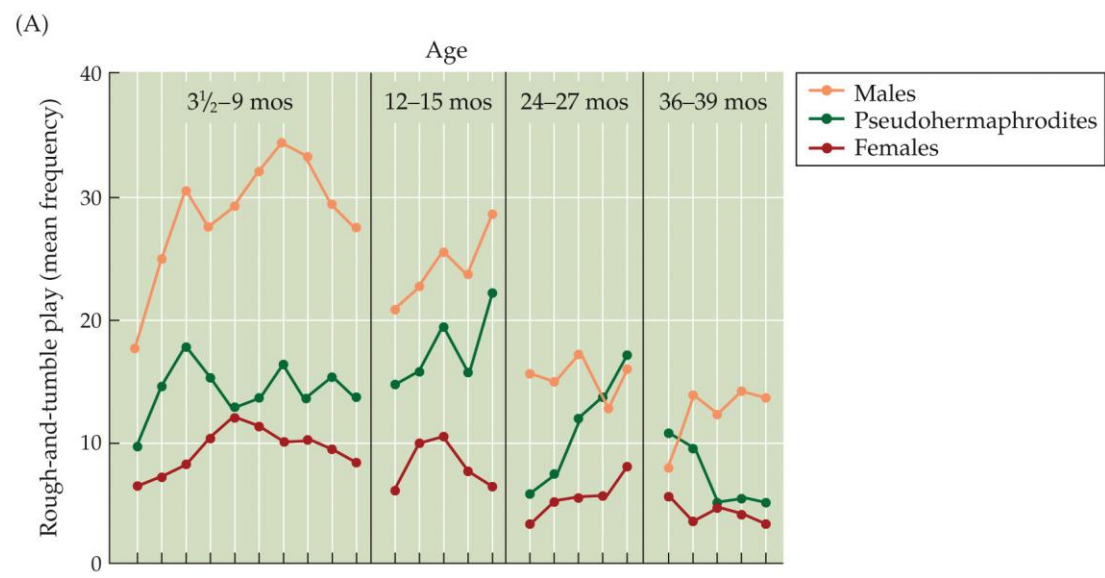


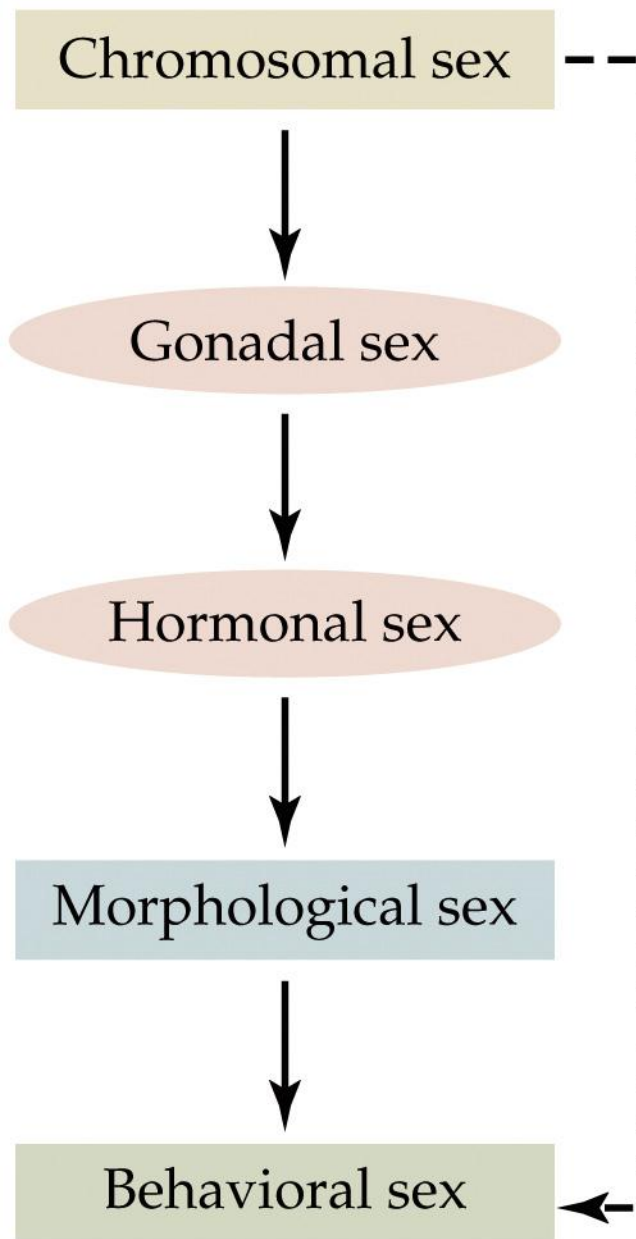


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The frequency of rough-and-tumble and pursuit play





Άνθρωποι: ταυτότητα φύλου, ρόλος, σεξουαλική προτίμηση/προσανατολισμός, νομικό φύλο

Asexual Reproduction	Sexual Reproduction
Many offspring fast	Longer to increase population size
100% genes passed on	50% genes passed on
Variation comes from mutations, so slow to adapt to environment	Faster adaptation to environment
No genders necessary	Need male and female

(A) Prairie voles



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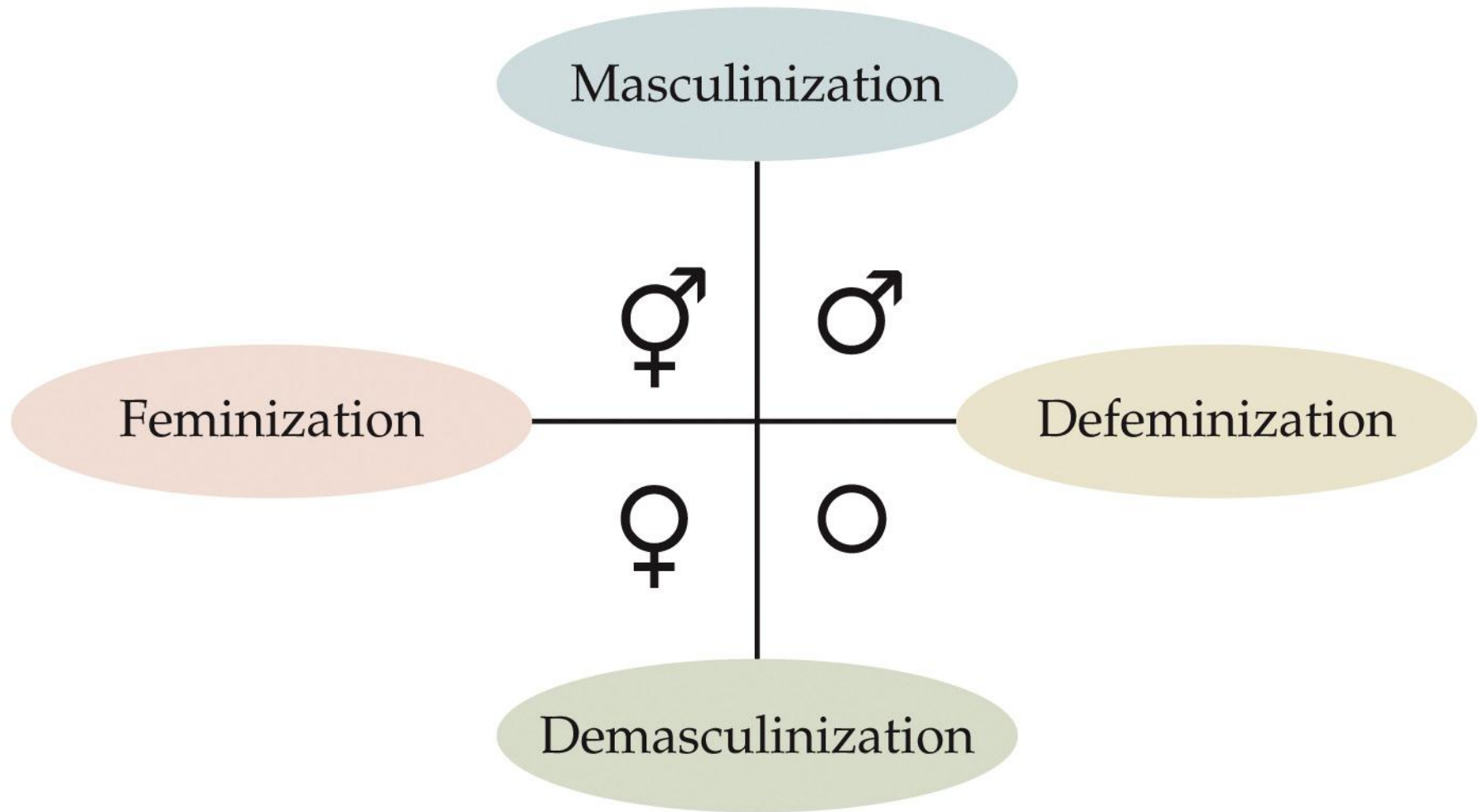
(B) Elk

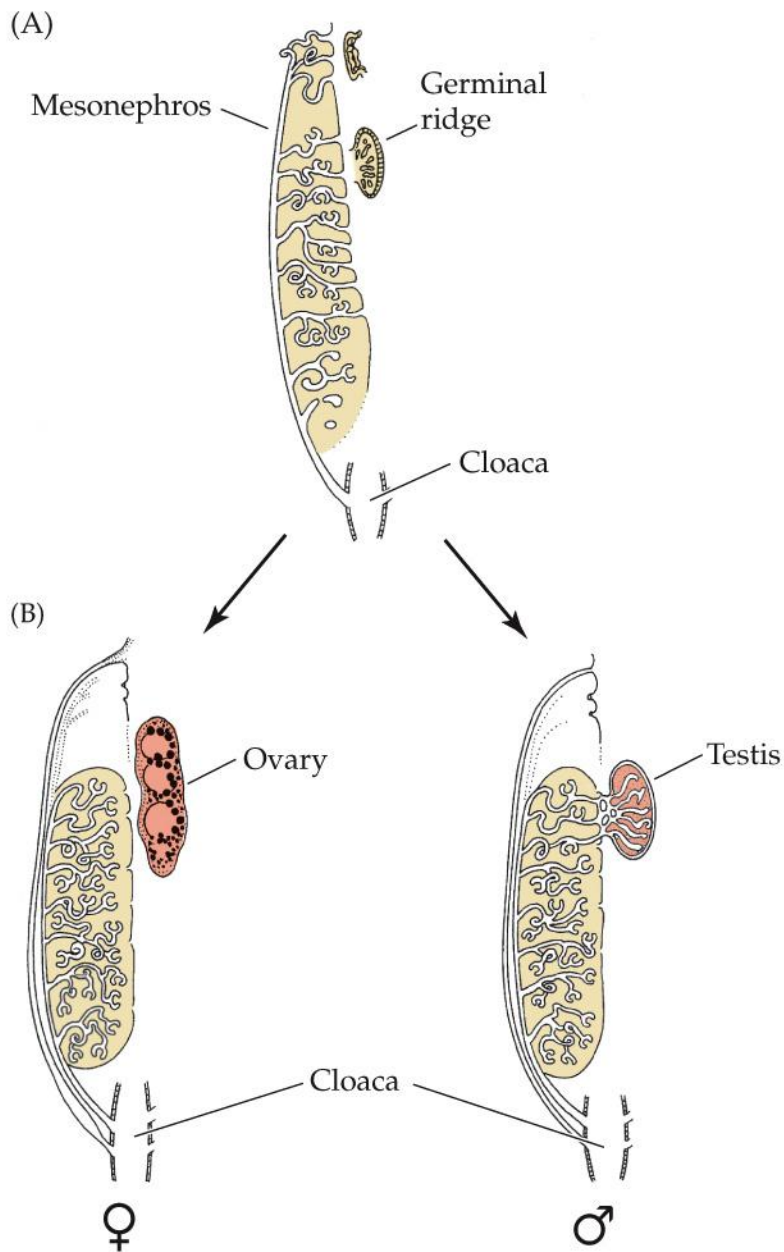




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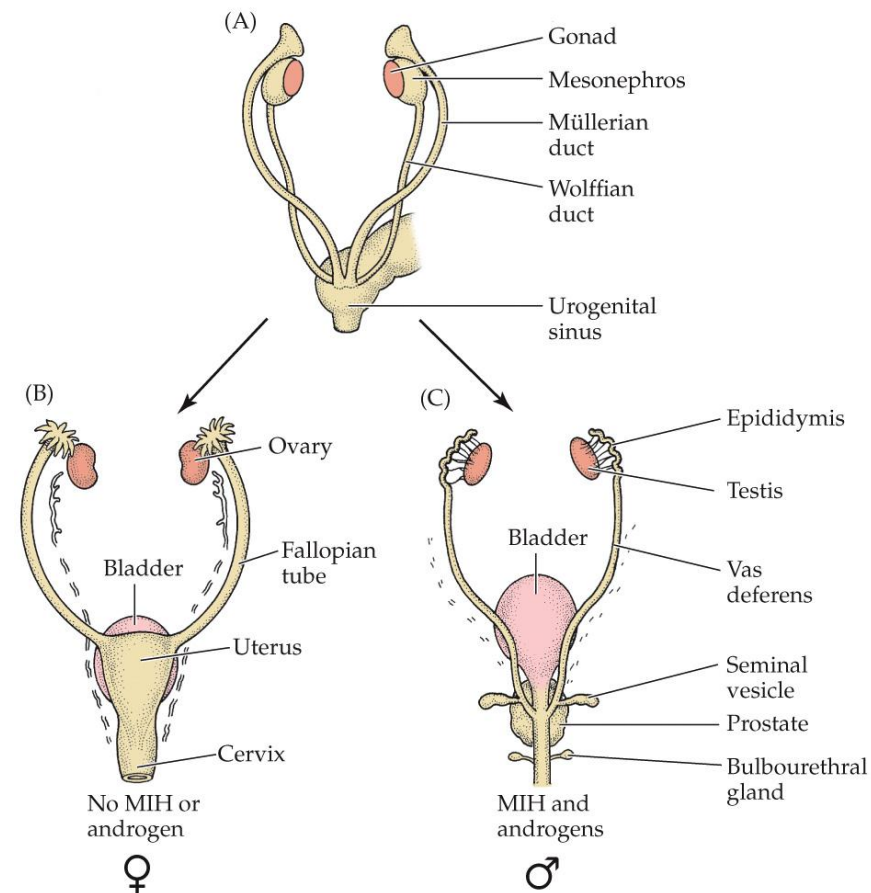
<https://www.youtube.com/watch?v=W7QZnwKqopo>





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Το γονίδιο *SRY* είναι απαραίτητο για τη δημιουργία των όρχεων



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Ανάπτυξη των εξωτερικών γεννητικών οργάνων

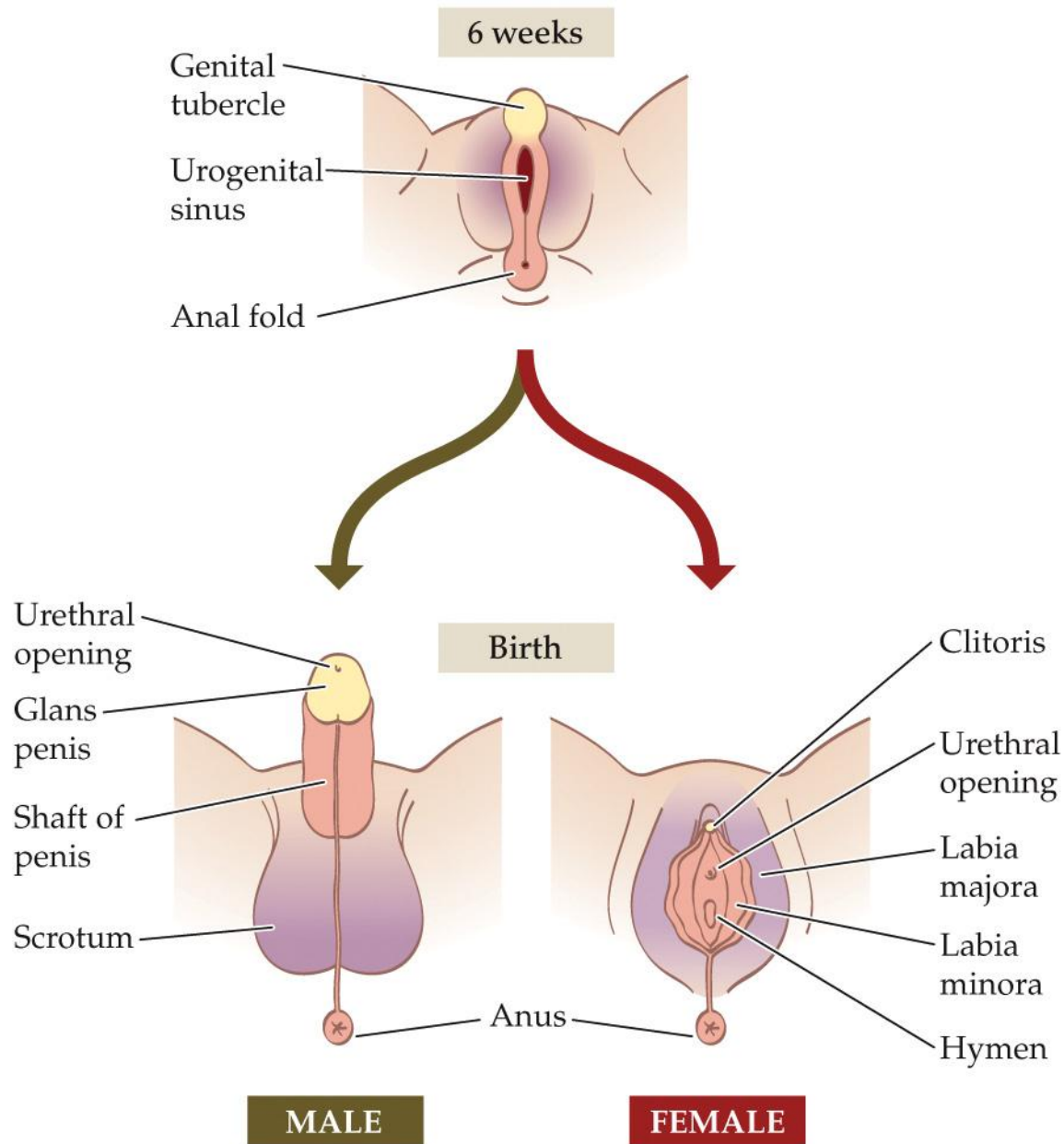
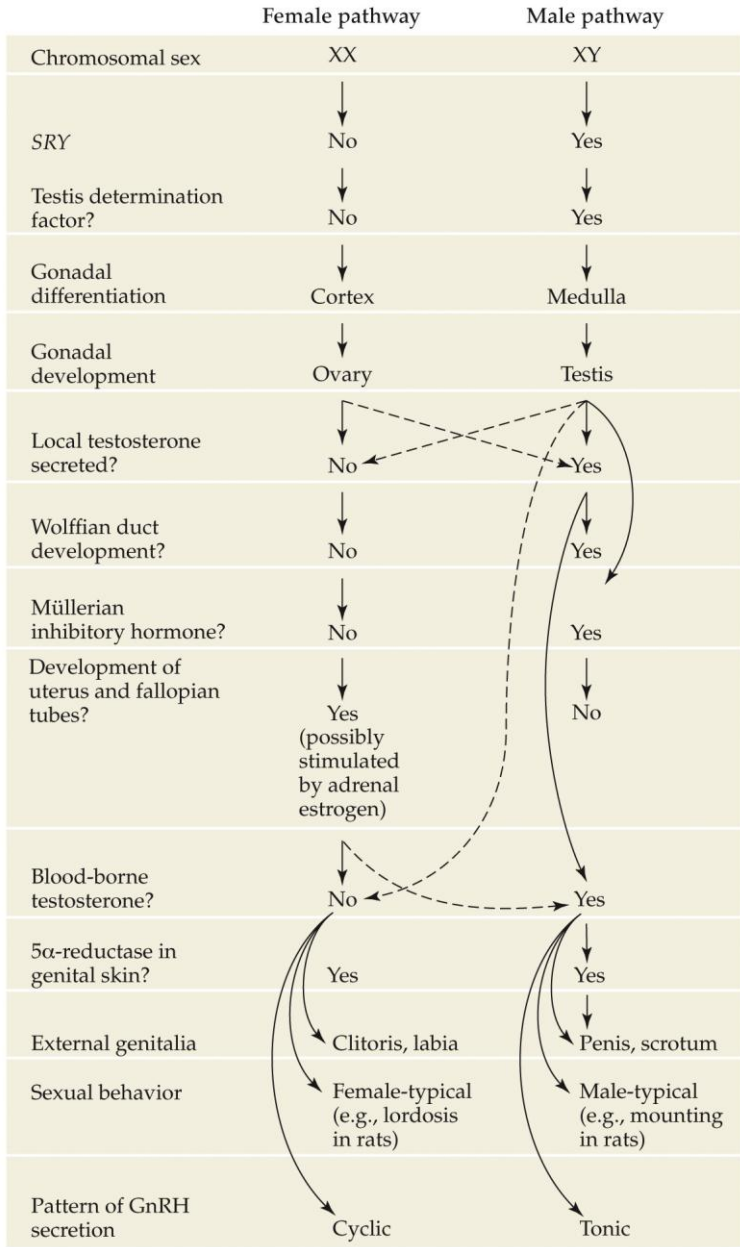


