

NEUROPEPTIDI

NEURONI PEPTIDERGICI

- I neuroni produttori di peptidi non si trovano solamente nell'ipotalamo, ma in tutto il SNC
- I neuropeptidi hanno il ruolo di neuromodulatori nella trasmissione sinaptica
- I recettori per i peptidi si trovano in diverse regioni dell'encefalo, anche distanti dai terminali peptidergici, in questo caso si pensa che agiscano attraverso meccanismi paracrini (volume transmission)
- I neuropeptidi inoltre influenzano molti comportamenti, per cui la loro azione parormonale si rivolge essenzialmente ai circuiti cerebrali

FAMIGLIE DI NEUROPEPTIDI

TABLE 1

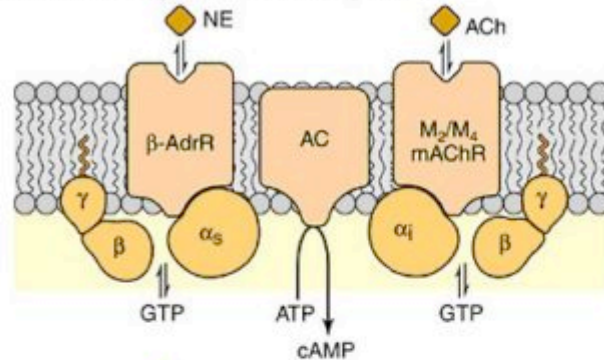
Families of Structurally and Functionally Related Peptides

- (1) VIP, secretin, glucagon, GIP, PHI, GRF
 - (2) Neurotensin, pancreatic polypeptide
 - (3) Cholecystokinin, gastrin, cerulein, phyllocerulein
 - (4) Vasopressin, oxytocin, vasotocin, etc.
 - (5) a. Bombesin, alytesin
b. Ranatensin, litorin
 - (6) Tachykinins: eledoisin, physalaemin, uperolein, phyllomedusin, kassinin, chylambatin, substance P
 - (7) a. ACTH, MSH, LPH, endorphins, Met-enkephalin
b. Leu-enkephalin, dynorphin, alpha- and beta-neo-endorphins, etc.
 - (8) Kinins
 - (9) Angiotensins
 - (10) Sauvagine, CRF
 - (11) Somatostatin, urotensin II
 - (13) Kyotorphin, neo-kyotorphin
 - (14) Atrial and brain natriuretic peptides
 - (15) Growth hormone, prolactin
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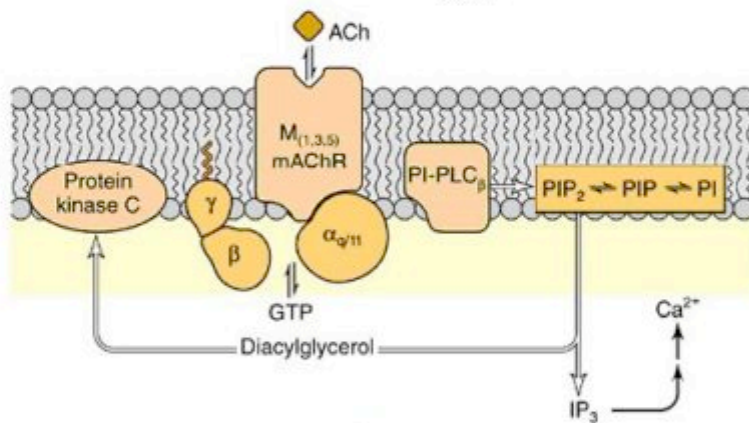
RECETTORI PER I PEPTIDI

Primary biochemical responses mediated by muscarinic acetylcholine receptors

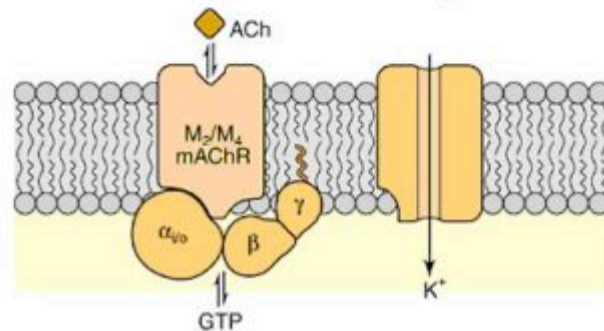
Inhibition of adenylyl cyclase



Stimulation of phospholipase C



Regulation of K $^+$ channels



I recettori per i neuropeptidi sono del tipo *transmembrana*. Attivano quindi una cascata di eventi metabolici intracellulari che possono influenzare non solo il potenziale di membrana, ma anche il metabolismo cellulare.

STUDI ATTUALI SUI NEUROPEPTIDI

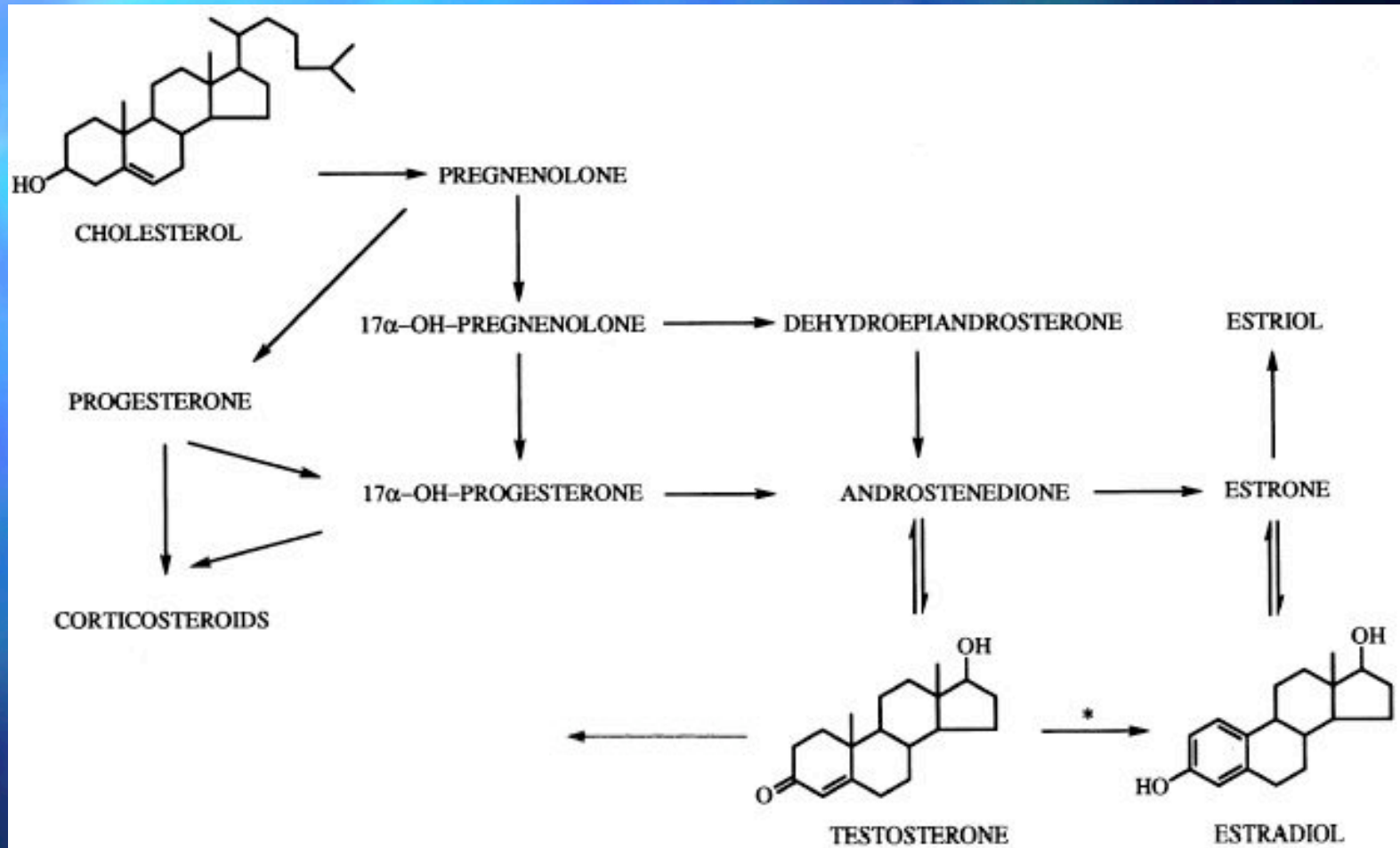
- (1) studies on neurotropic and behavioral actions of neuropeptides;
- (2) studies on physiological and pharmacological actions of neuropeptides;
- (3) studies on the mechanisms of action (including studies on receptors; receptor solubilization; the most promising technique is cloning of receptor cDNAs);
- (4) structure–activity studies, construction of synthetic analogs with predicted properties;
- (5) studies on neuropeptide localization and colocalization;
- (6) studies on neuroendocrine tumors;
- (7) molecular biology of neuropeptides and their life cycles, including processing by specific peptidases;
- (8) studies on neuropeptide-specific peptidases, including search for their specific activators and inhibitors as possible tools of regulation of the level of neuropeptides in the organism;
- (9) studies on neuropeptides in lower animals and in evolution;
- (10) neuroimmunoendocrinology.