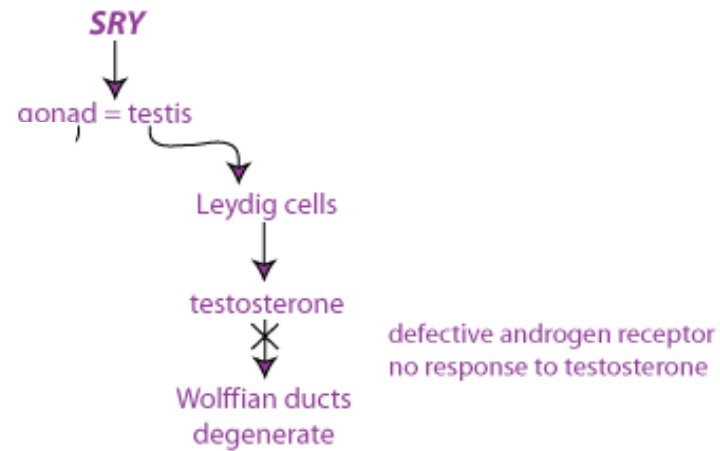
Figure 3.15 Sexual differentiation in humans

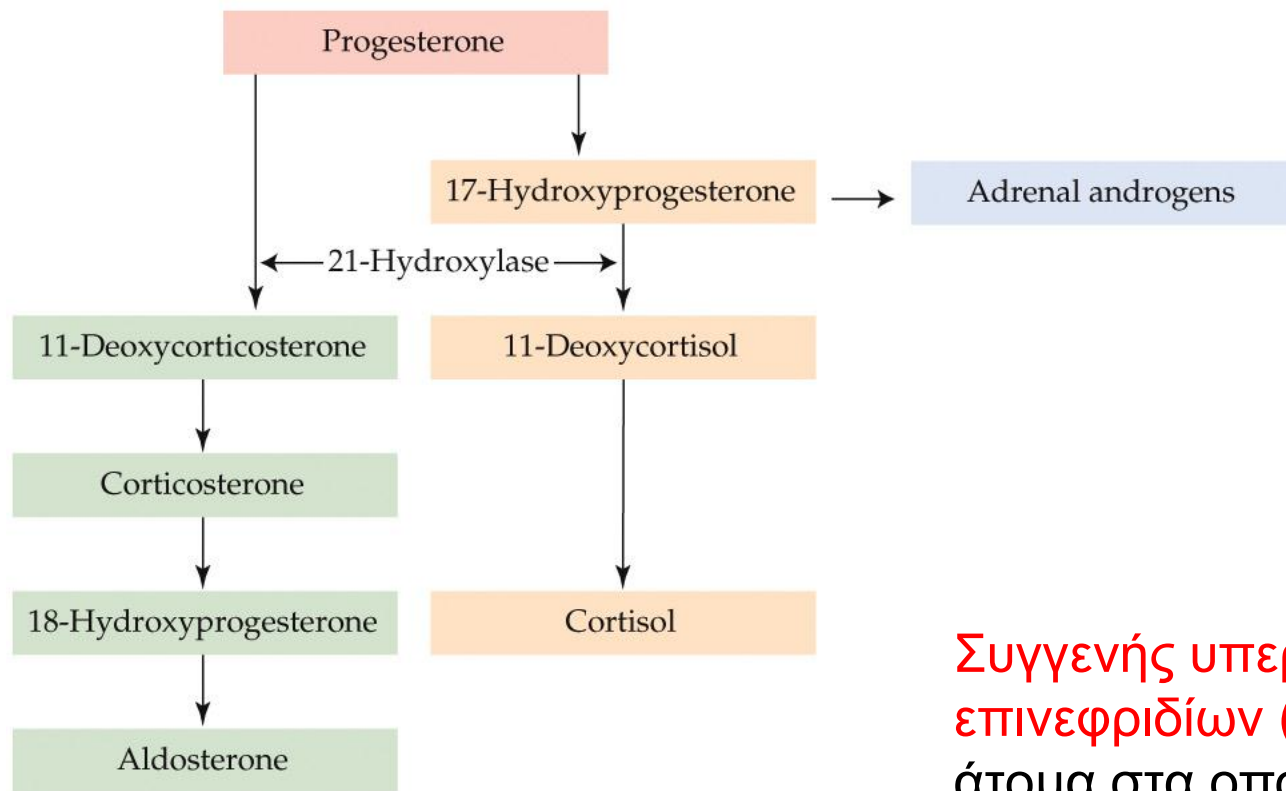




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ANDROGEN INSENSITIVITY SYNDROME (XY)



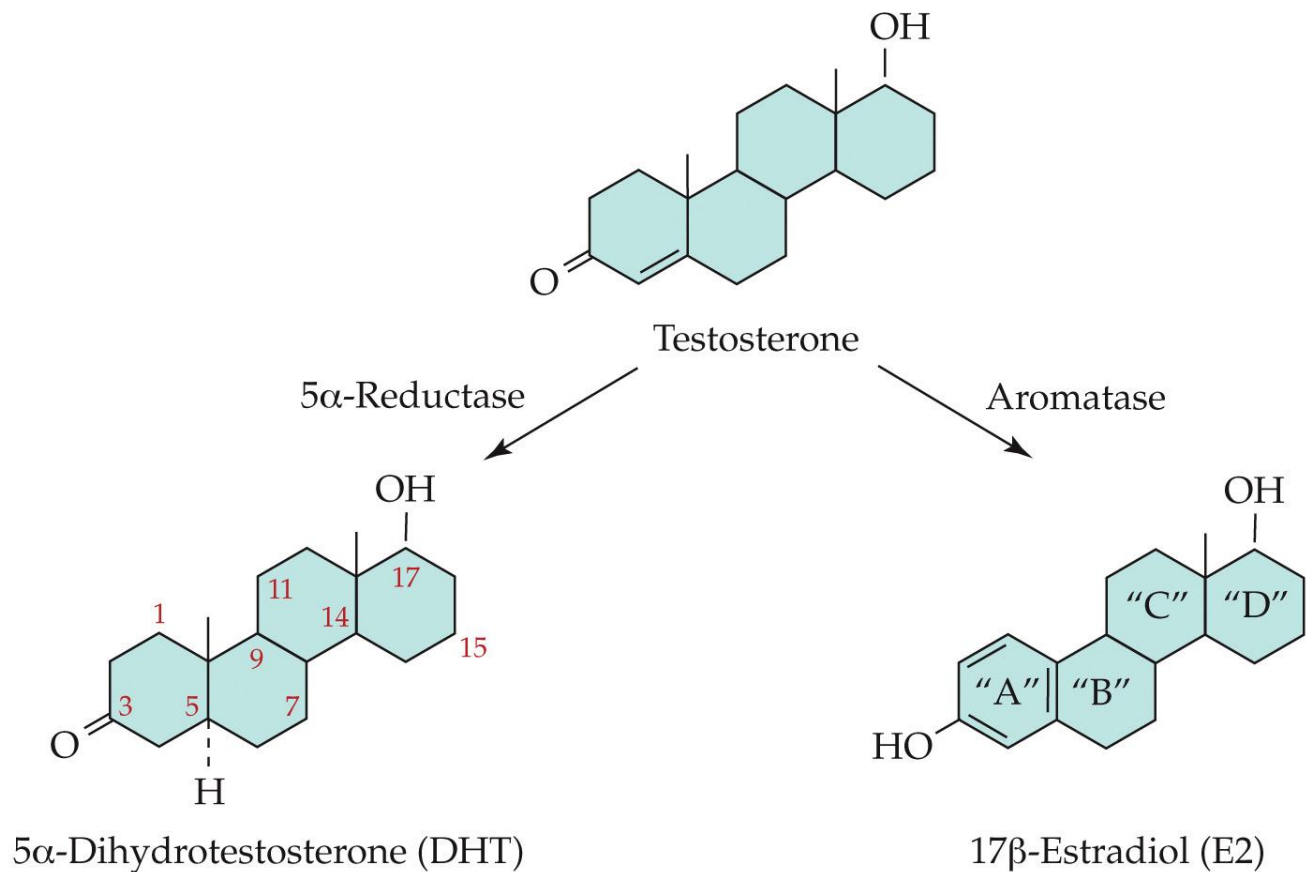


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Συγγενής υπερπλασία των επινεφριδίων (CAH): Θηλυκά άτομα στα οποία λείπει ένα ένζυμο (21-hydroxylase) και δεν μπορούν να μετατρέψουν την προγεστερόνη σε κορτιζόλη και αλδοστερόνη, παράγουν περισσότερα ανδρογόνα

Η θεωρία της οργάνωσης/ενεργοποίησης

Phoenix, Goy, Gerall, and Young (1959)

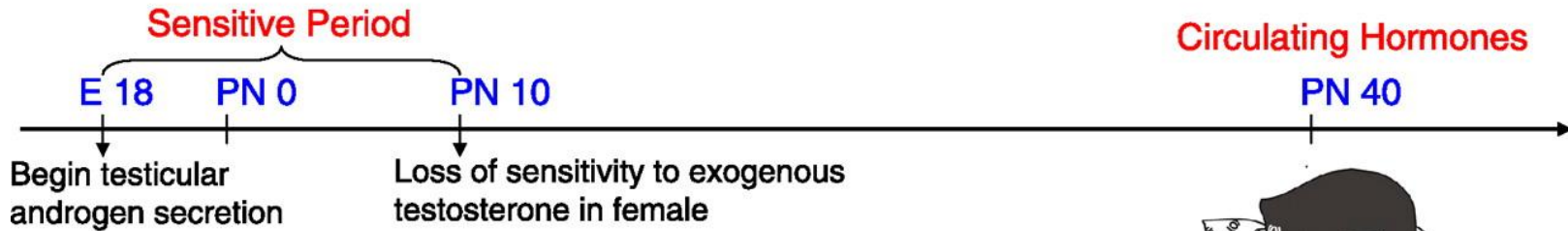


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α-φοιτοπρωτεΐνη: προσδένει τα οιστρογόνα της μητέρας, έτσι ώστε να μην εισέρχονται στο έμβρυο και επηρεάζουν τον εγκέφαλό του

Η θεωρία της οργάνωσης/ενεργοποίησης

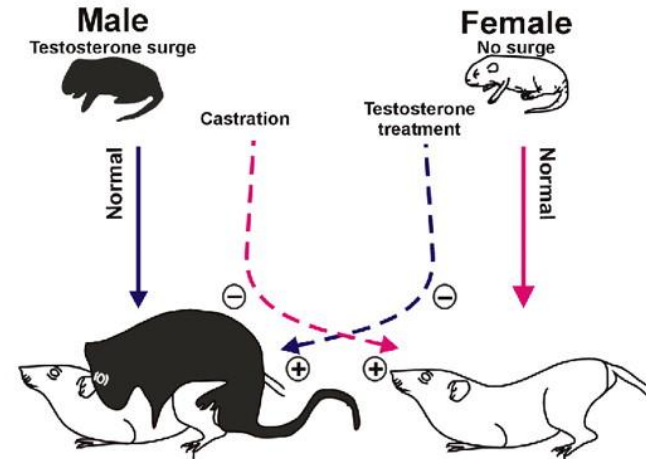
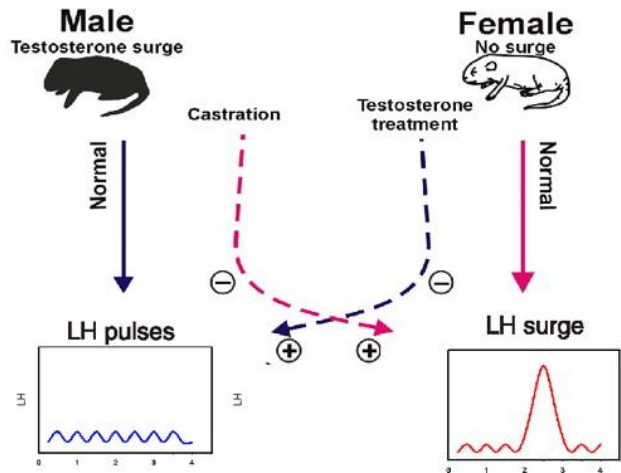
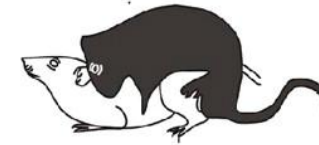
ORGANIZATION



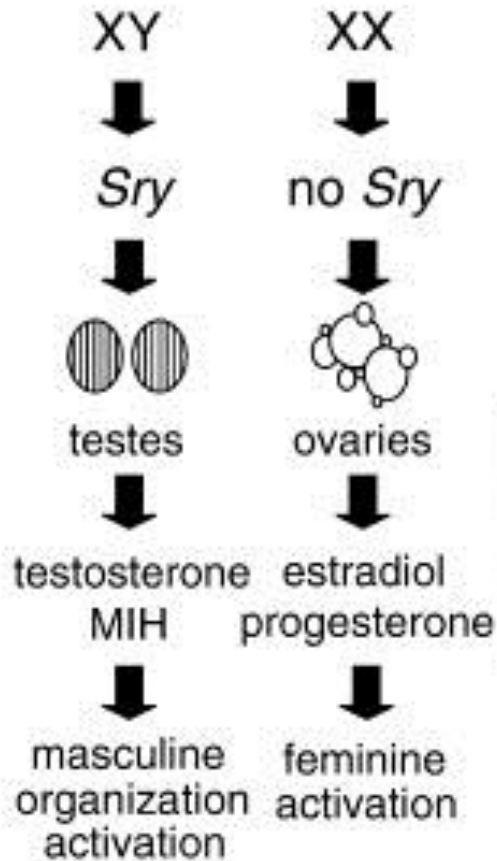
ACTIVATION

Circulating Hormones

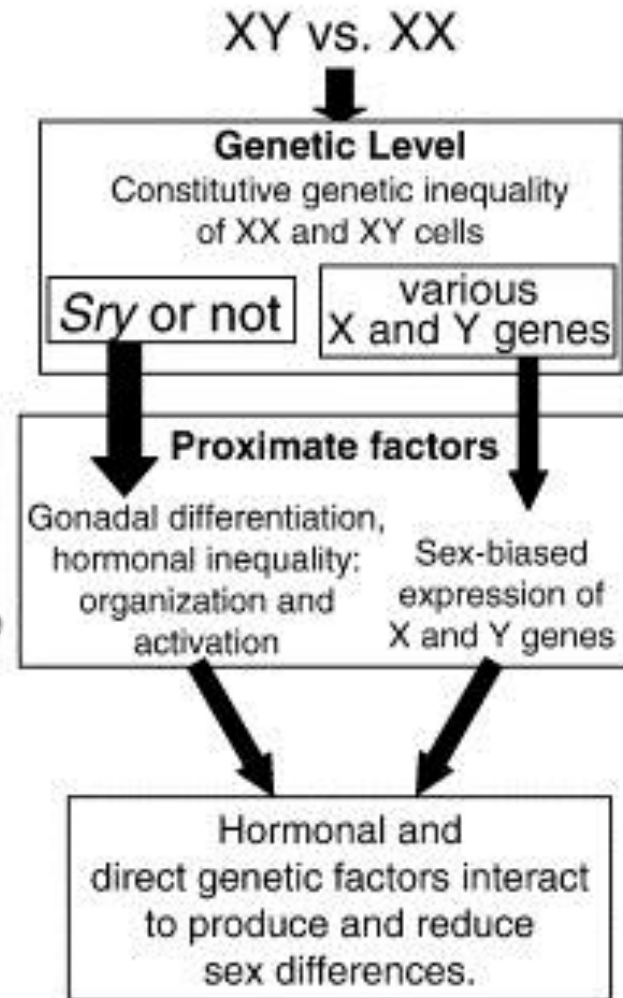
PN 40

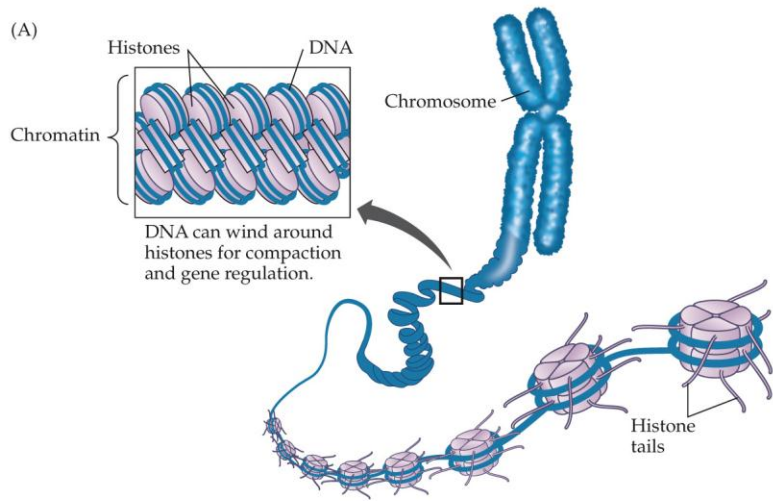


20th Century Model

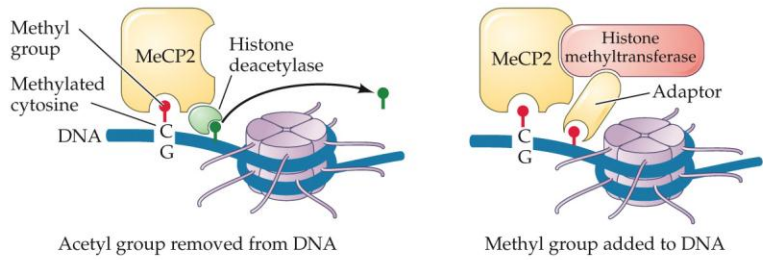


Unified Model





(B) DNA methylation

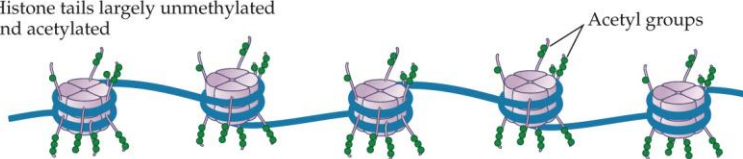


(C) Histone methylation/acetylation

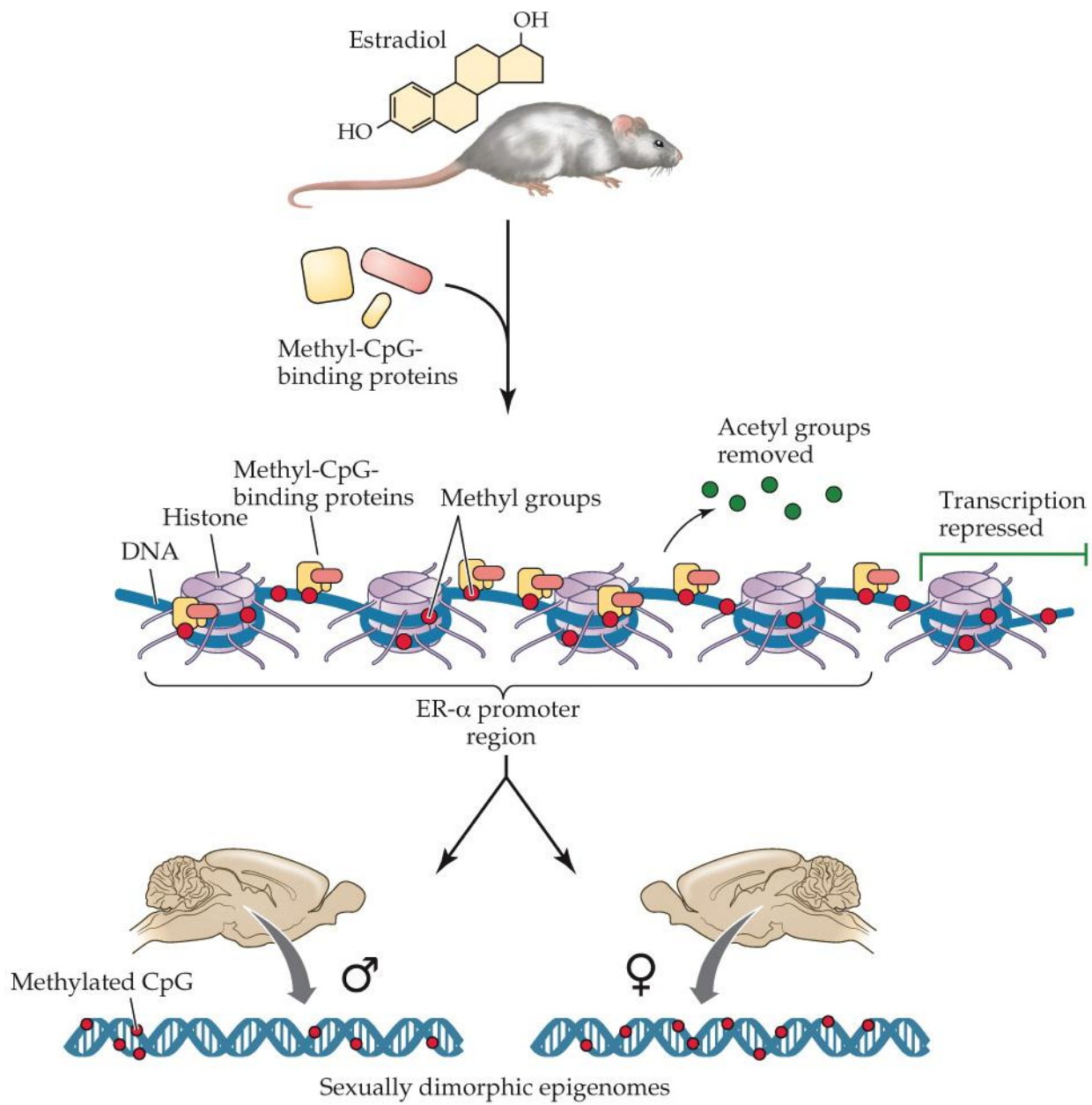
Inaccessible nucleosomes:
Histone tails largely methylated



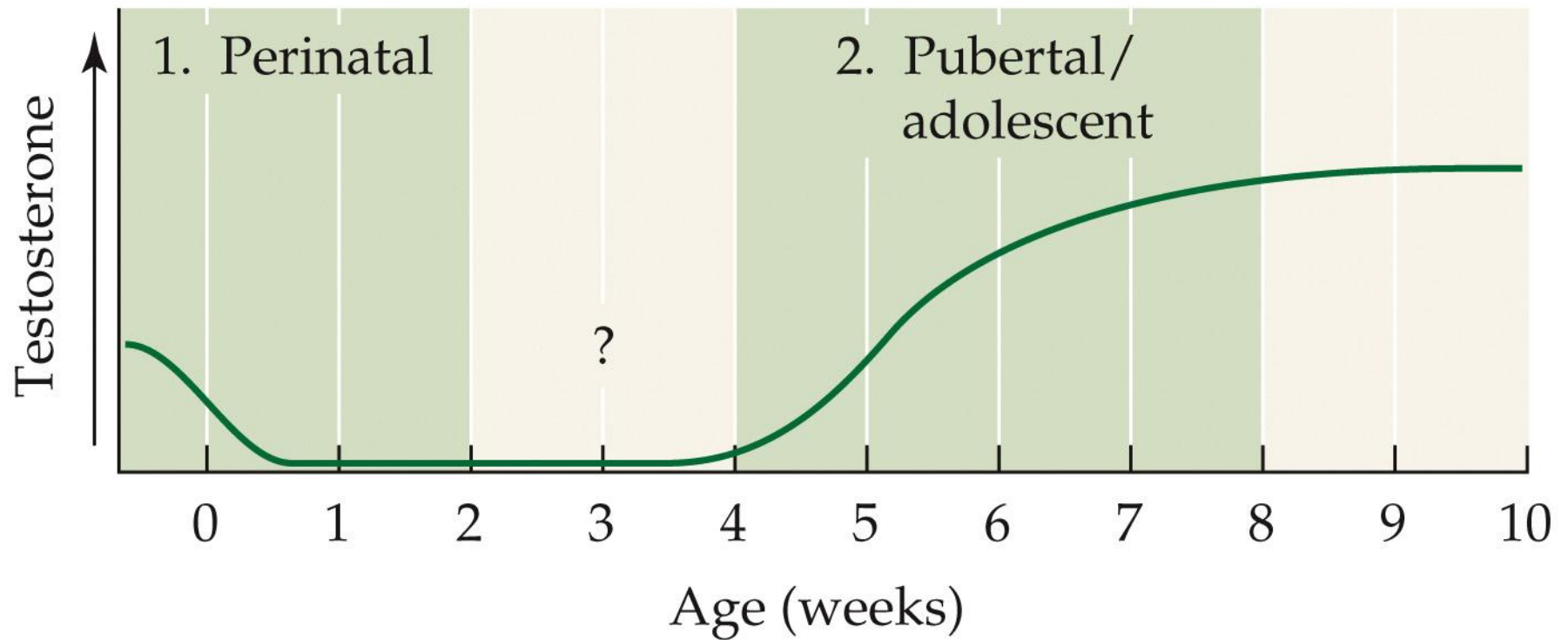
Accessible nucleosomes:
Histone tails largely unmethylated
and acetylated



Epigenetic sex differences



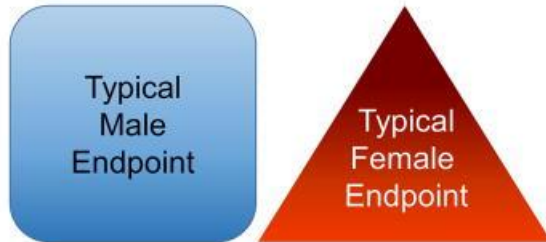
Two-stage model for organizational effects of steroids on behavior



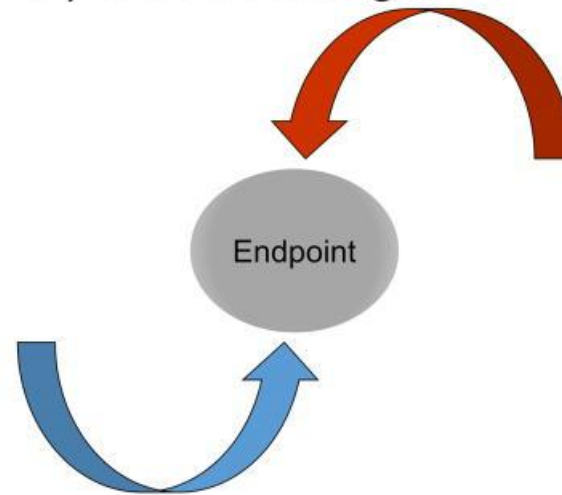
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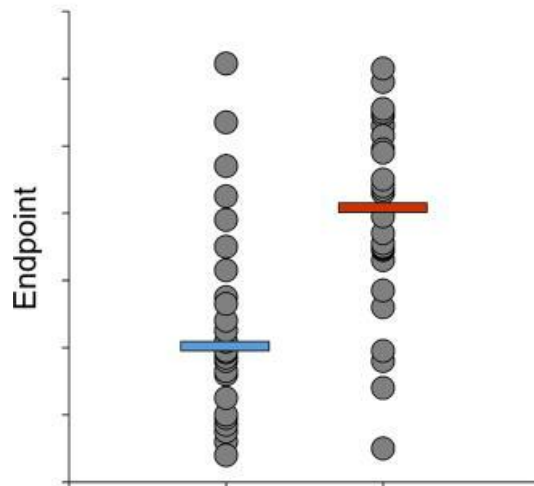
A) Sexual Dimorphism



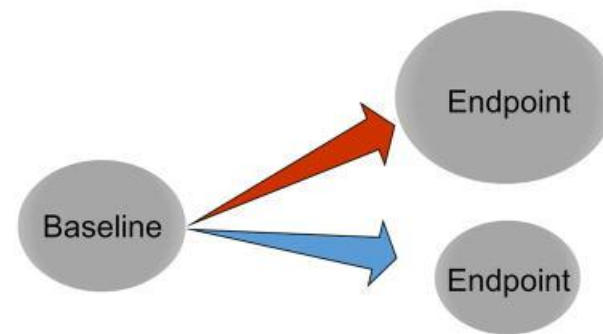
B) Sex Convergence

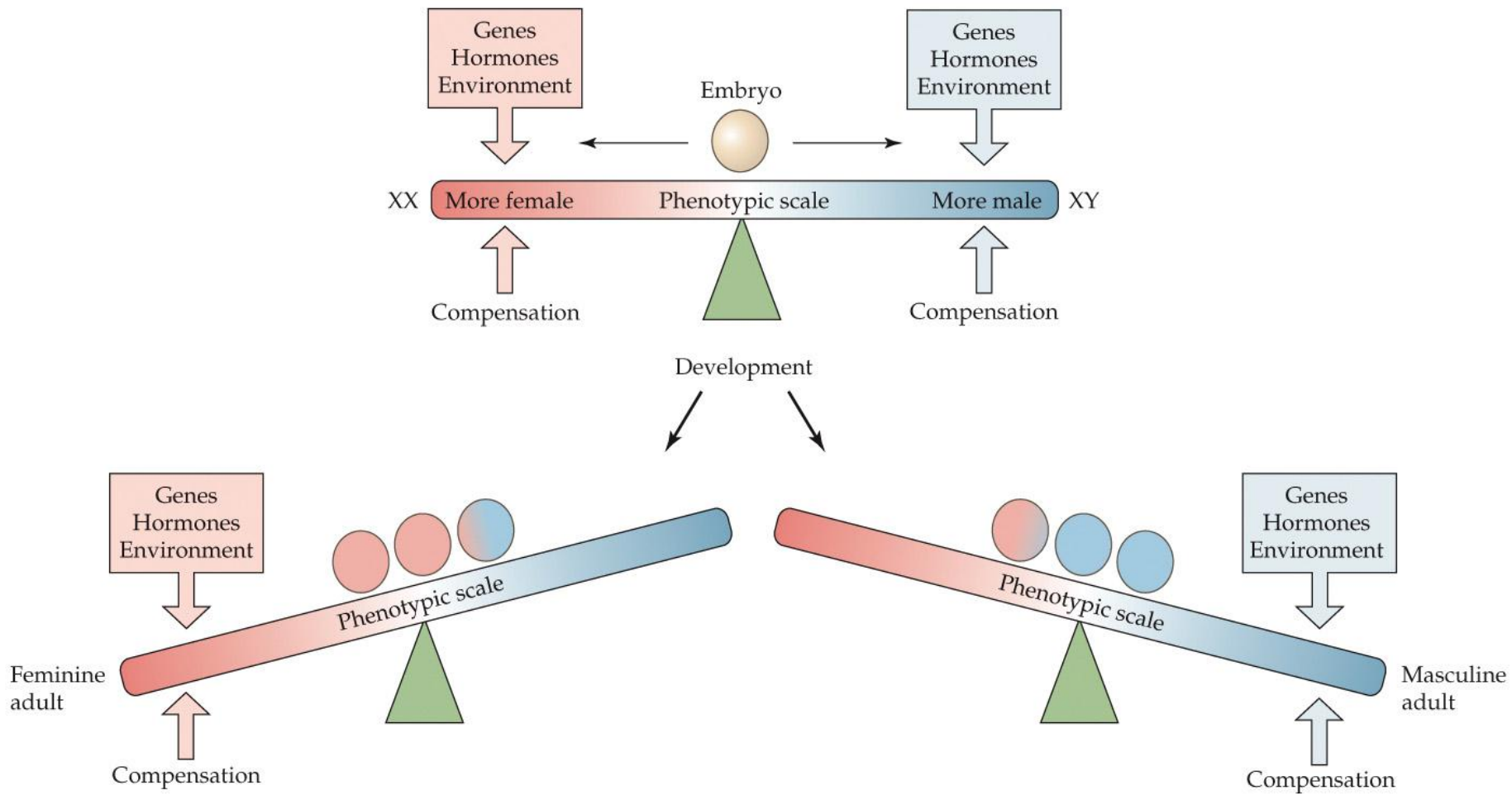


C) Sex Difference



D) Sex Divergence





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(A)



Male plumage



Female plumage

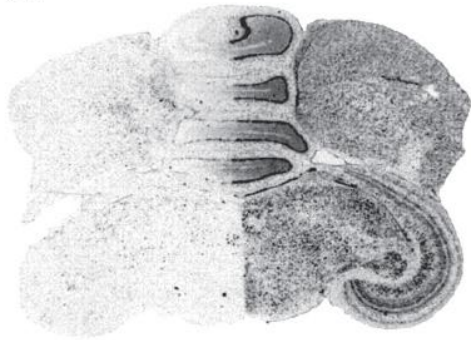


Πτηνά

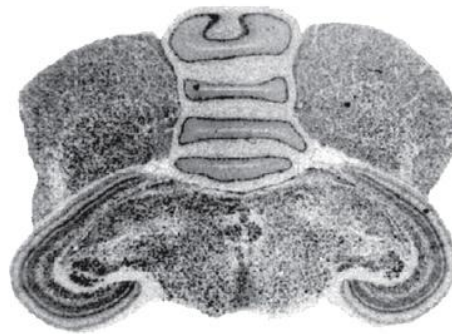
- Θηλυκά ZW χρωμοσώματα
- Αρσενικά ZZ χρωμοσώματα

Η συμπεριφορά του ήταν αρσενική!

(B)



ASW



PKCIZ

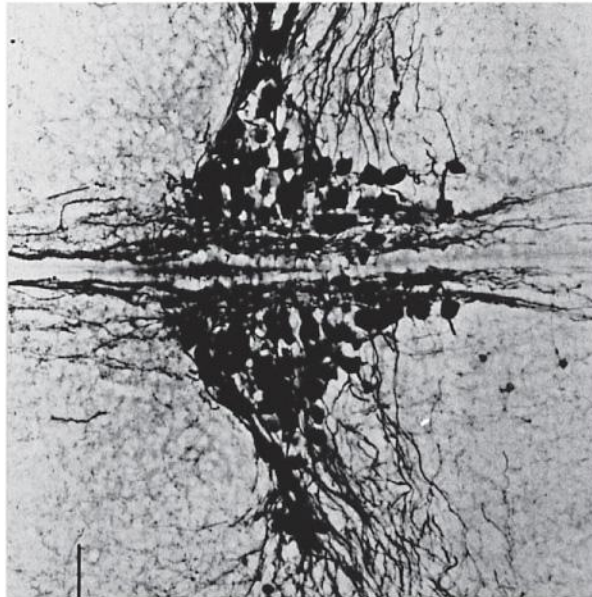
Sex differences in bullfrog brains mediate calling behavior

(A)

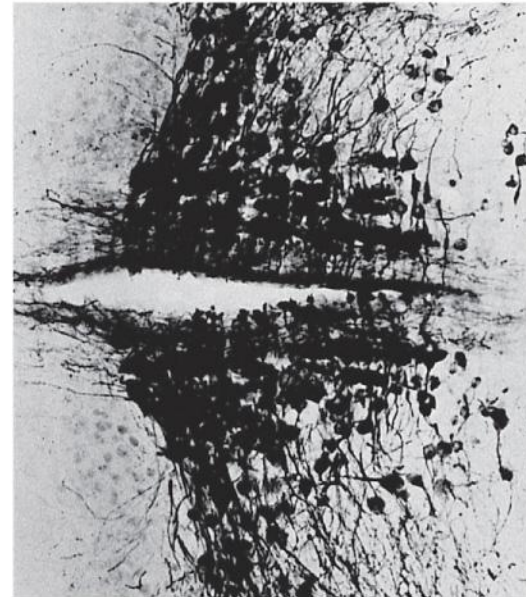


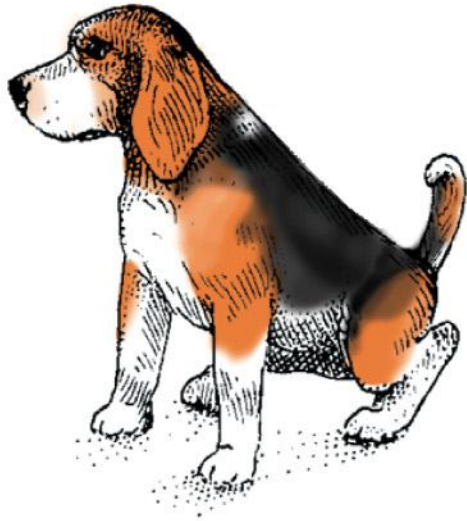
arginine vasotocin (AVT)

(B)

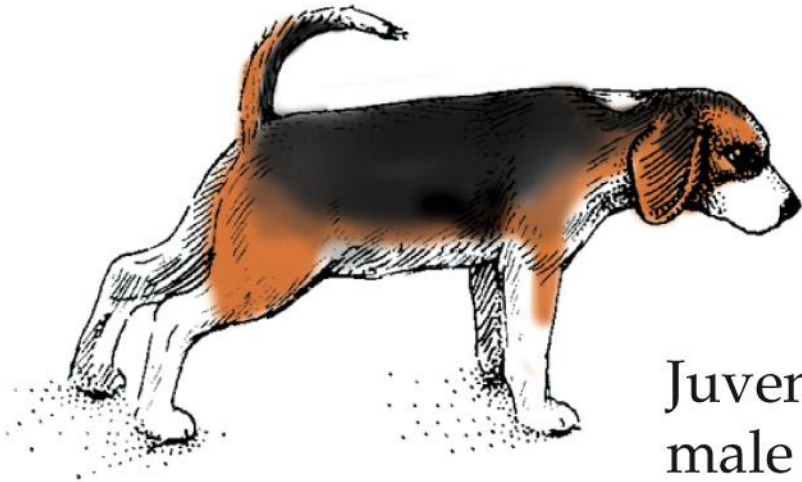


(C)

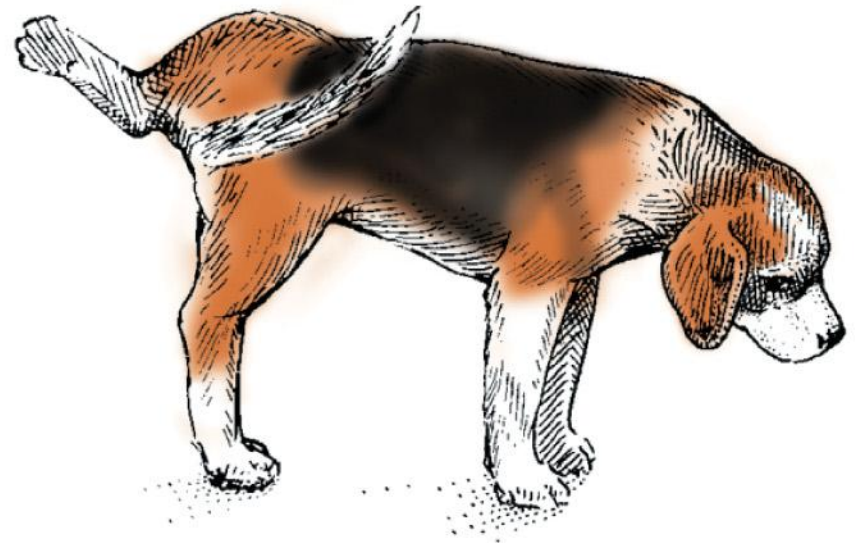




Female



Juvenile
male



Adult male

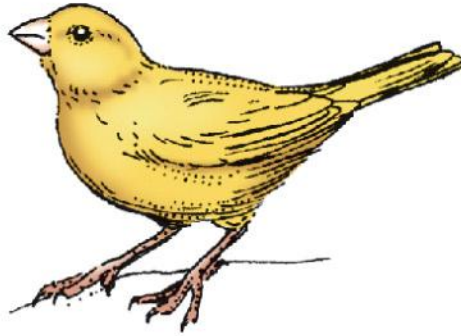
Singing in female songbirds

♀ Zebra finch



Never sing

♀ Canary



Sometimes sing

♀ Bay wren



Equal to male

TABLE 4.2 *Sexual dimorphism in songbird brains*

Brain structure	Species
Volumes of song system nuclei IMAN, DM, and nXIIIts^a	
IMAN volume ($\sigma > \text{♀}$)	Zebra finch, starling, dark-eyed junco
DM volume ($\sigma > \text{♀}$)	Zebra finch
nXIIIts volume ($\sigma > \text{♀}$)	Zebra finch, canary, red-winged blackbird
Number of neurons	
HVC and RA ($\sigma > \text{♀}$)	Zebra finch, bush shrike
RA neurons (σ slightly $> \text{♀}$)	White-browed robin chat, bay wren, buff-breasted wren
IMAN ($\sigma > \text{♀}$)	Zebra finch
Size of neurons	
Neuronal somata in HVC ($\sigma > \text{♀}$)	Zebra finch, Carolina wren, bush shrike
Neuronal somata in RA ($\sigma > \text{♀}$)	Zebra finch, Carolina wren
Neuronal somata in RA ($\sigma = \text{♀}$)	White-browed robin chat, bay wren, buff-breasted wren
Neuronal somata in IMAN ($\sigma > \text{♀}$)	Zebra finch
Dendritic fields in some HVC neurons ($\sigma > \text{♀}$)	Canary
Dendritic fields in RA ($\sigma > \text{♀}$)	Zebra finch and canary
Dendritic field sizes in RA ($\sigma = \text{♀}$)	Buff-breasted wren
Dendritic fields in IMAN ($\sigma > \text{♀}$)	Zebra finch

Source: Balthazart and Adkins-Regan, 2002.