NEUROSTEROIDI

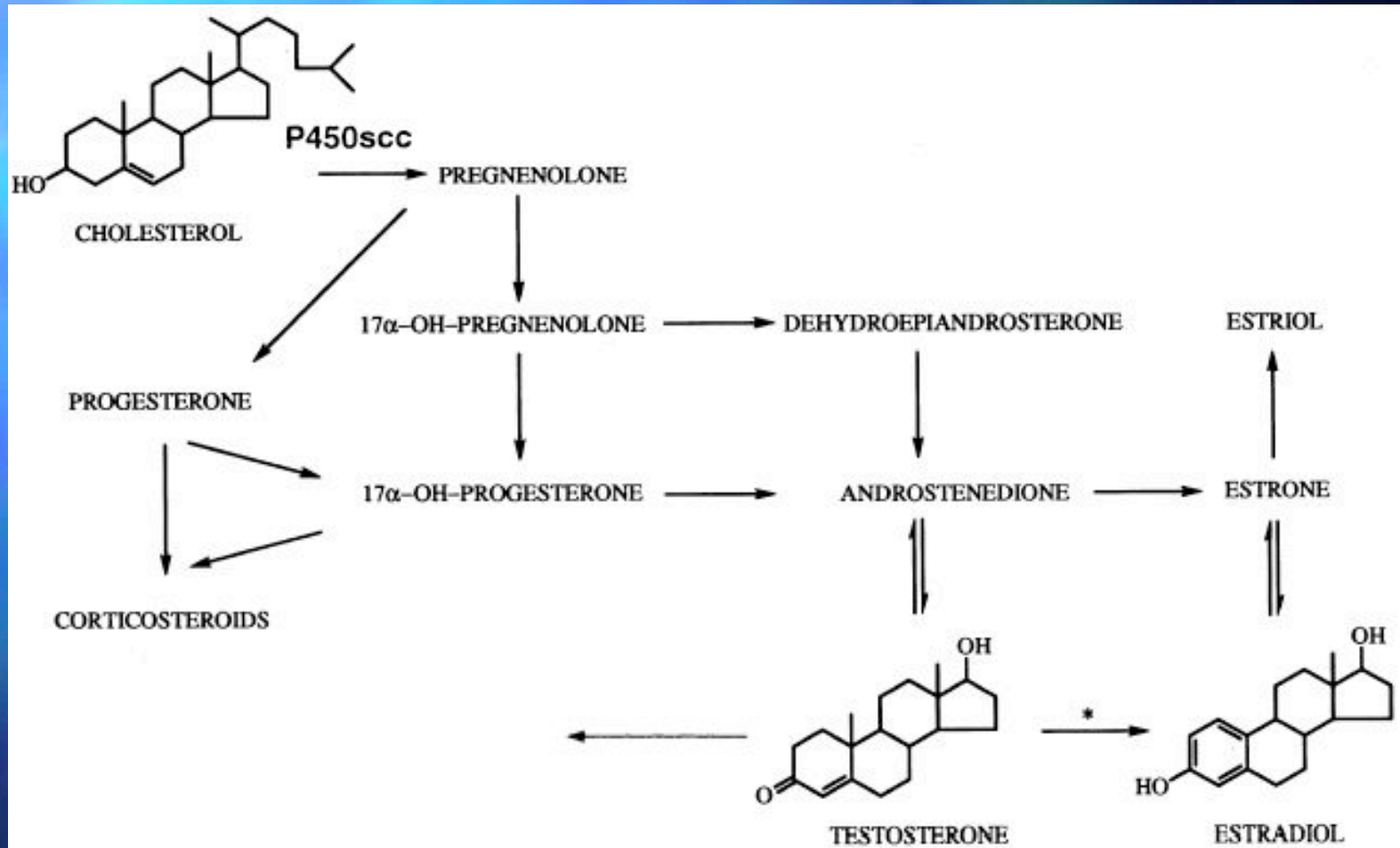
SIGNIFICATO DEL TERMINE

- Steroidi sintetizzati all'interno del sistema nervoso centrale (neuroni o glia)
 - Distinzione tra neosintesi e metabolismo
 - Azione "solo" sul SNC?
- Steroidi neuroattivi