^a IMAN = lateral magnocellular nucleus of the anterior nidopallium; nXIIIts = tracheosyringeal division of the nucleus of the hypoglossal nerve
HVC = high vocal center; RA = robust nucleus of the archistriatum, aka robustus archistriatum; area X = a forebrain nucleus located in the parolfactory lobe

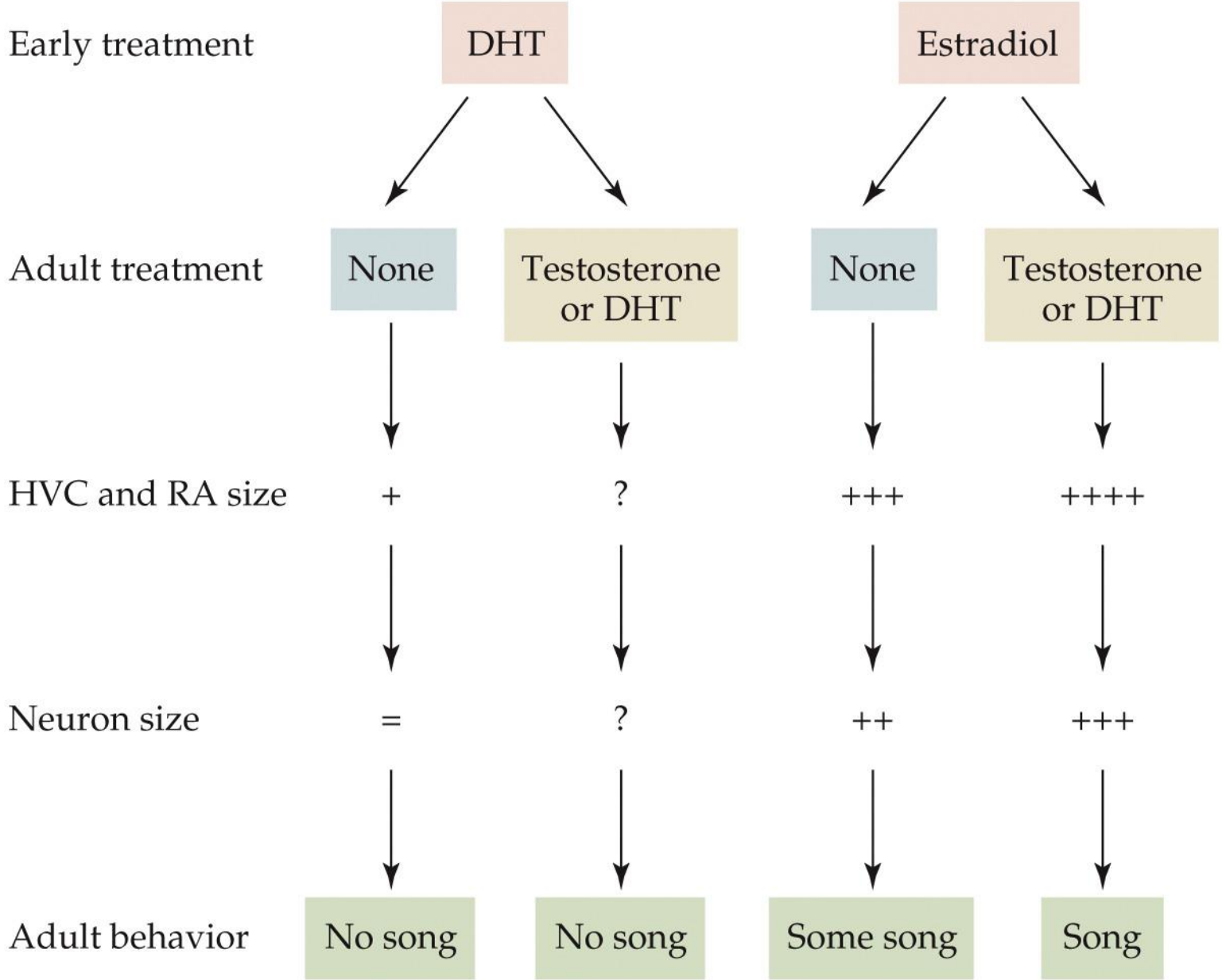
TABLE 4.2 *Sexual dimorphism in songbird brains*

Brain structure	Species
Number of neurons with sex steroid receptors	
Cells with androgen receptors in HVC and IMAN ($\sigma^{\circ} > \text{♀}$)	Zebra finch
Cells with androgen and estrogen receptors in HVC ($\sigma^{\circ} > \text{♀}$)	Canary
Cells with androgen receptors in HVC and IMAN ($\sigma^{\circ} = \text{♀}$)	Bay wren, rufous-and-white wren
Connectivity	
HVC neurons projecting to RA ($\sigma^{\circ} > \text{♀}$)	Zebra finch
HVC neurons projecting to area X ($\sigma^{\circ} > \text{♀}$)	Zebra finch
IMAN neurons projecting to RA ($\sigma^{\circ} > \text{♀}$)	Zebra finch
Neurochemistry	
RA activity induced by GABA _A receptor antagonist ($\sigma^{\circ} = \text{♀}$)	Zebra finch
Ascending catecholaminergic and enkephalinergic projections to area X ($\sigma^{\circ} > \text{♀}$)	Zebra finch
Acetylcholinesterase staining in area X ($\sigma^{\circ} > \text{♀}$)	Zebra finch

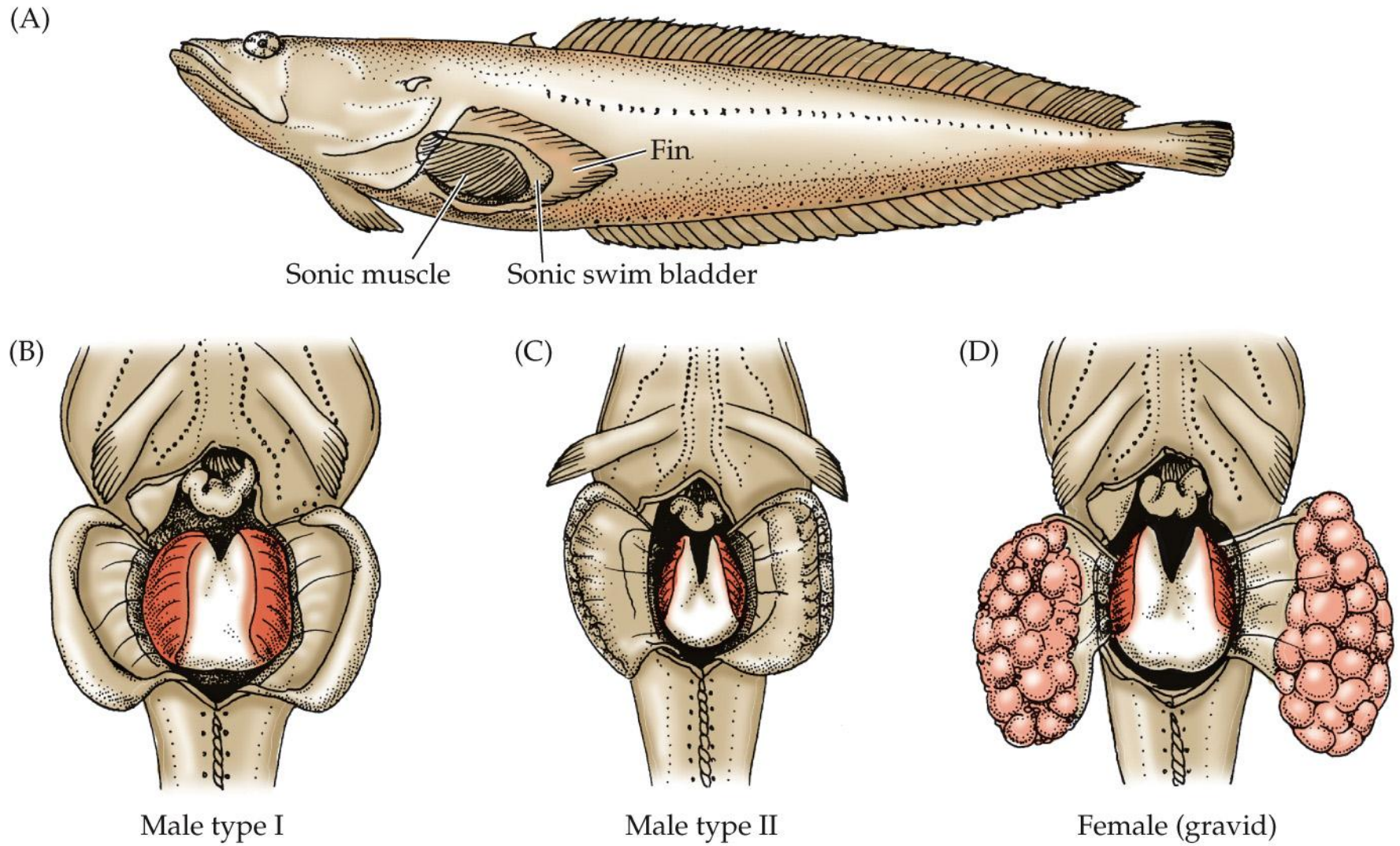
Source: Balthazart and Adkins-Regan, 2002.

^a IMAN = lateral magnocellular nucleus of the anterior nidopallium; nXIIts = tracheosyringeal division of the nucleus of the hypoglossal nerve
HVC = high vocal center; RA = robust nucleus of the archistriatum, aka robustus archistriatum; area X = a forebrain nucleus located in the parolfactory lobe

Singing in zebra finches



The sonic organs are used by type I male midshipman fish to attract females to their nests



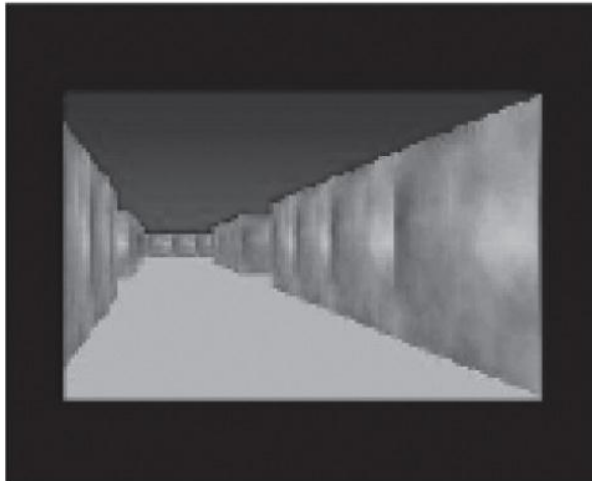
Cichlid fish change cell size in response to social conditions



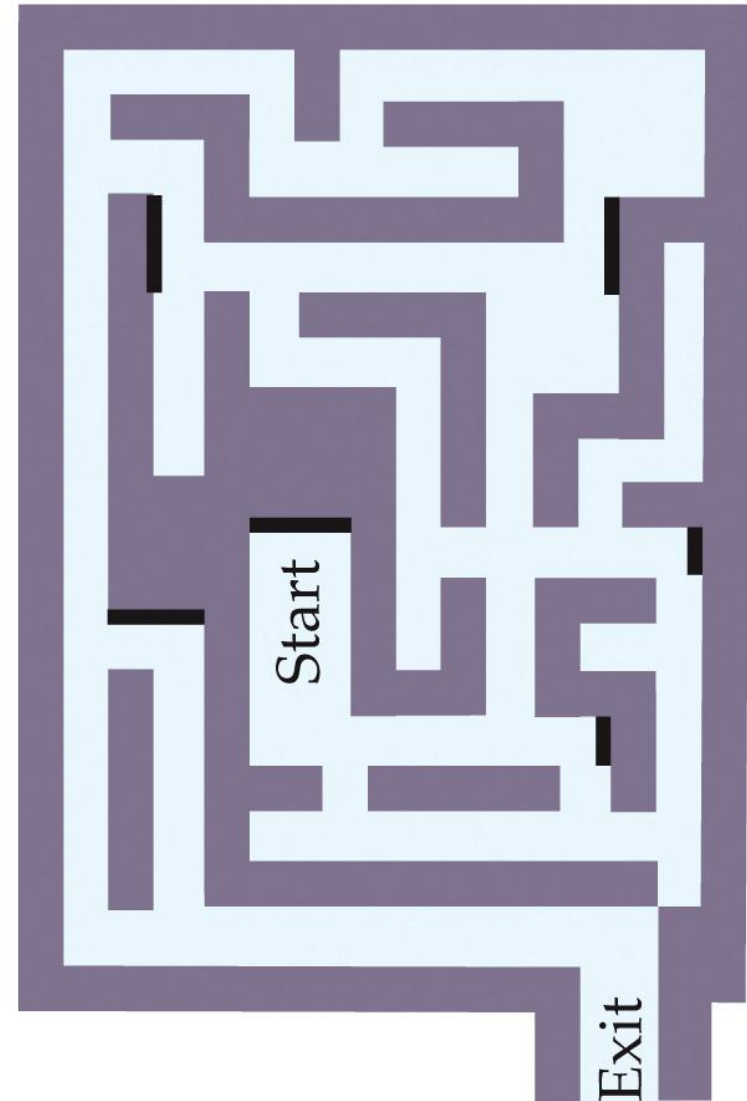
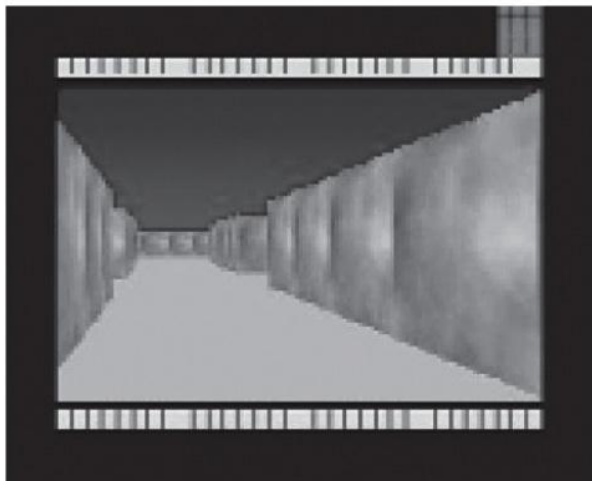
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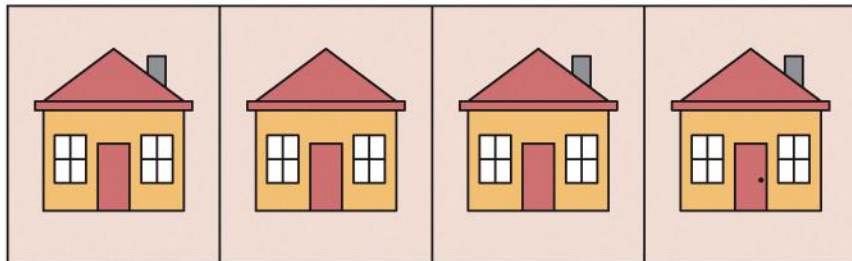
Active



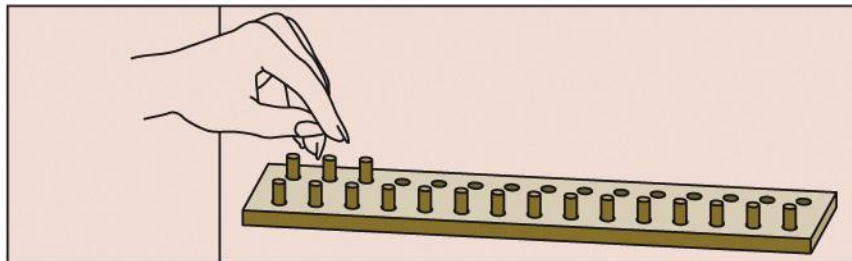
Control



(A)



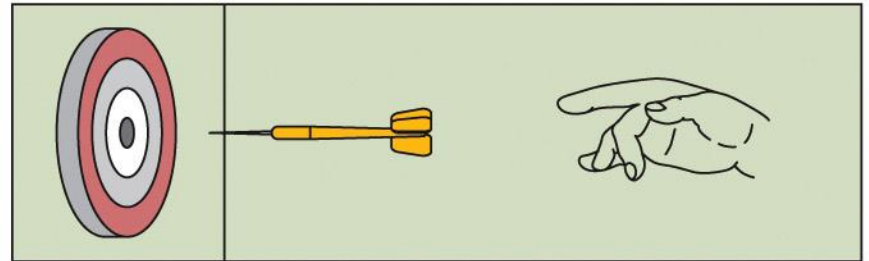
(B)



(C)

77	$14 \times 3 - 17 + 52$
43	$2(15 + 3) + 12 - \frac{15}{3}$

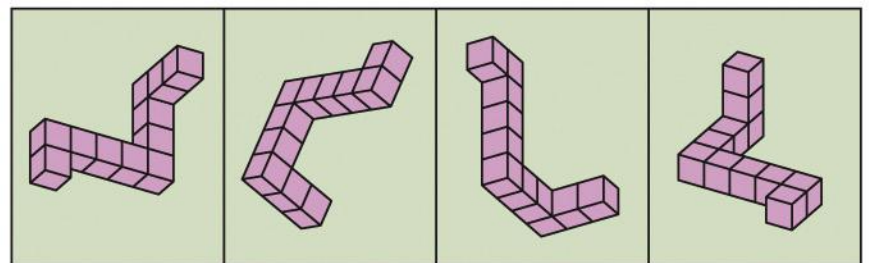
(D)



(E)

1,100	If only 60% of seedlings will survive, how many must be planted to obtain 660 trees?
-------	--

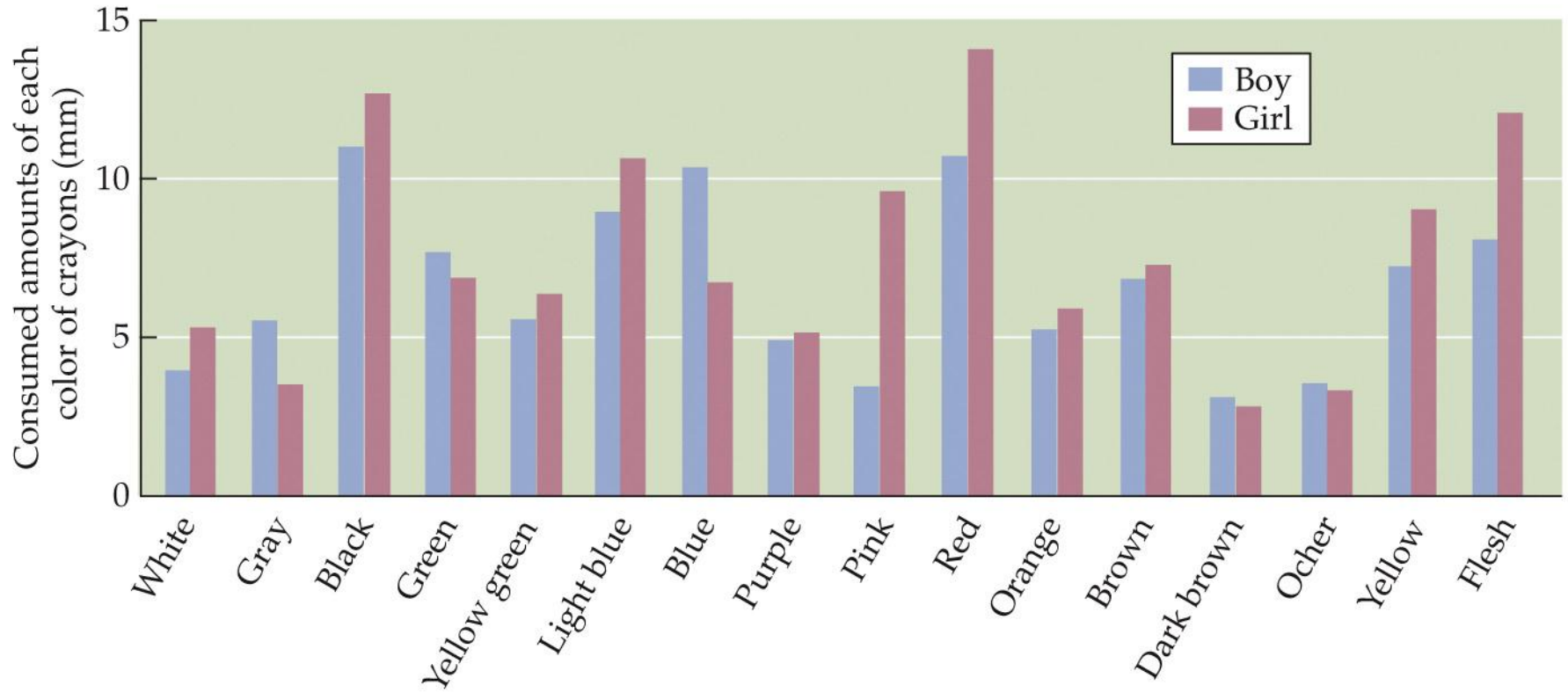
(F)



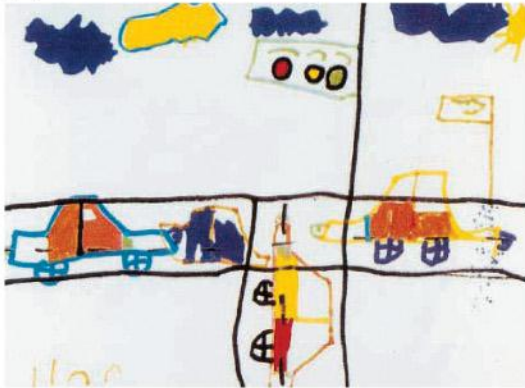
Motifs in Children's Drawings

Motif	Boys (%)	Girls (%)
Moving objects (vehicle, train, aircraft, etc.)	92.4	04.6
Person	26.5	96.6
Flower	07.2	57.0
Butterfly	03.2	23.4
Sun	50.8	76.5
Mountain	14.5	03.1
House and building	17.7	33.5
Tree	09.6	23.4
Ground	42.7	57.8
Cloud	25.0	32.8
Sky	41.9	49.2

(A)



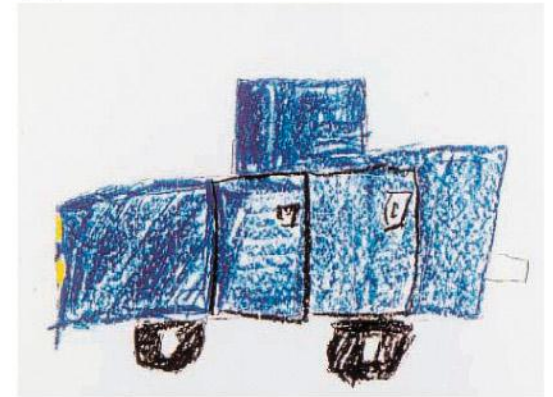
(B)



(D)



(F)



(C)



(E)




(G)



The title for this Special Section is **Meta-analysis and Individual Participant Data Synthesis in Child Development**, edited by Glenn I. Roisman and Marinus H. van IJzendoorn

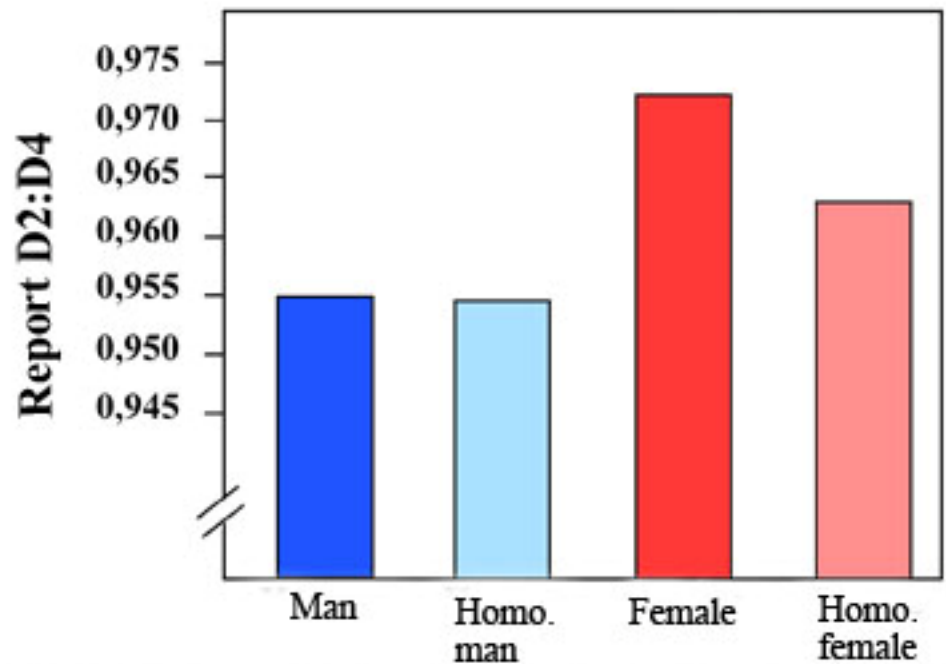
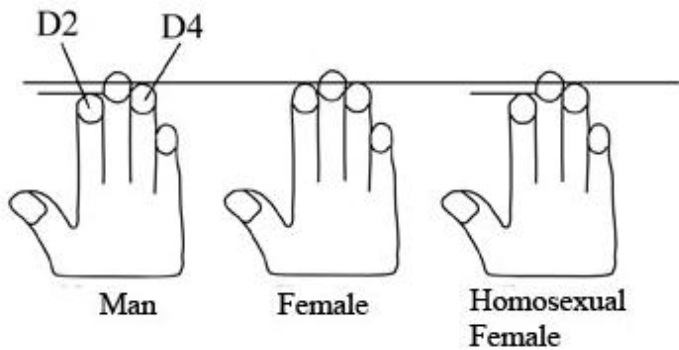
The Development of Children's Gender-Science Stereotypes: A Meta-analysis of 5 Decades of U.S. Draw-A-Scientist Studies

David I. Miller , Kyle M. Nolla, Alice H. Eagly, and David H. Uttal
Northwestern University

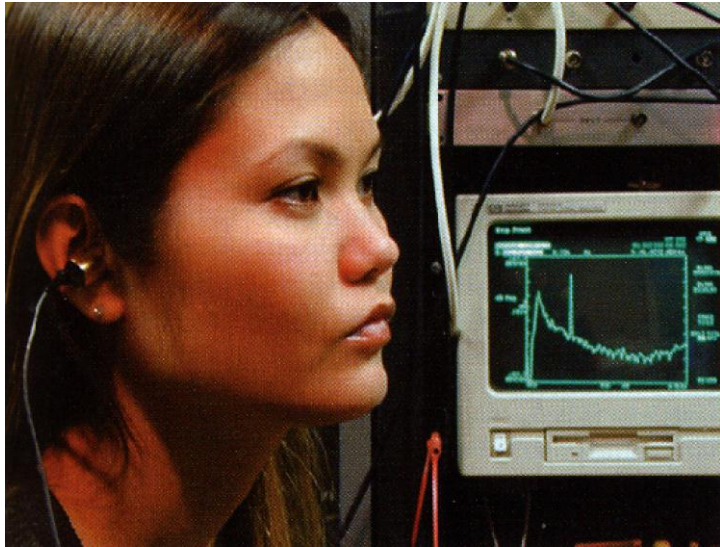
This meta-analysis, spanning 5 decades of Draw-A-Scientist studies, examined U.S. children's gender-science stereotypes linking science with men. These stereotypes should have weakened over time because women's representation in science has risen substantially in the United States, and mass media increasingly depict female scientists. Based on 78 studies ($N = 20,860$; grades K-12), children's drawings of scientists depicted female scientists more often in later decades, but less often among older children. Children's depictions of scientists therefore have become more gender diverse over time, but children still associate science with men as they grow older. These results may reflect that children observe more male than female scientists in their environments, even though women's representation in science has increased over time.



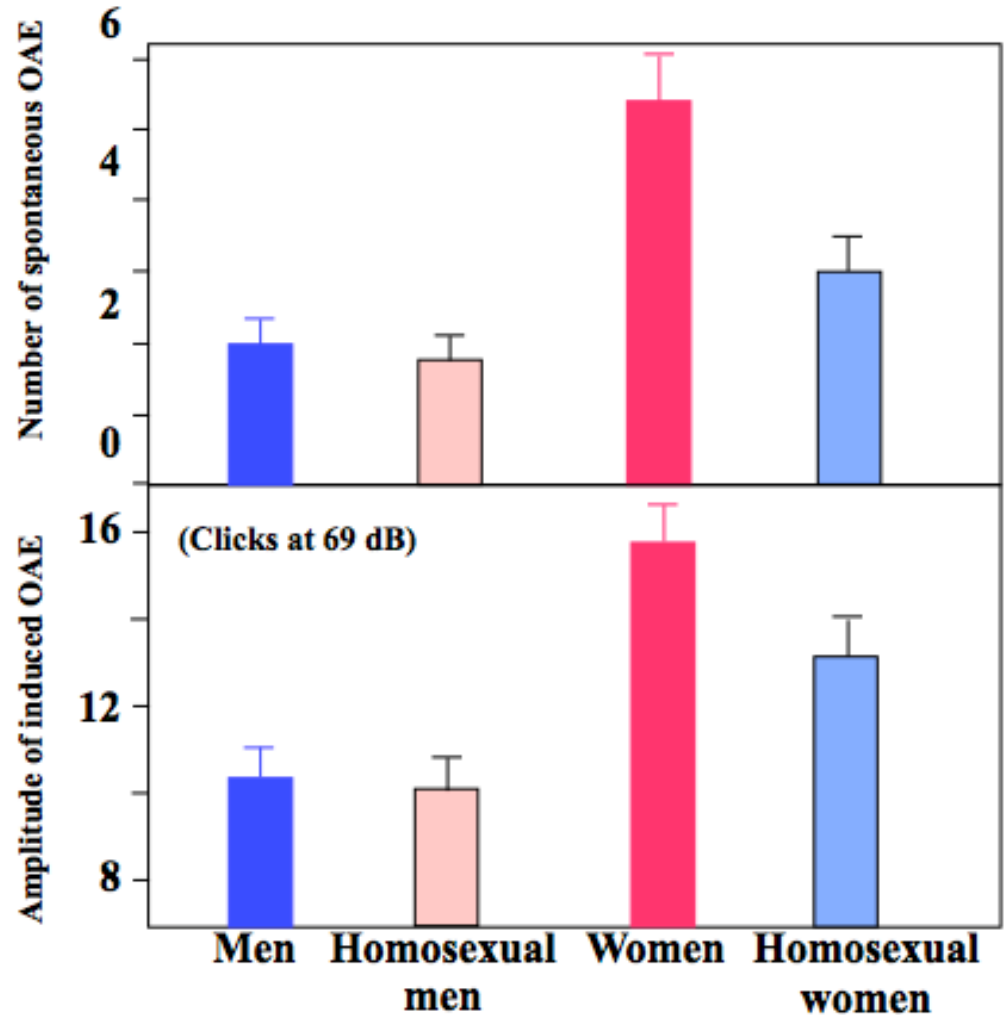
The 2D:4D ratio as a measure of exposure to androgens



Otoacoustic emissions



Dennis McFadden
UT Austin



Average sex differences in behavior often reflect significant overlap between the sexes

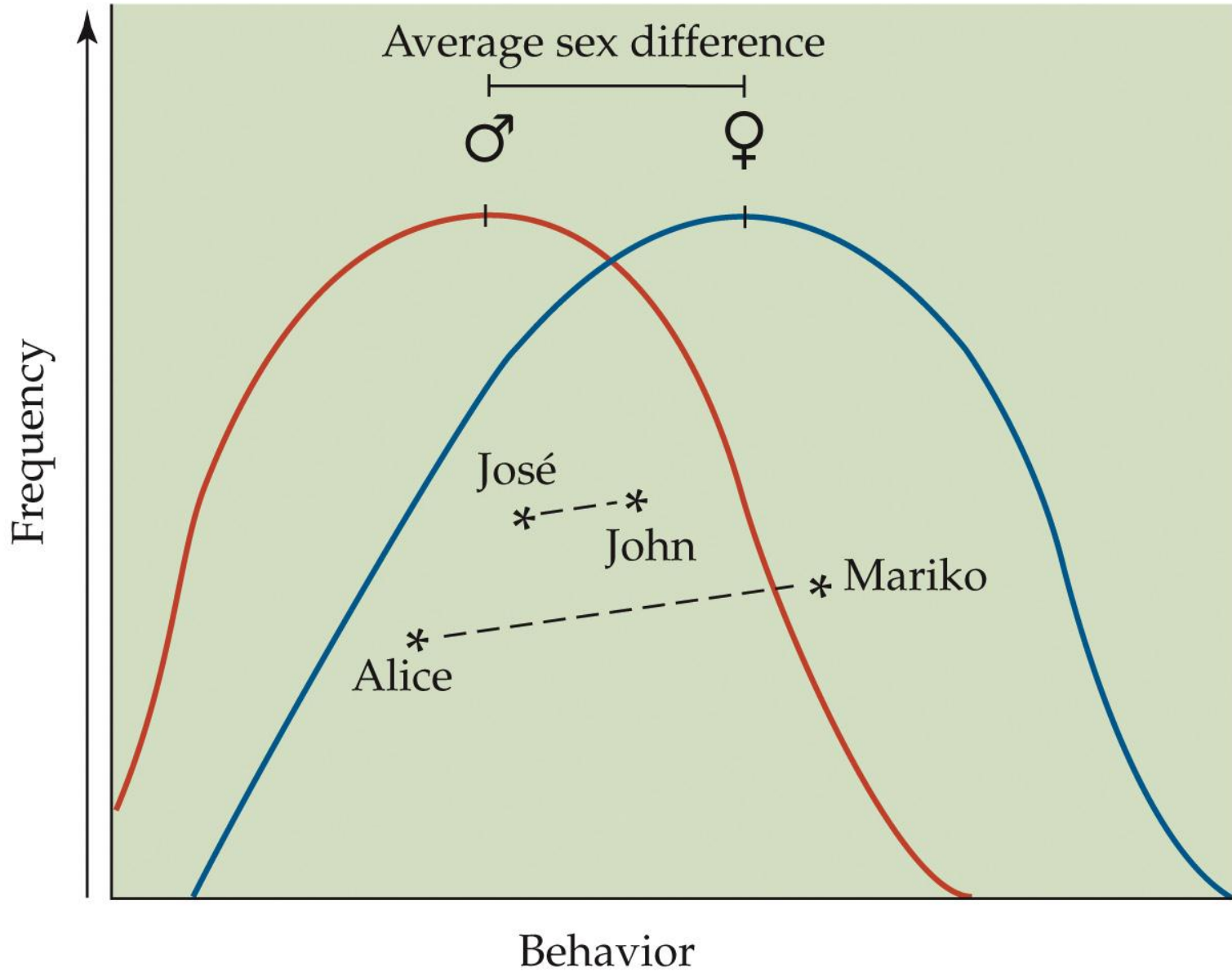


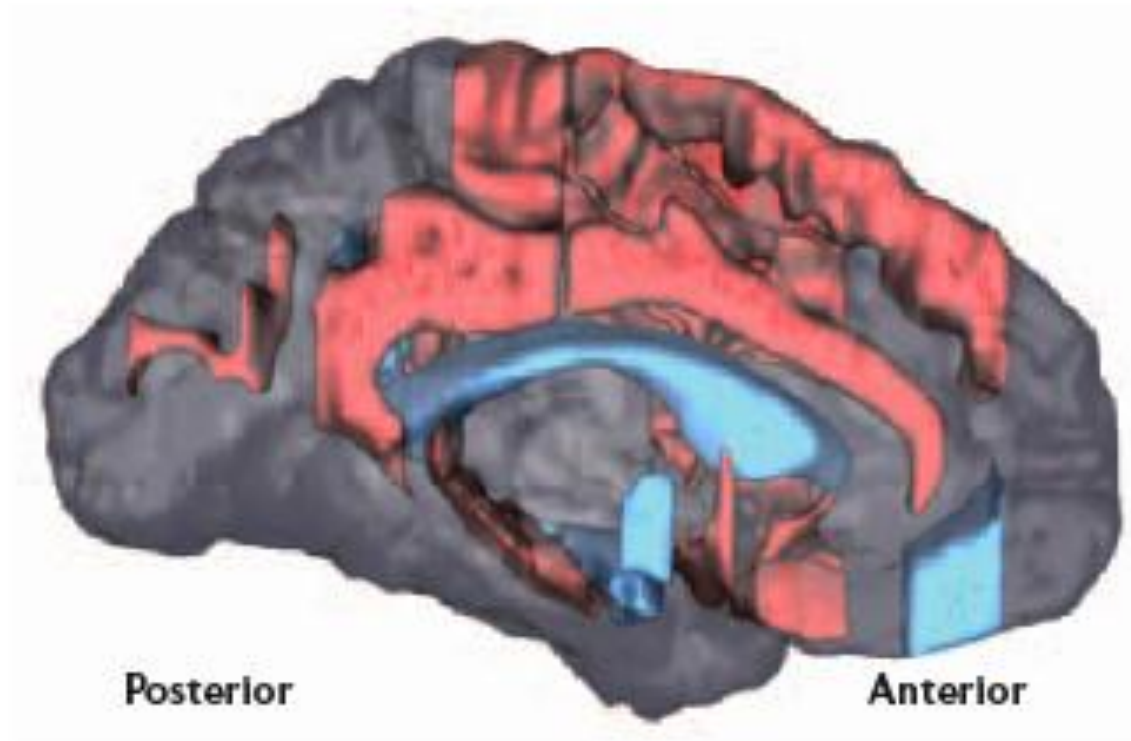
TABLE 4.4 *Effect size for behavioral sex differences in humans*

Behavior	Approximate effect size^a
Aggression	Moderate ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)
Rough-and-tumble play	Moderate–large ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)
Childhood activity levels	Moderate–large ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)
Overall verbal abilities	Negligible–small ($\sigma^{\text{♂}} < \sigma^{\text{♀}}$)
Speech production	Small ($\sigma^{\text{♂}} < \sigma^{\text{♀}}$)
Verbal fluency	Moderate ($\sigma^{\text{♂}} < \sigma^{\text{♀}}$)
Perceptual speed	Moderate ($\sigma^{\text{♂}} < \sigma^{\text{♀}}$)
3-D visual rotation	Large ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)
2-D visual rotation	Small ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)
Spatial perception	Small–moderate ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)
Overall quantitative abilities	Small–moderate ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)
Quantitative problem solving	Small–moderate ($\sigma^{\text{♂}} > \sigma^{\text{♀}}$)

Sources: After Collaer and Hines, 1988; data from J. Cohen, 1977; Forger, 1998; Kimura, 1992.