SINTESI

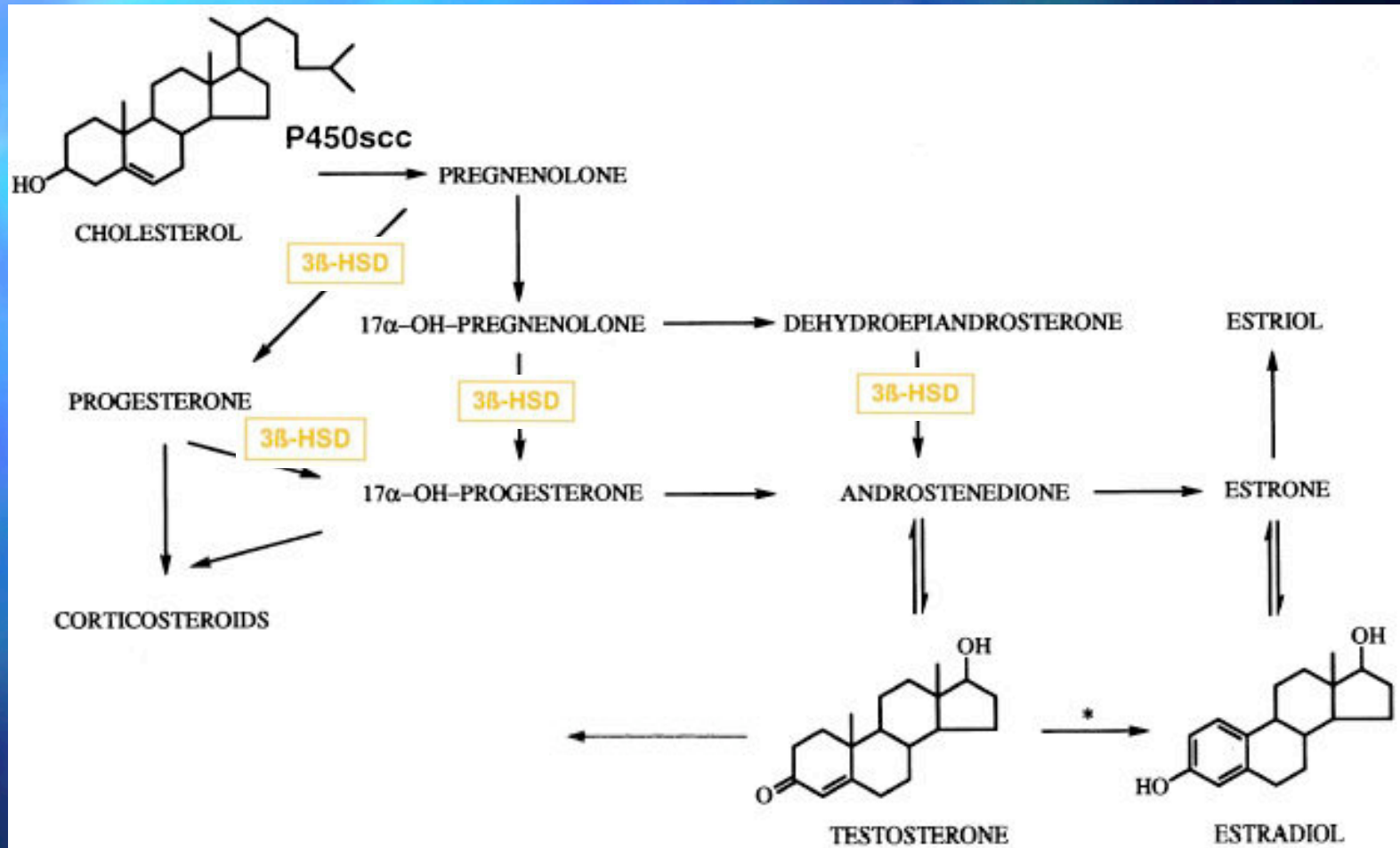


SINTESI



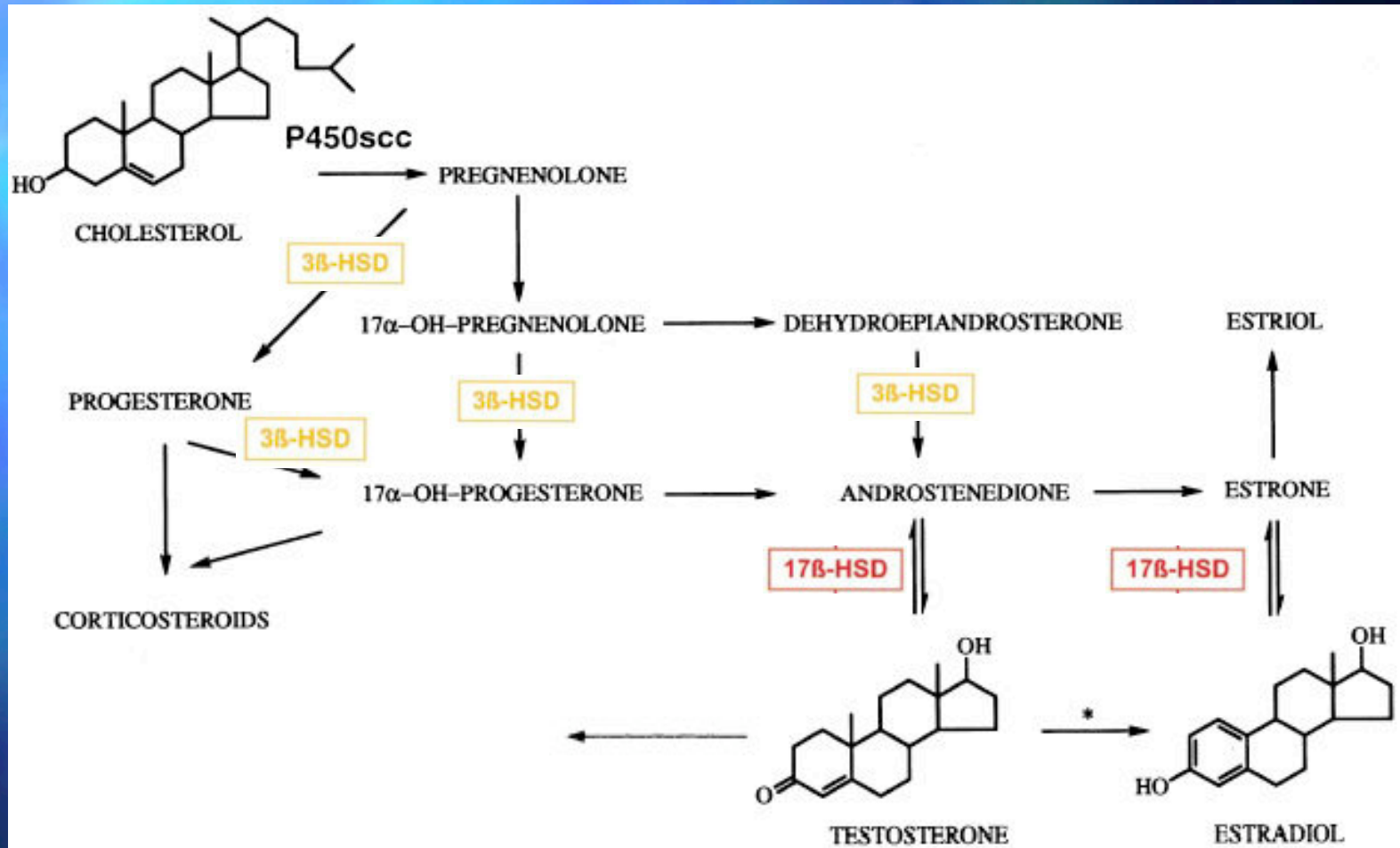
P450-side chain cleavage enzyme

SINTESI



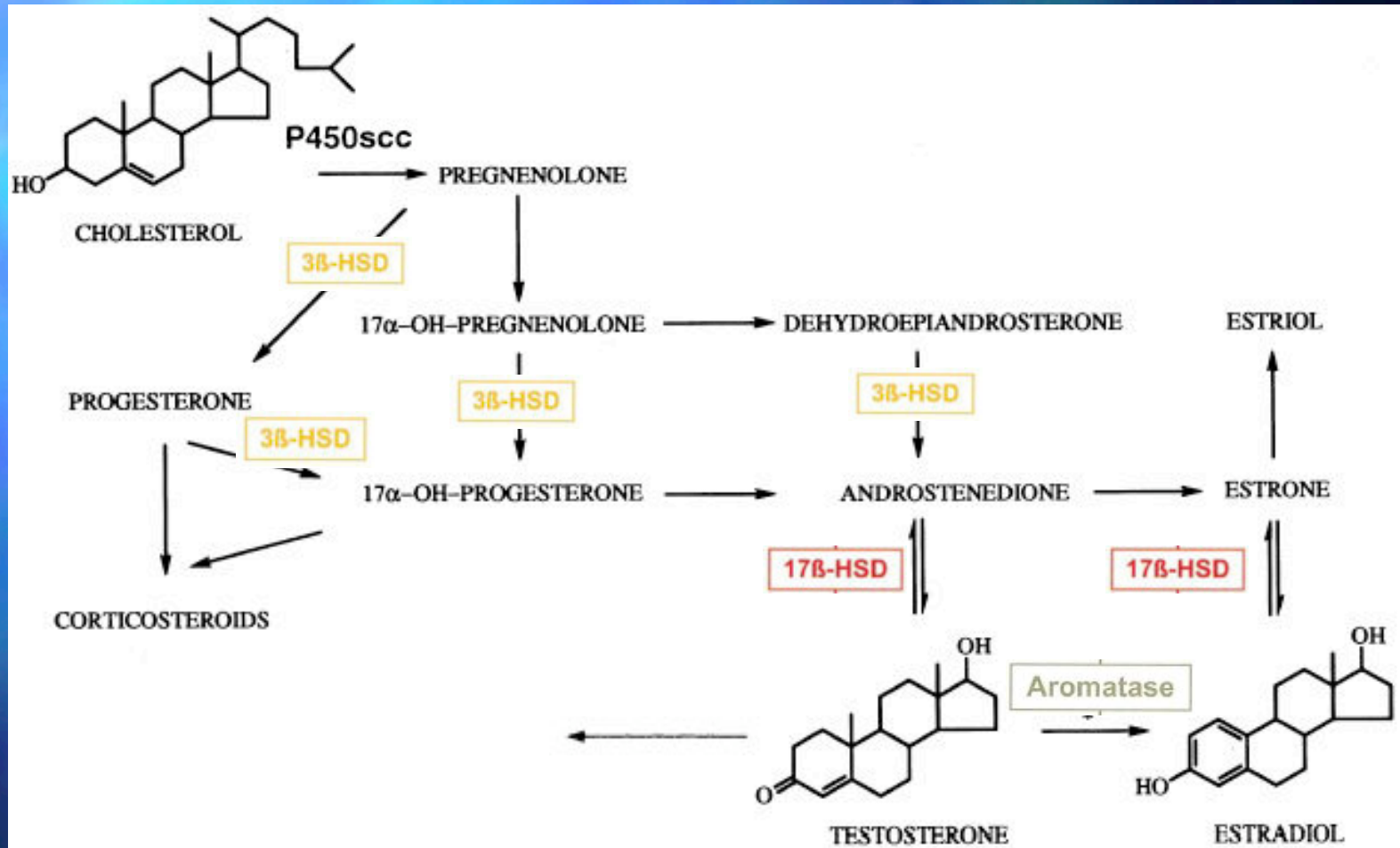
3-beta idrossisteroide deidrogenasi

SINTESI



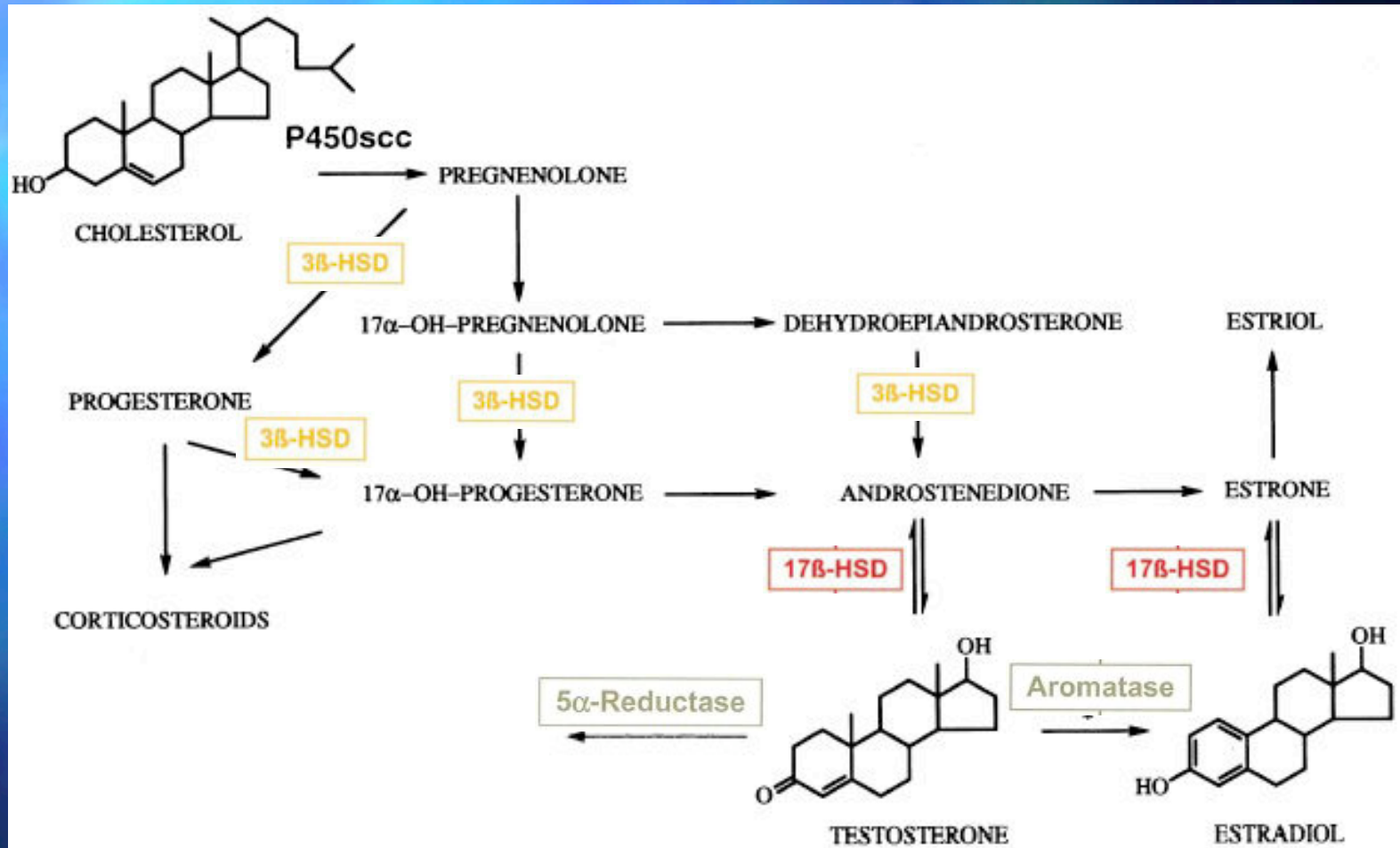
17-beta idrossisteroide deidrogenasi

SINTESI



aromatasi

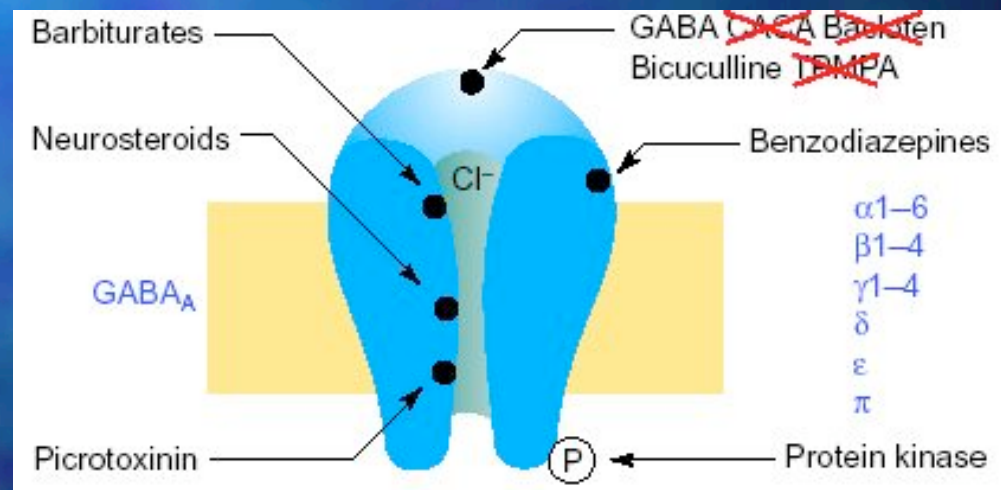
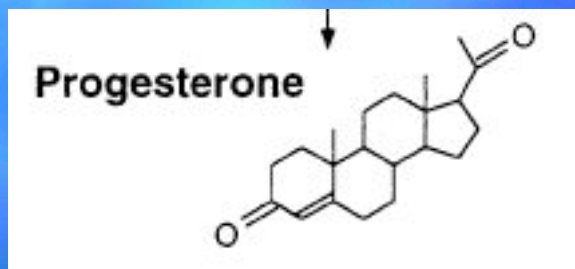
SINTESI



5alfa riduttasi

PROGESTERONE

- Può legarsi al recettore GABA_A e modulare la trasmissione GABAergica



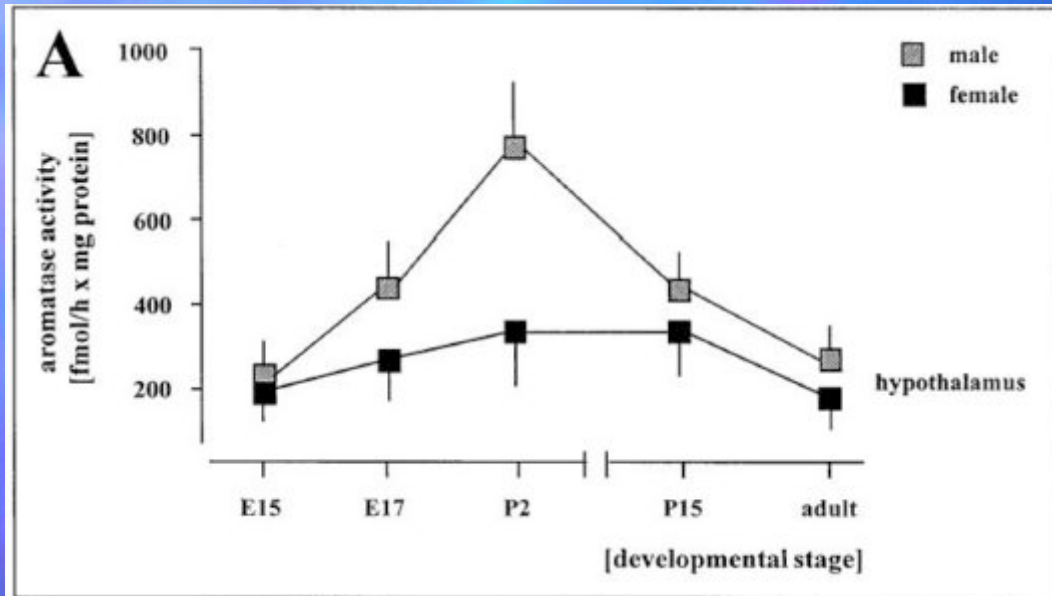
TESTOSTERONE E DHT