^aEffect sizes of ≥ 0.8 standard deviations are considered large, of ~ 0.5 standard deviations, moderate; of ~ 0.2 , small; and of < 0.2 , negligible.

Διαφορές του φύλου στη δομή και λειτουργία του εγκεφάλου





-  Περιοχές του εγκεφάλου που φυσιολογικά είναι μεγαλύτερες στα θηλυκά
-  Περιοχές του εγκεφάλου που φυσιολογικά είναι μεγαλύτερες στα αρσενικά

TABLE 4.1 *Structural sex differences in the central nervous system of humans*

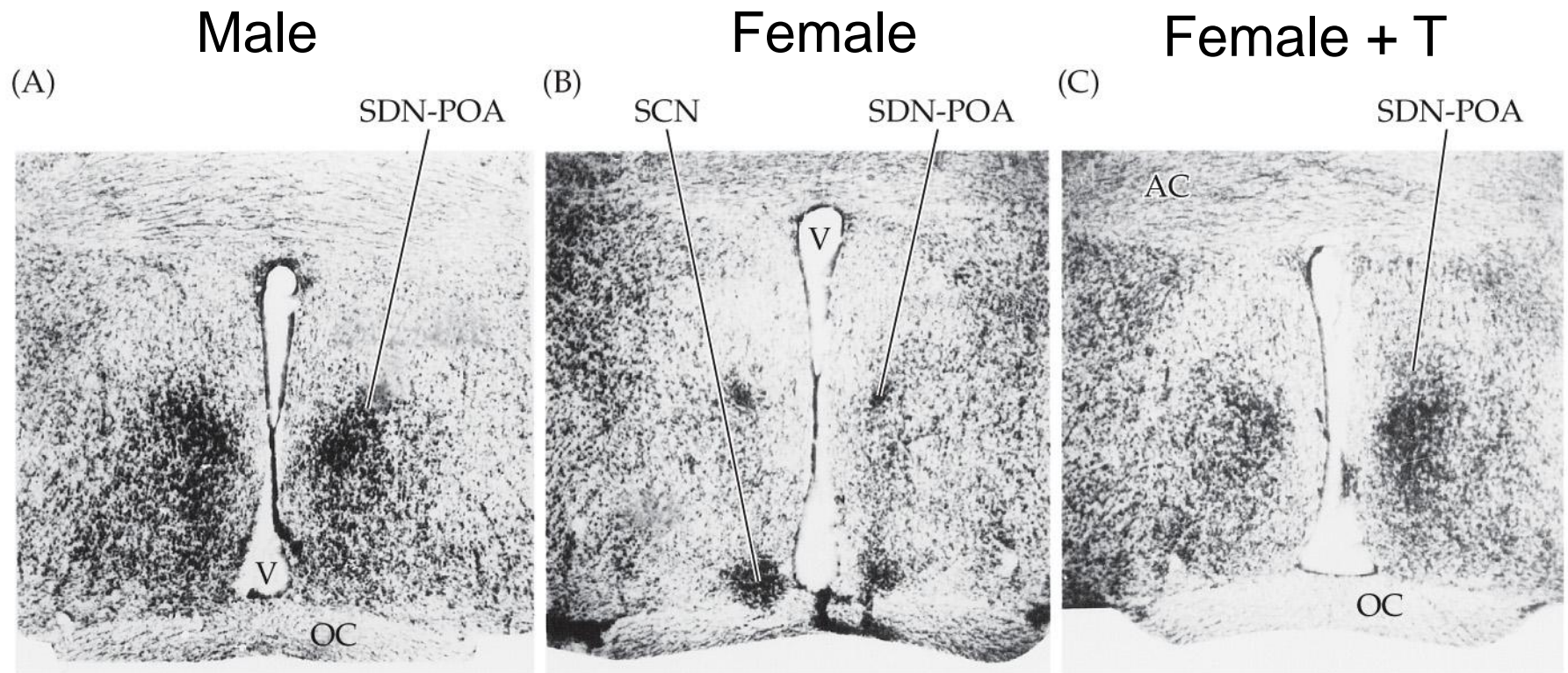
Brain region	Difference
Hypothalamus	
SDN-POA	♂ > ♀
Interstitial nucleus of the anterior hypothalamus-3 (INAH-3)	♂ > ♀
Bed nucleus of the stria terminalis (BNST)	♂ > ♀
Suprachiasmatic nuclei (SCN)	♂ < ♀ ^a
Spinal cord	
Onuf's nucleus (no. of motor neurons)	♂ > ♀
Structures associated with language	
Planum temporale	♂ < ♀ ^b
Dorsolateral prefrontal cortex	♂ < ♀
Superior temporal gyrus	♂ < ♀
Structures connecting the hemispheres	
Corpus callosum (posterior portion)	♂ < ♀ ^c
Anterior commissure	♂ < ♀
Massa intermedia of thalamus	♂ < ♀

Source: After Forger, 1998.

^aMore elongated in ♀.

^bLeft and right more symmetrical in size in ♀.

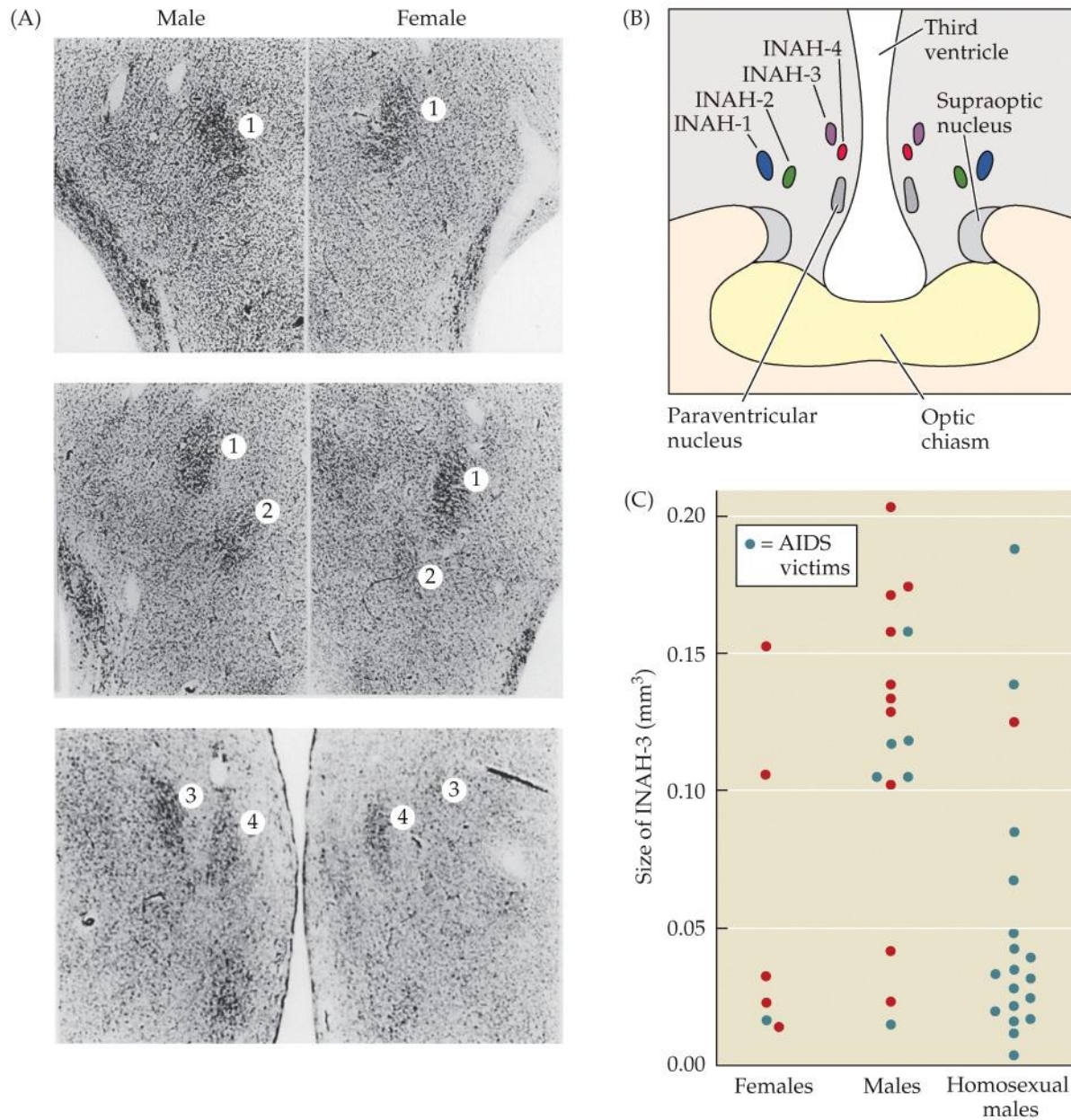
^cMore bulbous in ♀.



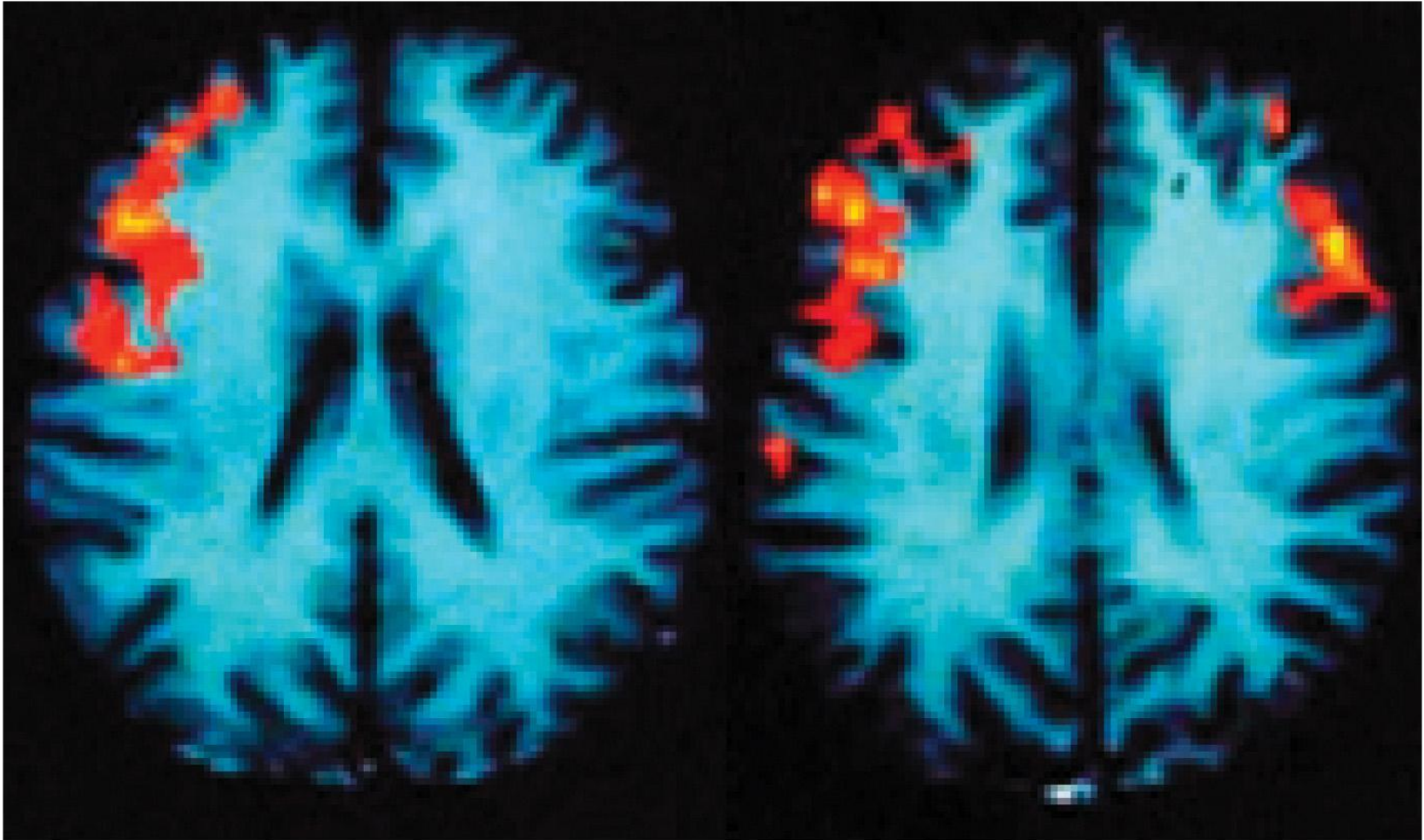
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 4.5

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The interstitial nuclei of the anterior hypothalamus



Οι άνδρες και οι γυναίκες χρησιμοποιούν διαφορετικά μέρη του εγκεφάλου για επίλυση προβλημάτων



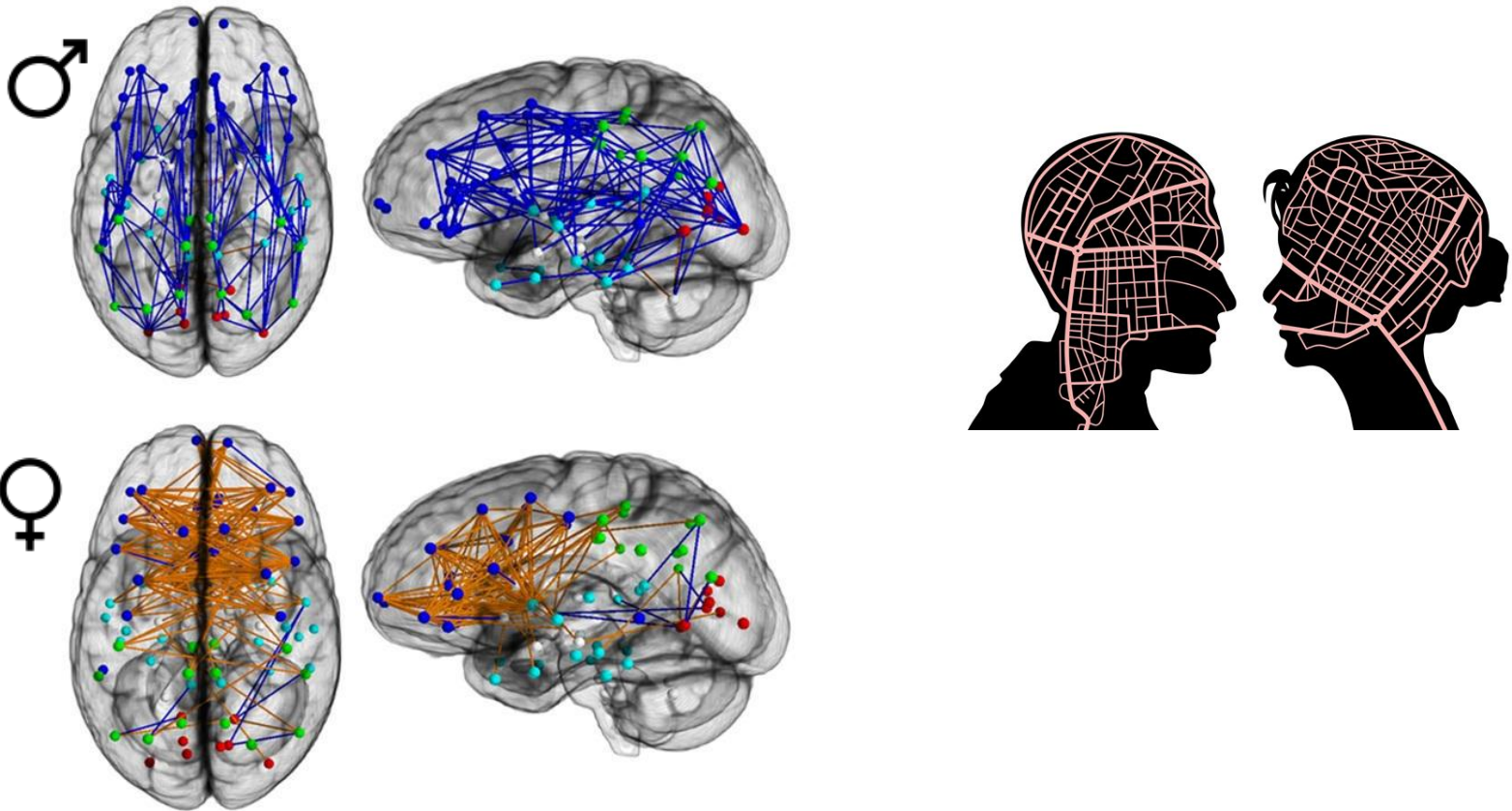
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 4.25

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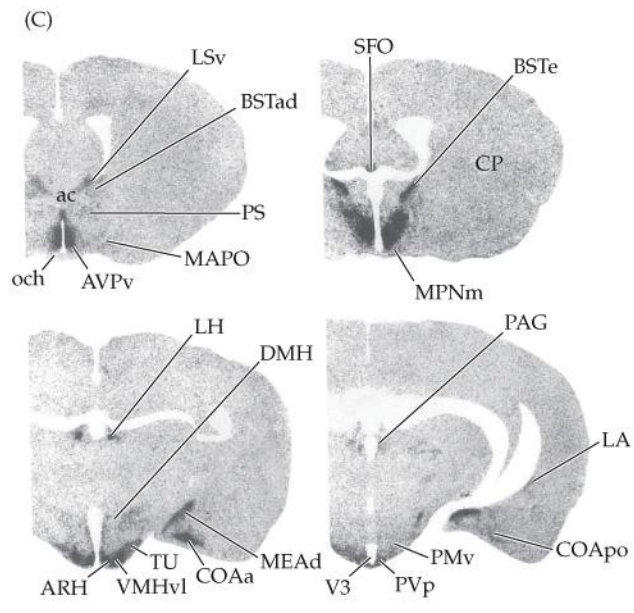
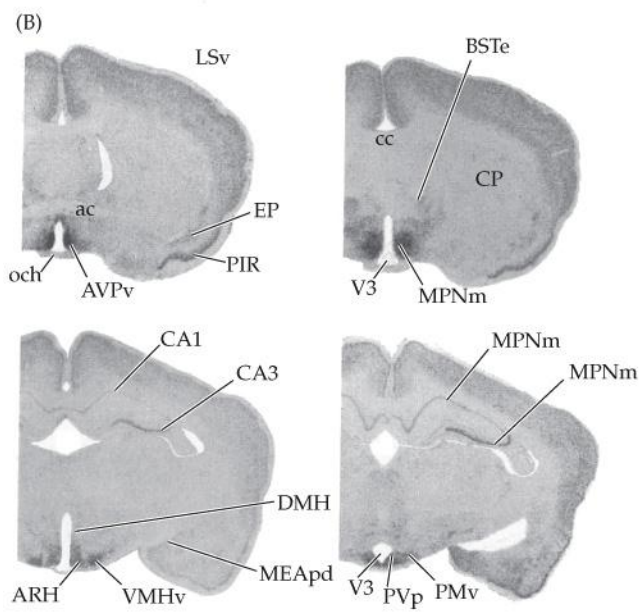
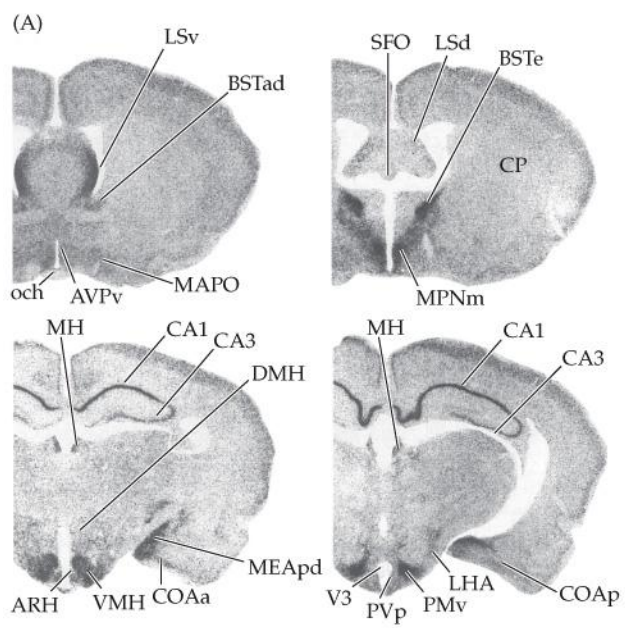
Males (left): left inferior frontal gyrus in rhyming tasks