- Possono legarsi ai recettori per gli androgeni presenti in varie aree encefaliche

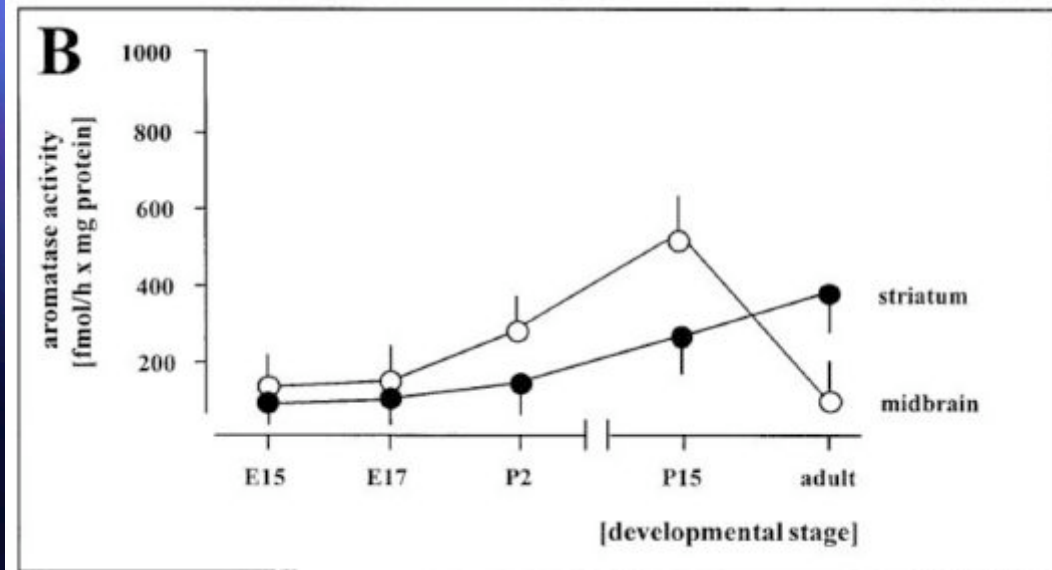
ESTRADIOLO

- Può legarsi ai recettori per gli estrogeni diffusi in numerosissime regioni cerebrali
- Può legarsi a recettori di membrana e dare origine ad effetti a brevissimo o a breve termine

VARIAZIONI DELL'ATTIVITA' AROMATASICA NEL CORSO DELLO SVILUPPO

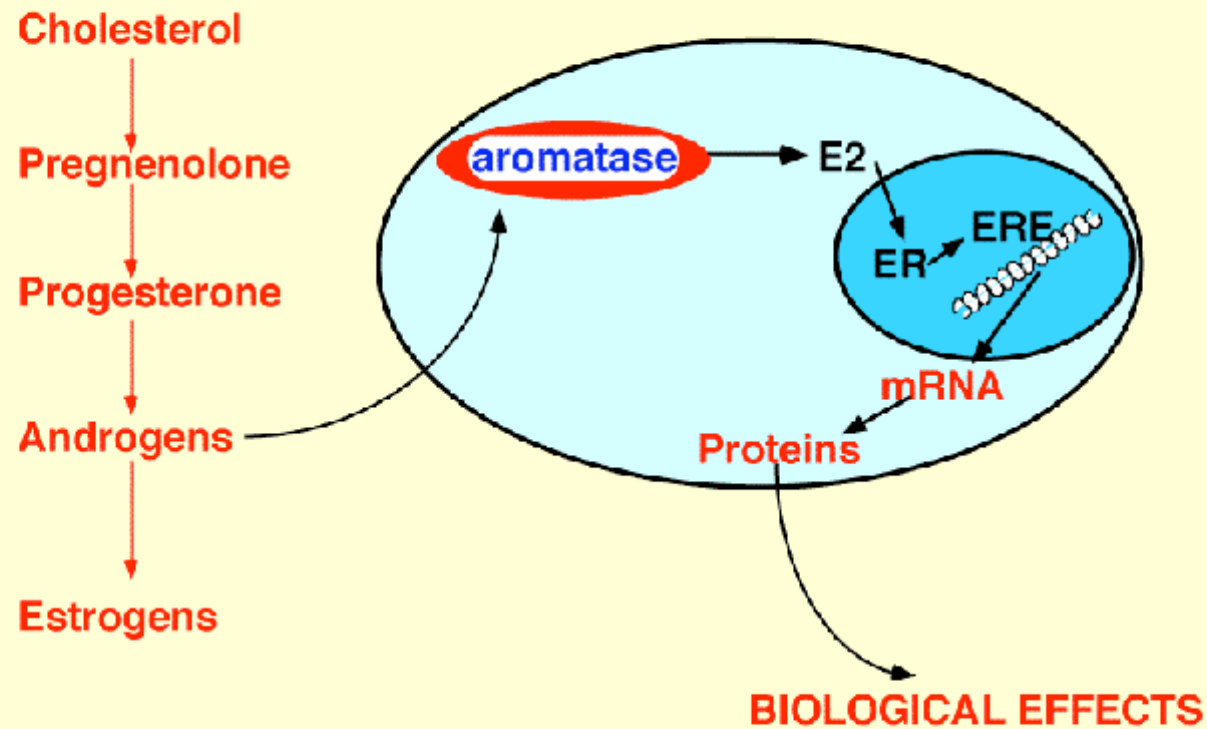


Gli enzimi che servono alla sintesi dei neurosteroidi possono avere una espressione diversa a seconda della regione e dell'età.

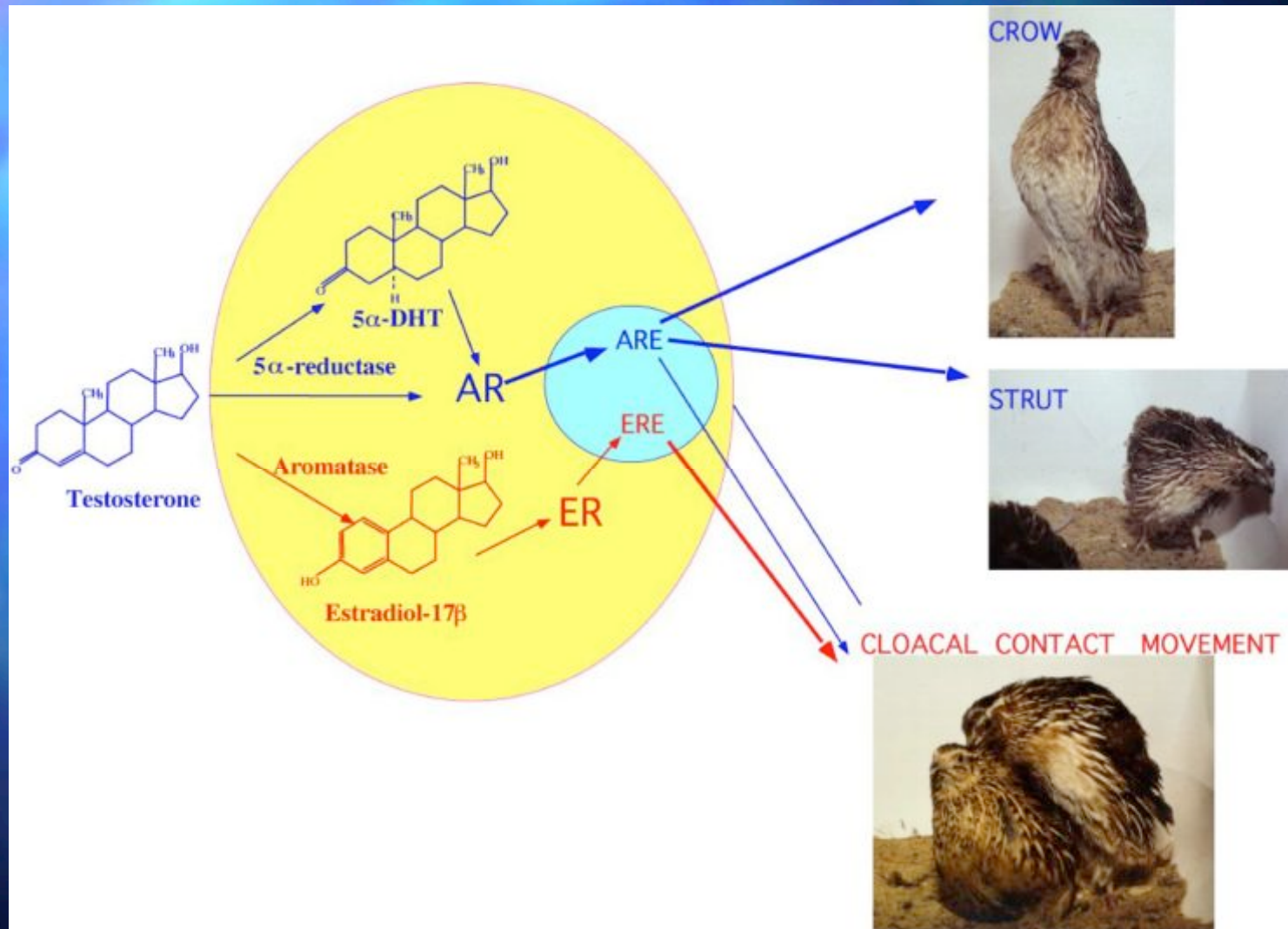


A. Presenza di dimorfismo nella espressione dell'aromatasi ipotalamica nella prima settimana di vita.
B. Inversione nella quantità di aromatasi tra striato e mesencefalo