Females (right): both the left and right inferior frontal gyri are activated

Διαφορές του φύλου στη συνδεσιμότητα των εγκεφαλικών περιοχών

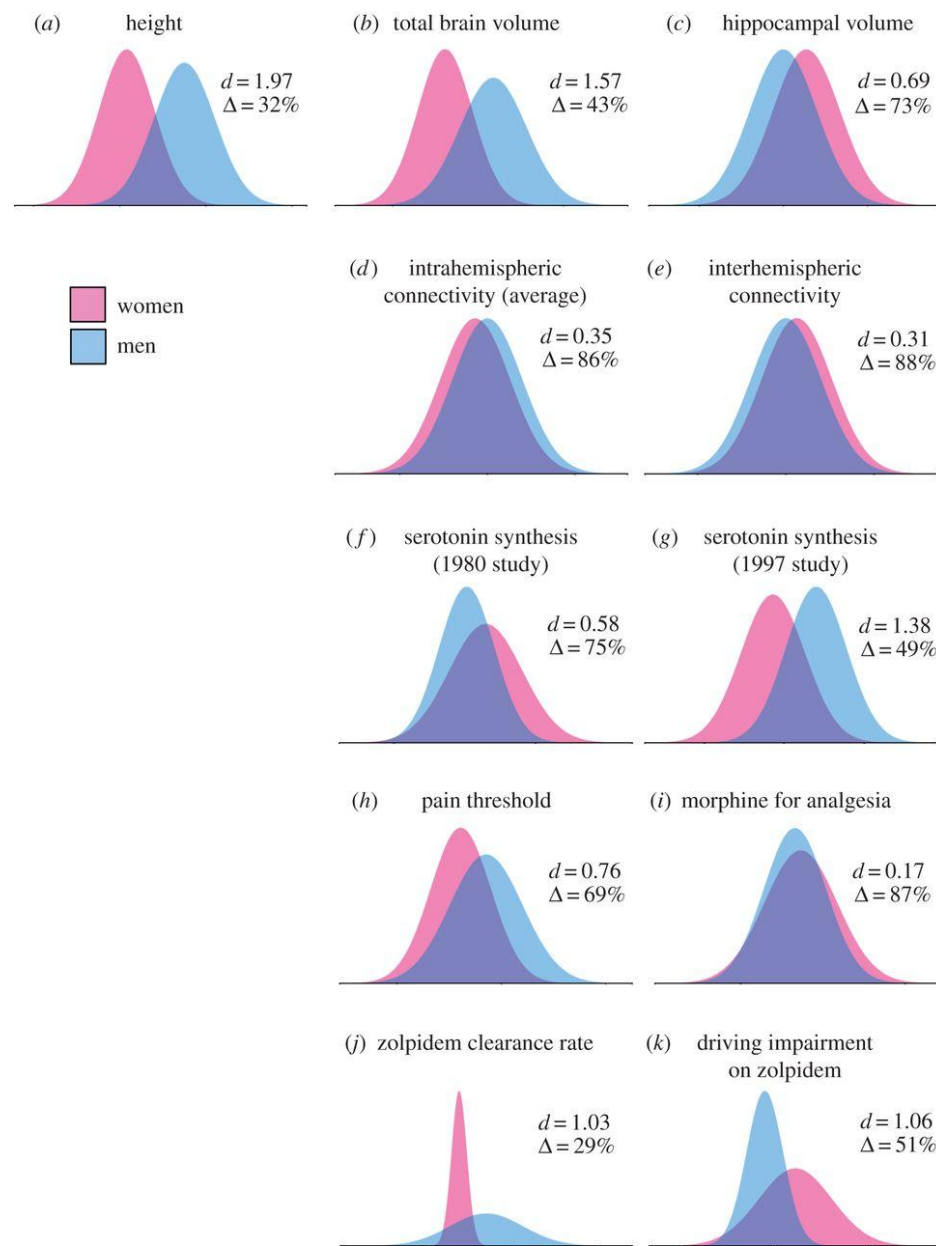


Οι υποδοχείς στεροειδών στον εγκέφαλο – Αλληλοεπικάλυψη



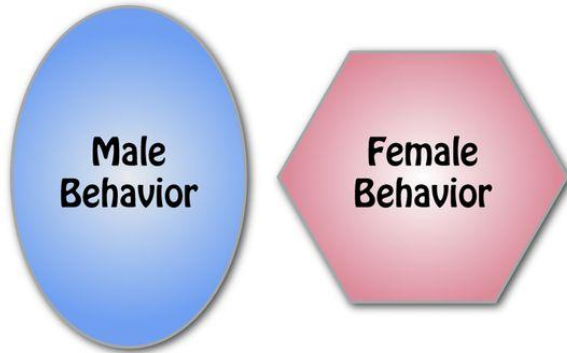
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY 5e, Figure 4.8
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Η ιδέα του «μωσαϊκού»

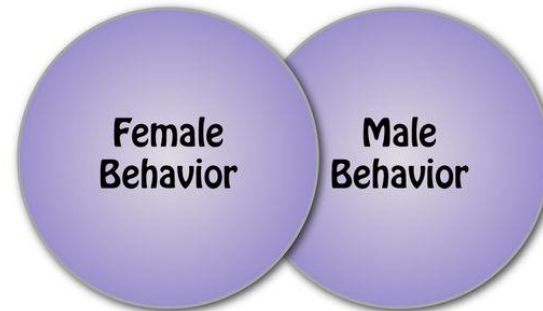


**Illustration of the four types of sex differences that can be observed in animal models:
qualitative, quantitative, population, and mechanistic.**

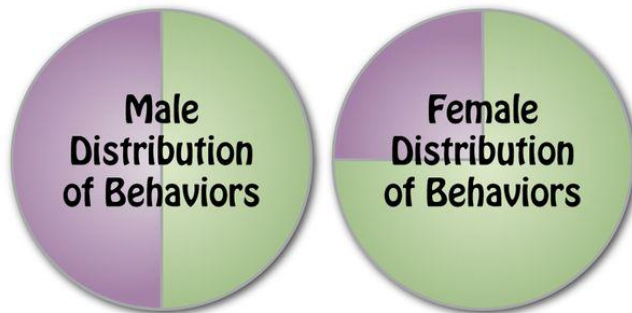
A Qualitative Differences



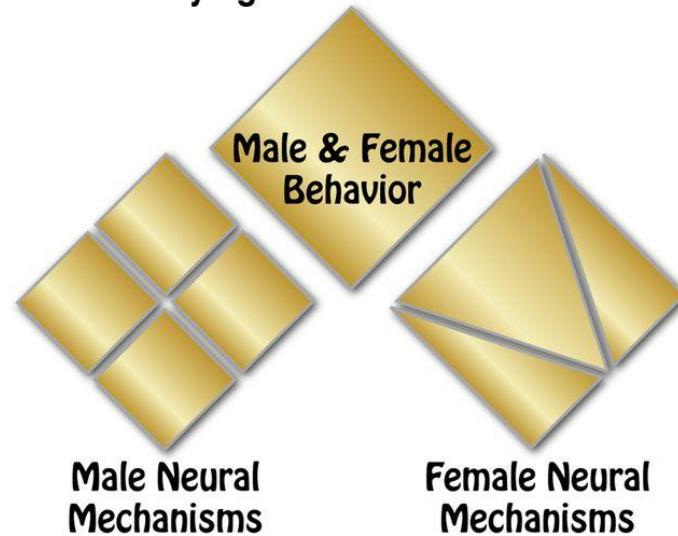
B Quantitative Differences



C Population Differences

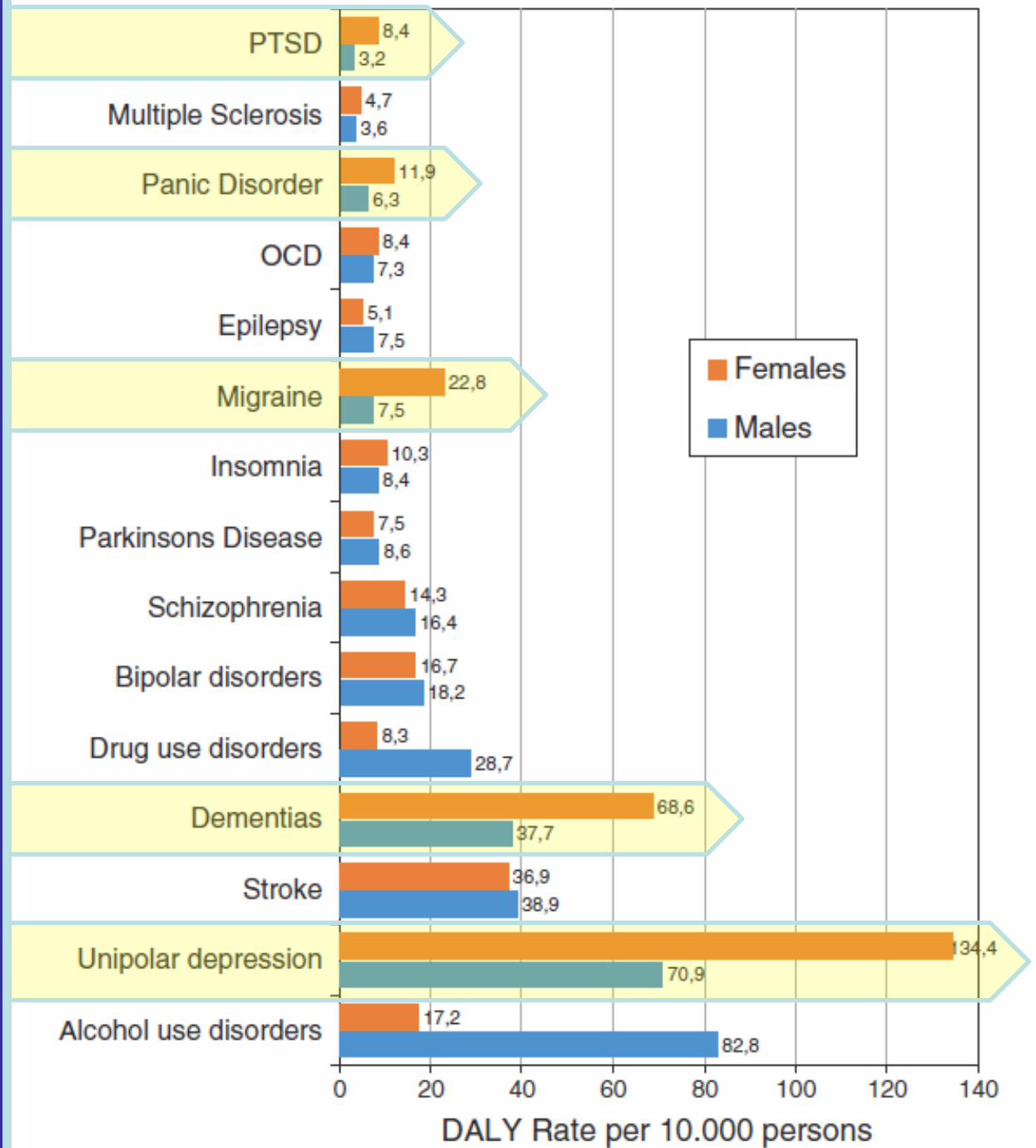


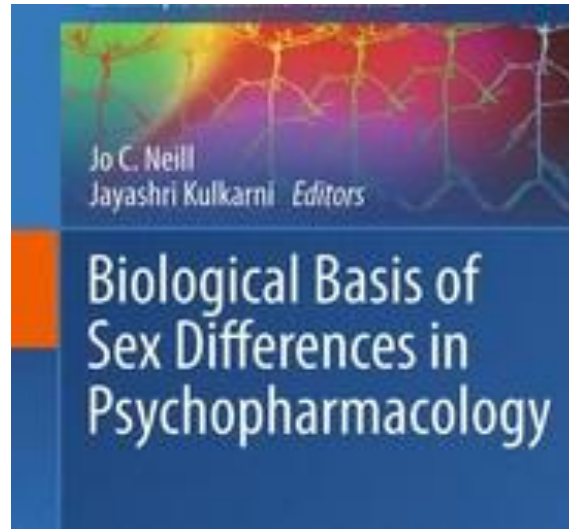
D Underlying Mechanisms Differ



Jill B. Becker, and George F. Koob Pharmacol Rev
2016;68:242-263

**Διαφορές του φύλου
στις Νευρο-
ψυχιατρικές
διαταραχές**





1993: *NIH Revitalization Act to increase representation of women in clinical trials.*

Review

Female psychopharmacology matters! Towards a sex-specific psychopharmacology

**Blanca Bolea-Alamanac¹, Sarah J Bailey²,
Thelma A Lovick³, Dirk Scheele⁴ and Rita Valentino⁵**

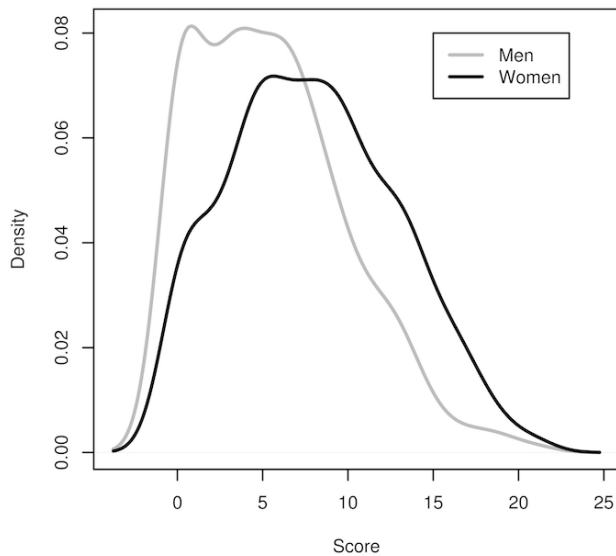


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2018, Vol. 32(2) 125-130
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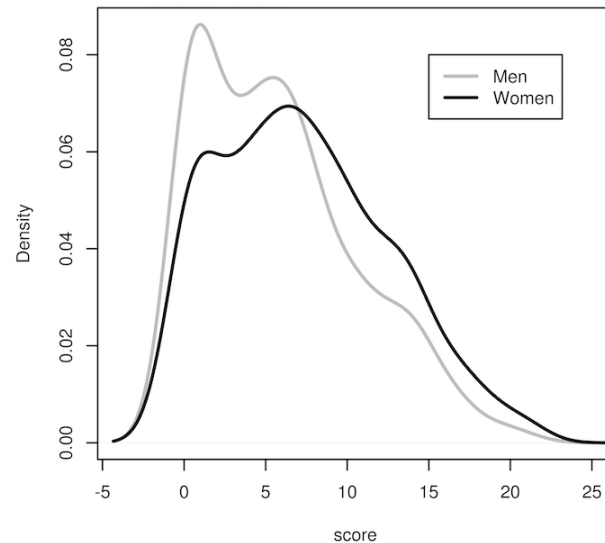


Οι γυναίκες εμφανίζουν υψηλότερα επίπεδα κατάθλιψης, άγχους και αϋπνίας υπό το στρες νοσηλείας σε σχέση με τους άνδρες

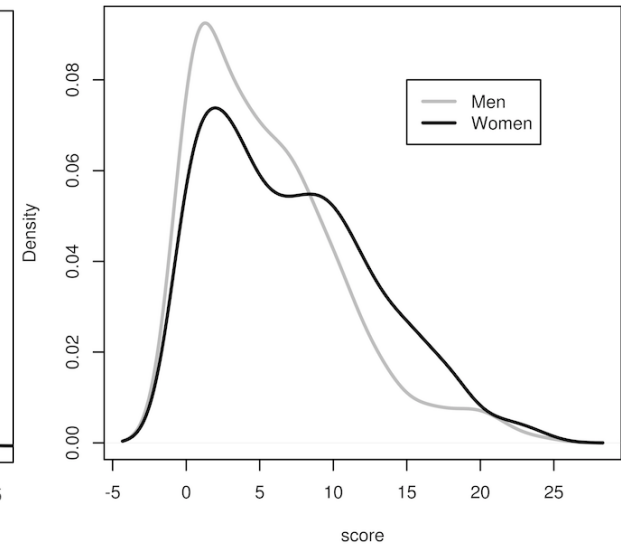
Anxiety



Depression



Insomnia



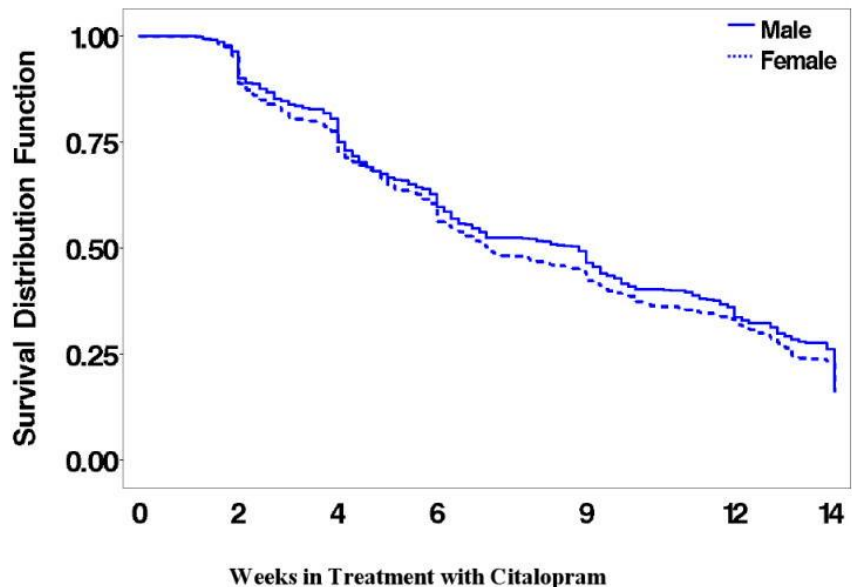
Διαφορές των δύο φύλων στην απόκριση στην αντικαταθλιπτική αγωγή

Οι γυναίκες απαντούν καλύτερα στους **SSRI** σε σχέση με τα TCA και τους SNRI.

Μετα-εμμηνοπαυσιακές γυναίκες έχουν χαμηλότερα ποσοστά ανάρρωσης με **SSRI** σε σχέση με νεώτερες γυναίκες. **ΔΕΝ** ισχύει για τα **SNRI** (βενλαφαξίνη).

Δεν υπάρχουν διαφορές στους άνδρες μεταξύ SSRI, SNRI, TCA.

Οι άνδρες ανέχονται όμως καλύτερα τα **TCA** σε σχέση με τις γυναίκες.