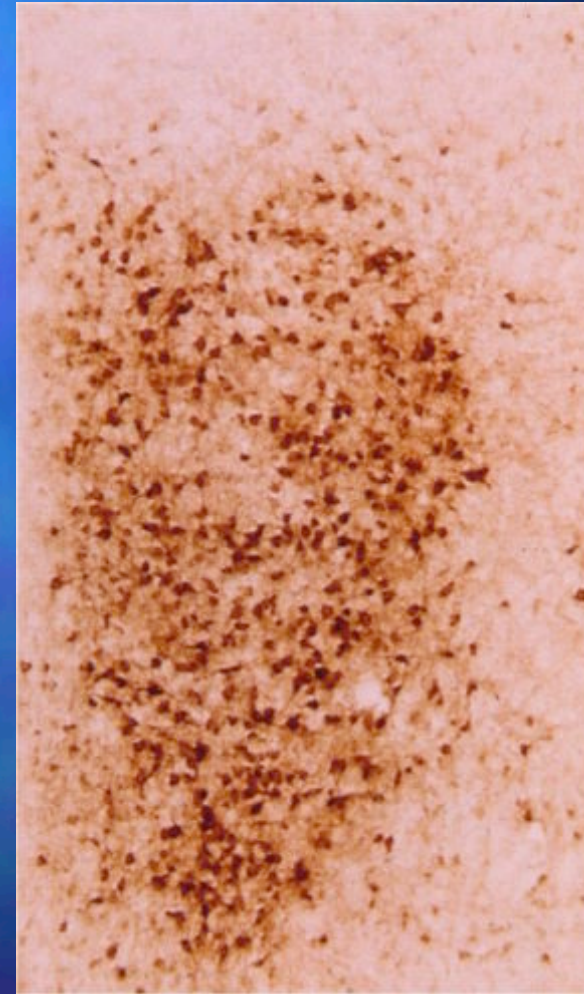
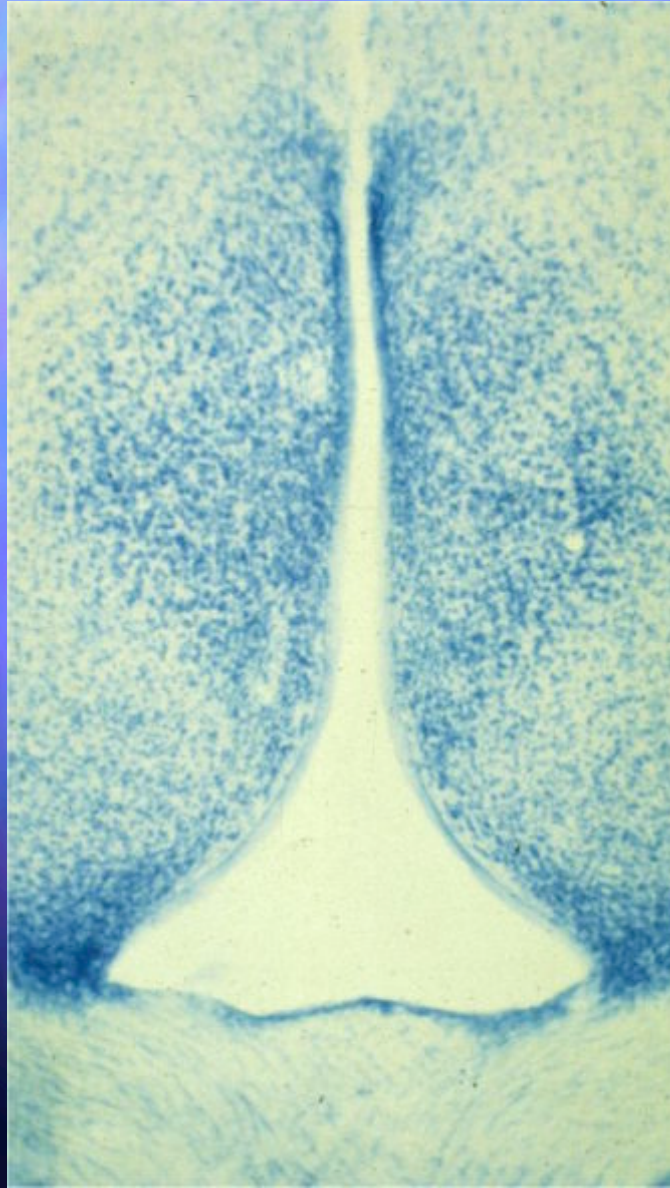
MOLTI EFFETTI DEL T NEL SNC SONO MEDIATI DA ESTROGENI PRODOTTI LOCALMENTE