Number of Participants							
Male	1023	963	754	528	332	153	57
Female	1788	1674	1246	885	550	282	100
Total	2811	2637	2000	1413	882	435	157

Log-Rank Statistic=2.81: p=0.0935

Sex differences in pharmacokinetics of antidepressants

Nikolaos Kokras, Christina Dalla & Zeta Papadopoulou-Daifoti[†]

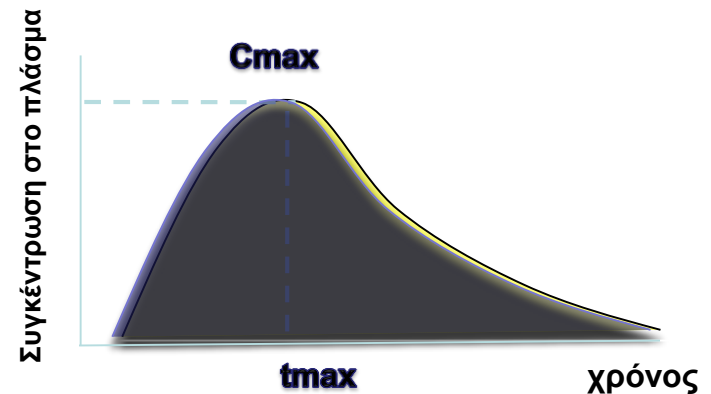
*Expert
Opinion*

- Διαφορές του φύλου στη **φαρμακοκινητική** των αντικαταθλιπτικών: συνήθως υψηλότερα επίπεδα στις γυναίκες

Διαφορές του φύλου στη Φαρμακοκινητική

Οι γυναίκες έχουν σε σχέση με τους άνδρες:

- Χαμηλότερο σωματικό βάρος
- Χαμηλότερη αιματική ροή
- Μικρότερη μυϊκή μάζα
- Υψηλότερα ποσοστά λίπους (~ 11%)
- Διαφορετικό όγκο κατανομής
- Διαφορετική πρωτεϊνική σύνδεση
- Διαφορετικό μεταβολισμό
- Χαμηλότερη κάθαρση
- **Μεγαλύτερη βιοδιαθεσιμότητα**



Κατά τη χορήγηση της ίδιας δόσης πιθανόν οι γυναίκες να εκτίθενται σε υψηλότερα επίπεδα για μεγαλύτερο χρονικό διάστημα



Μεταβολισμός αντικαταθλιπτικών: διαφορές του φύλου

P450 isozymes	Sex difference in activity	Influence of sex hormones	Reported substrates
CYP1A2	F < M	Yes	Fluvoxamine, duloxetine, clomipramine
CYP2A6	F > M	Yes	
CYP2B6	F > M	-	Bupropion
CYP2C9	F = M	-	Fluoxetine
CYP2C19	F ≤ M	Yes	Citalopram, fluoxetine, fluvoxamine
CYP2D6	F ≥ M	Yes	Desipramine, mirtazapine, venlafaxine
CYP2E1	F < M	-	
CYP3A4	F > M	-	Venlafaxine

Ορισμένα ισοένζυμα (π.χ. CYP2A6) επηρεάζονται από τα οιστρογόνα


Mini-Review

Preclinical sex differences in depression and antidepressant response: Implications for clinical research

Nikolaos Kokras, Christina Dalla 

First published: 7 November 2016 [Full publication history](#)

DOI: 10.1002/jnr.23861 [View/save citation](#)

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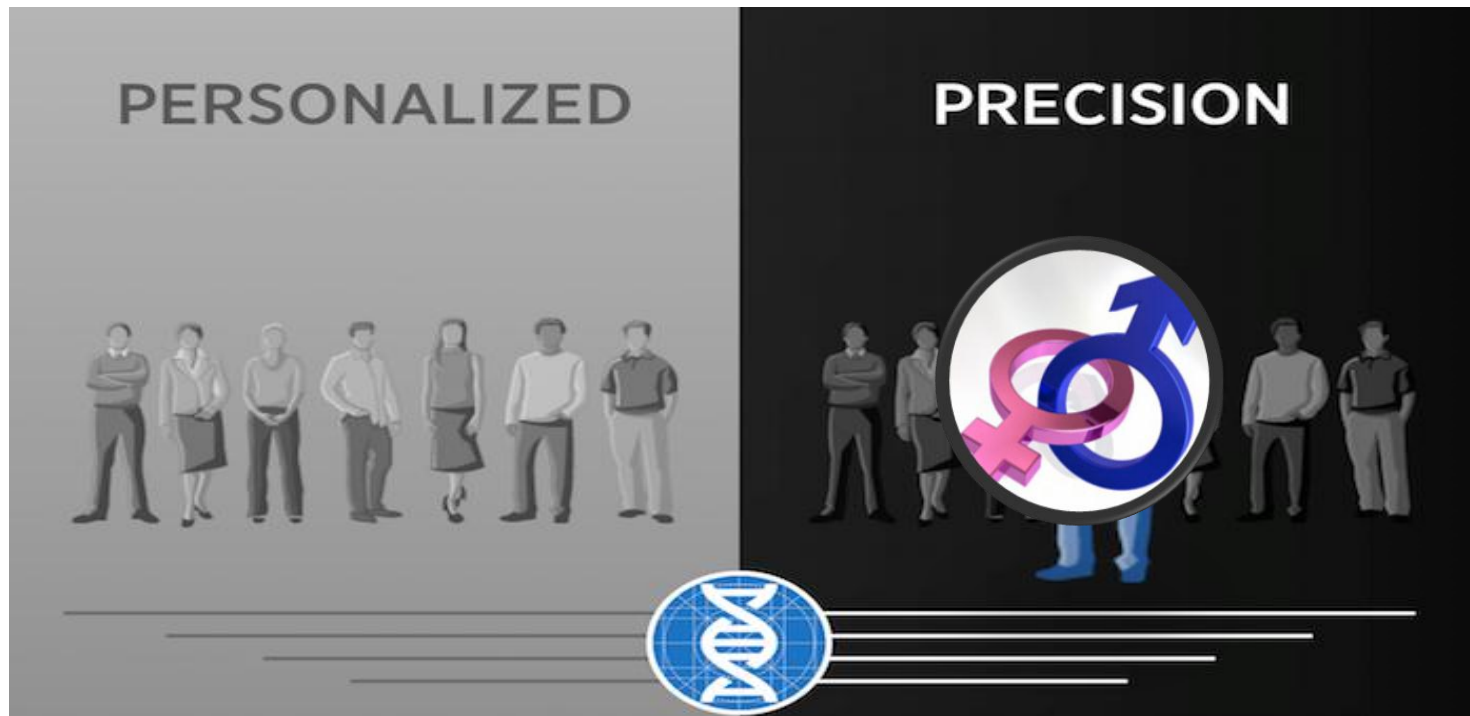


3

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Volume 95, An Issue Whose
Time Has Come:
Sex/Gender Influences on
Nervous System Function
Pages 731–736





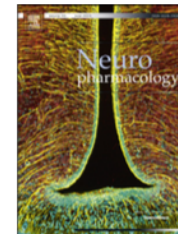
**ΥΠΑΡΧΟΥΝ ΔΙΑΦΟΡΕΣ ΤΟΥ
ΦΎΛΟΥ ΣΤΑ ΜΟΝΤΕΛΑ?**



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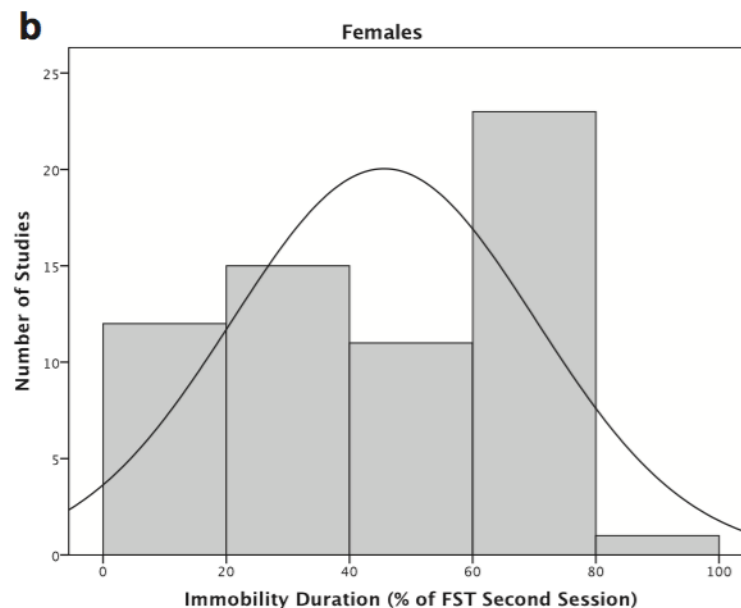
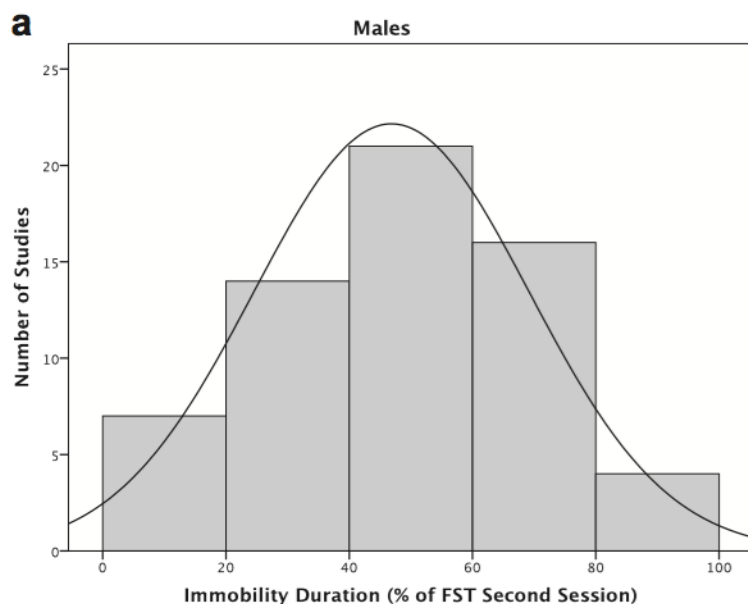


Nikolaos Kokras ^{a, b}, Katerina Antoniou ^c, Hudu G. Mikail ^a, Vasilios Kafetzopoulos ^a, Zeta Papadopoulou-Daifoti ^a, Christina Dalla ^{a, *}

^a Department of Pharmacology, Medical School, University of Athens, Greece

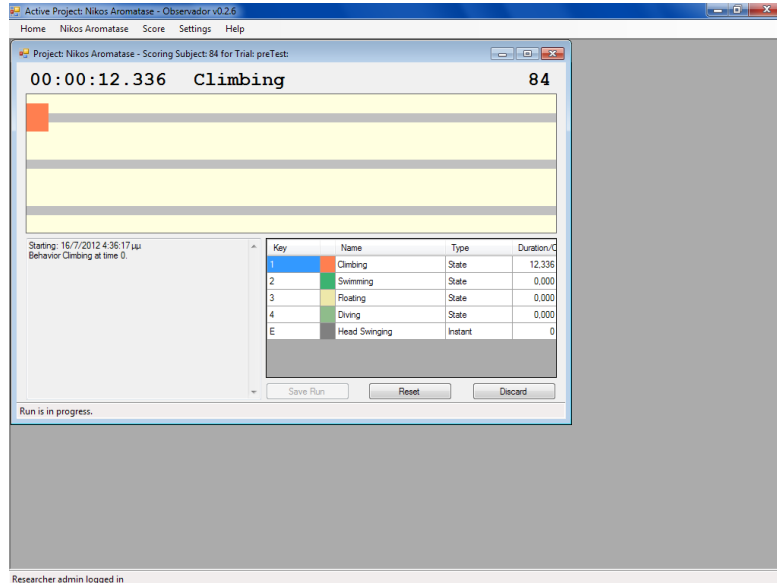
^b First Department of Psychiatry, Eginition Hospital, Medical School, University of Athens, Greece

^c Department of Pharmacology, Medical School, University of Ioannina, Greece

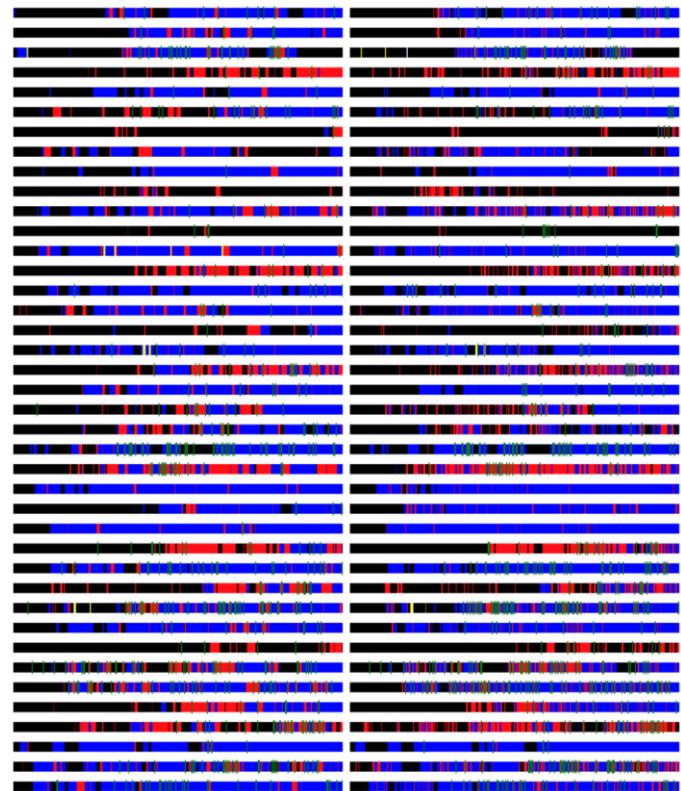


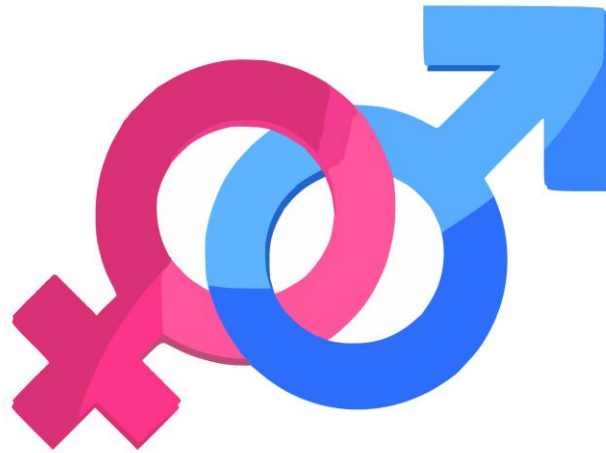
Kinoscope: ένα λογισμικό για την καταγραφή της συμπεριφοράς

For manual scoring and analysis
Open Source
Sourceforge.net/projects/kinoscope



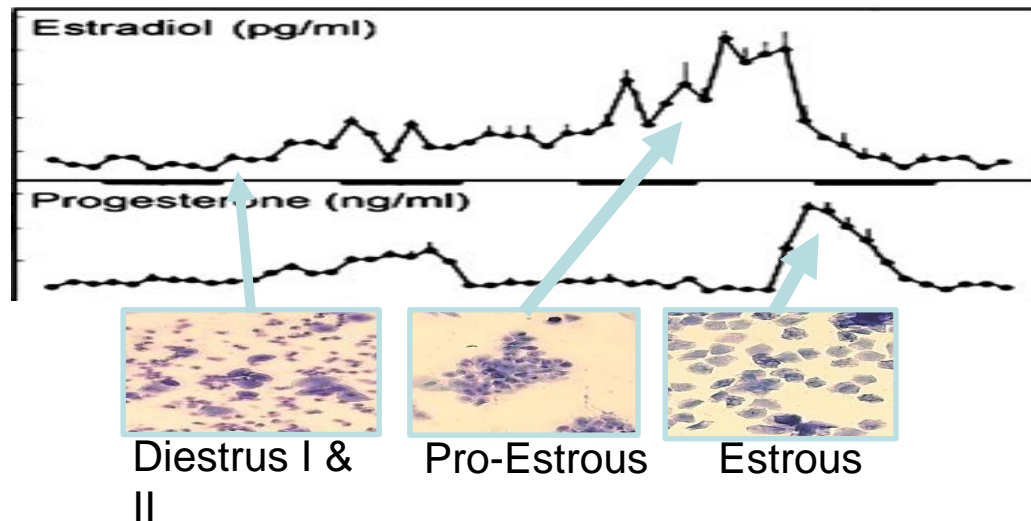
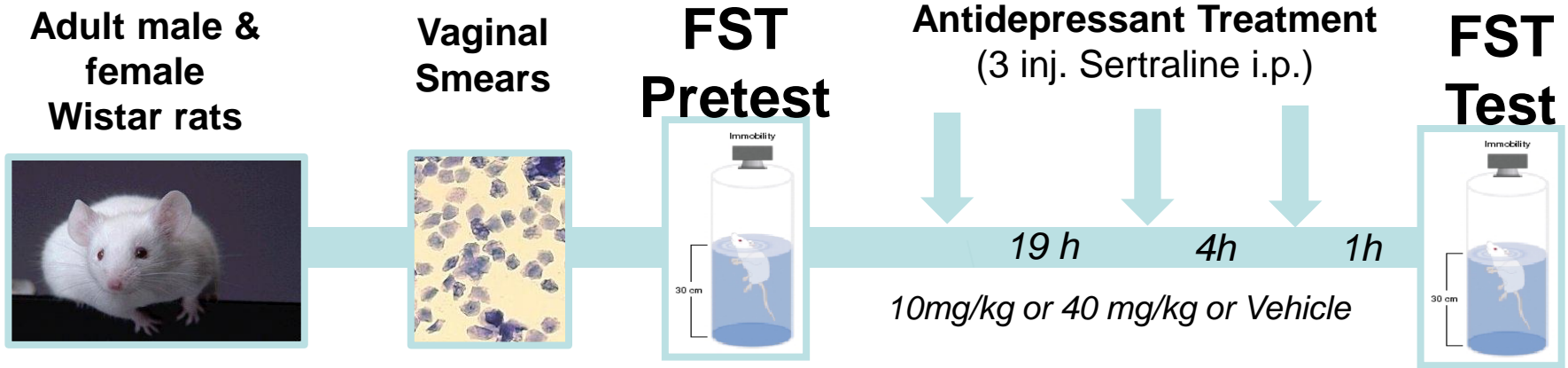
Behavioral Maps

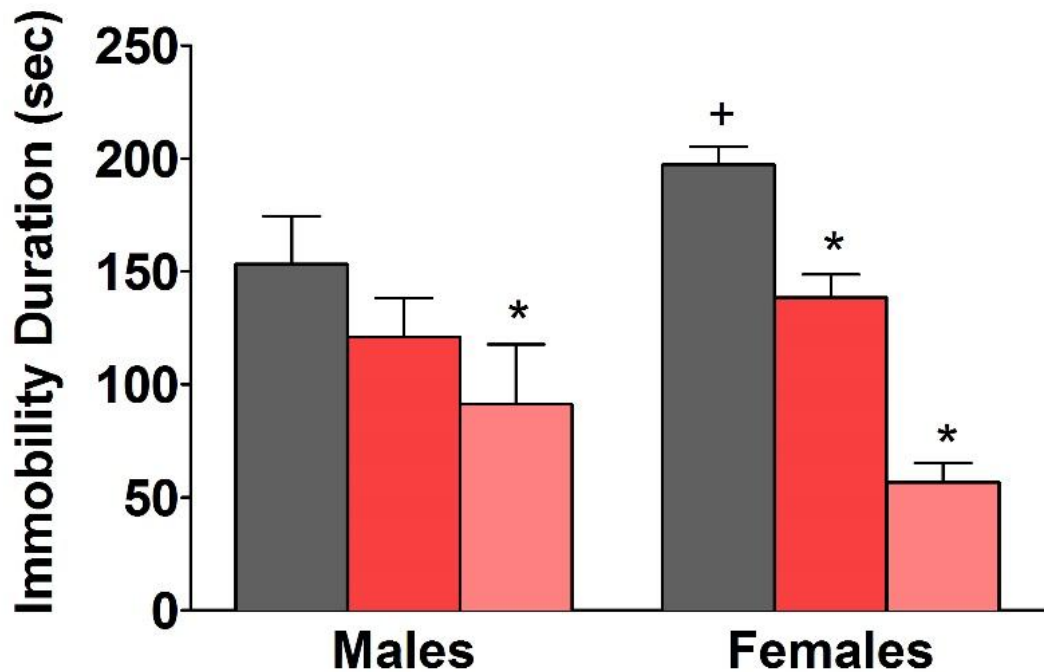




**ΠΟΙΟΣ Ο ΡΟΛΟΣ ΤΩΝ
ΟΡΜΟΝΩΝ ΤΟΥ ΦΥΛΟΥ?**

Η απάντηση στην αντικαταθλιπτική αγωγή επηρεάζεται από τις ορμόνες?





Τα θηλυκά εμφανίζουν περισσότερο ακινησία από ότι τα αρσενικά

Οι διαφορές του φύλου εξαφανίζονται μετά από τη χορήγηση σερτραλίνης