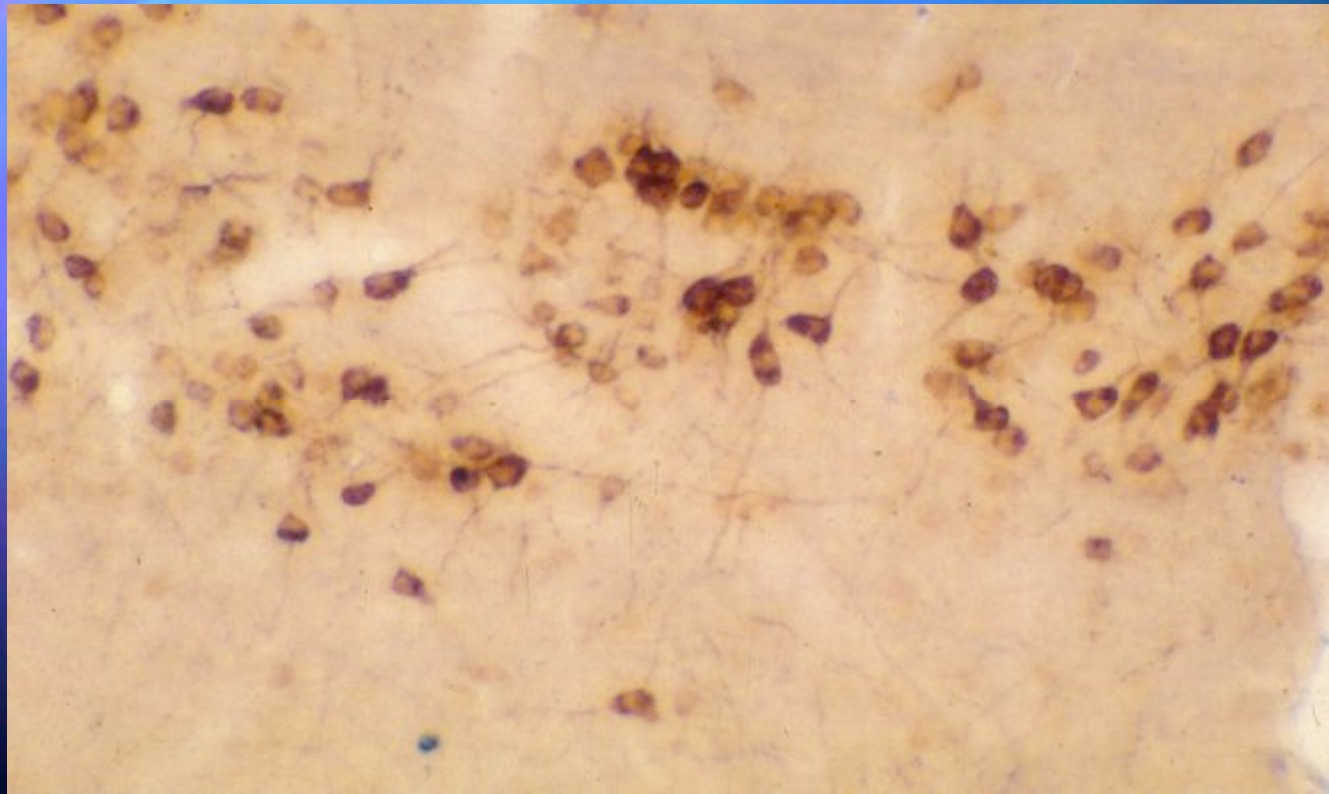
STEROIDI E COMPORTAMENTO MASCHILE



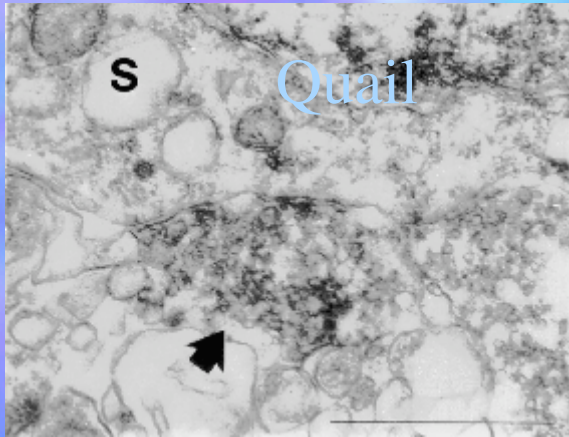
**CELLULE ARO-ir MARCANO
IN MANIERA SPECIFICA IL
POM**



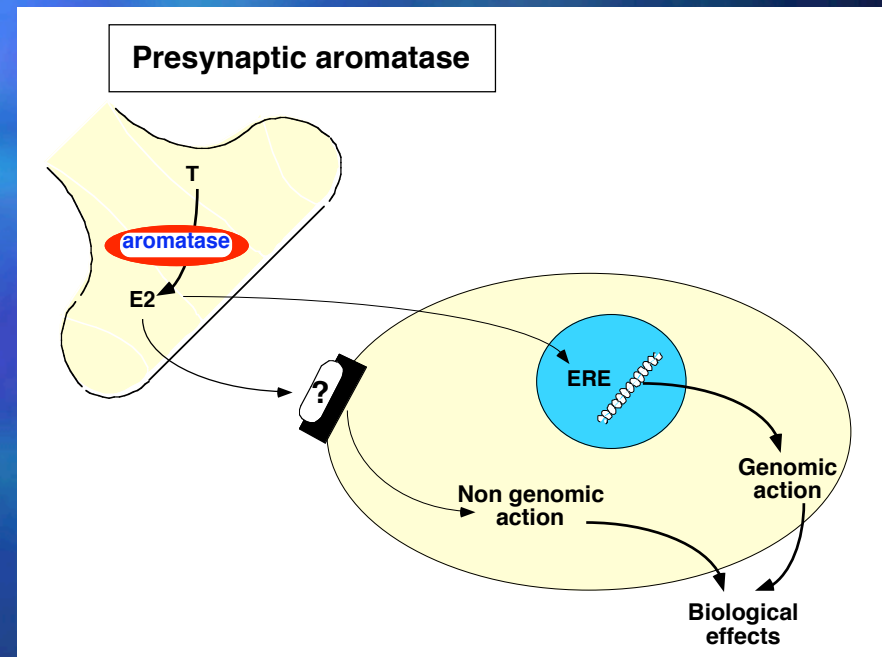
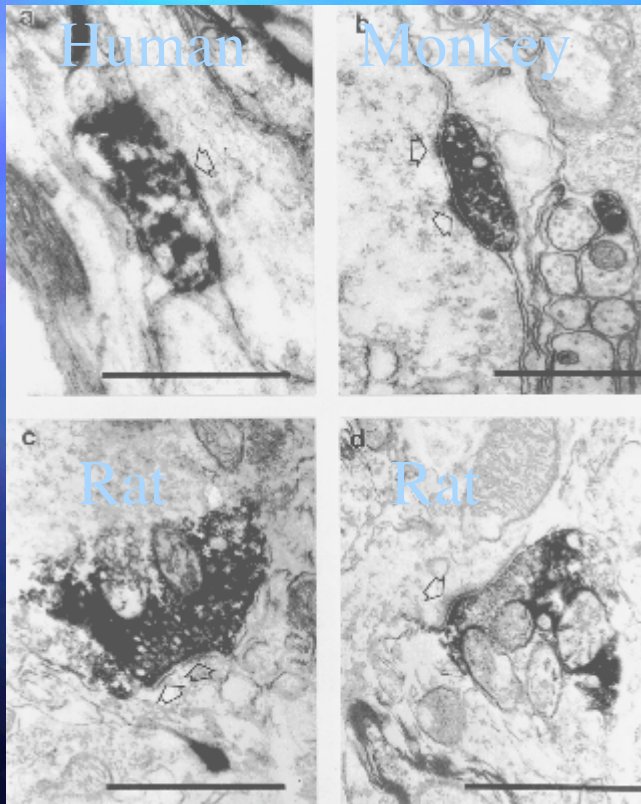
Organizzazione anatomica: Localizzazione subcellulare



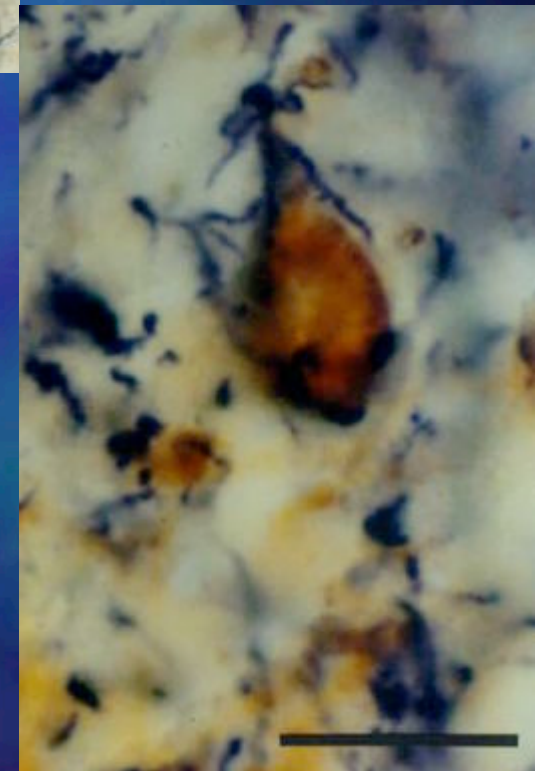
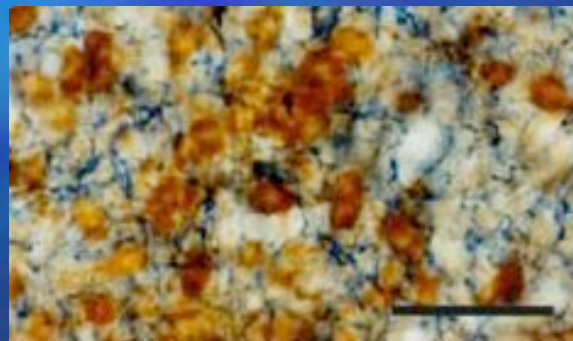
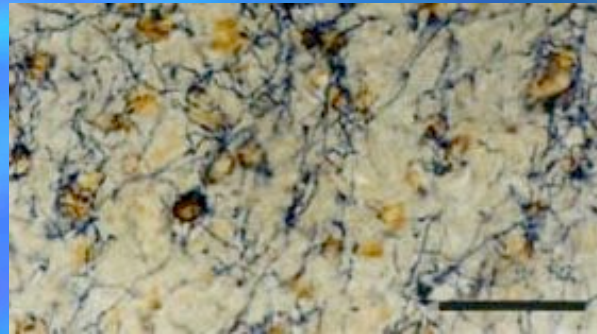
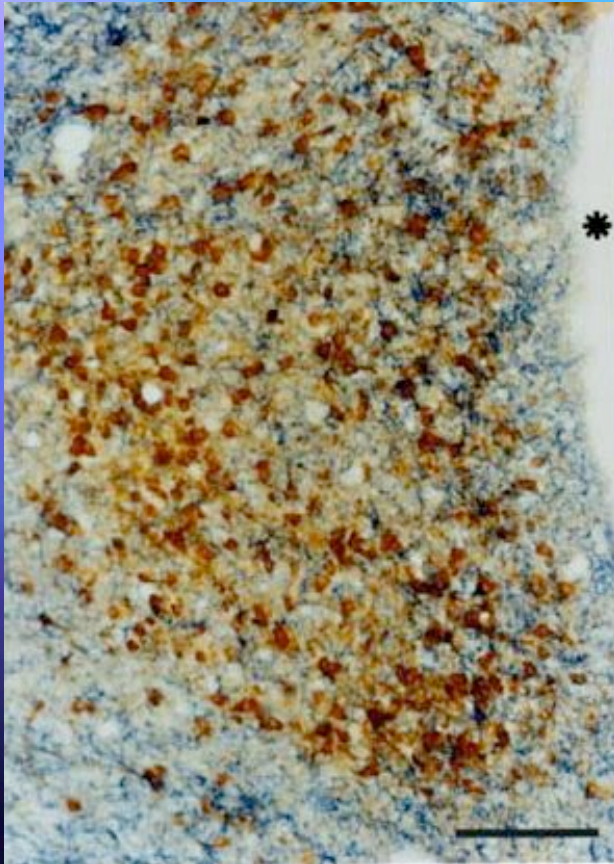
Corpo cellulare
Processi



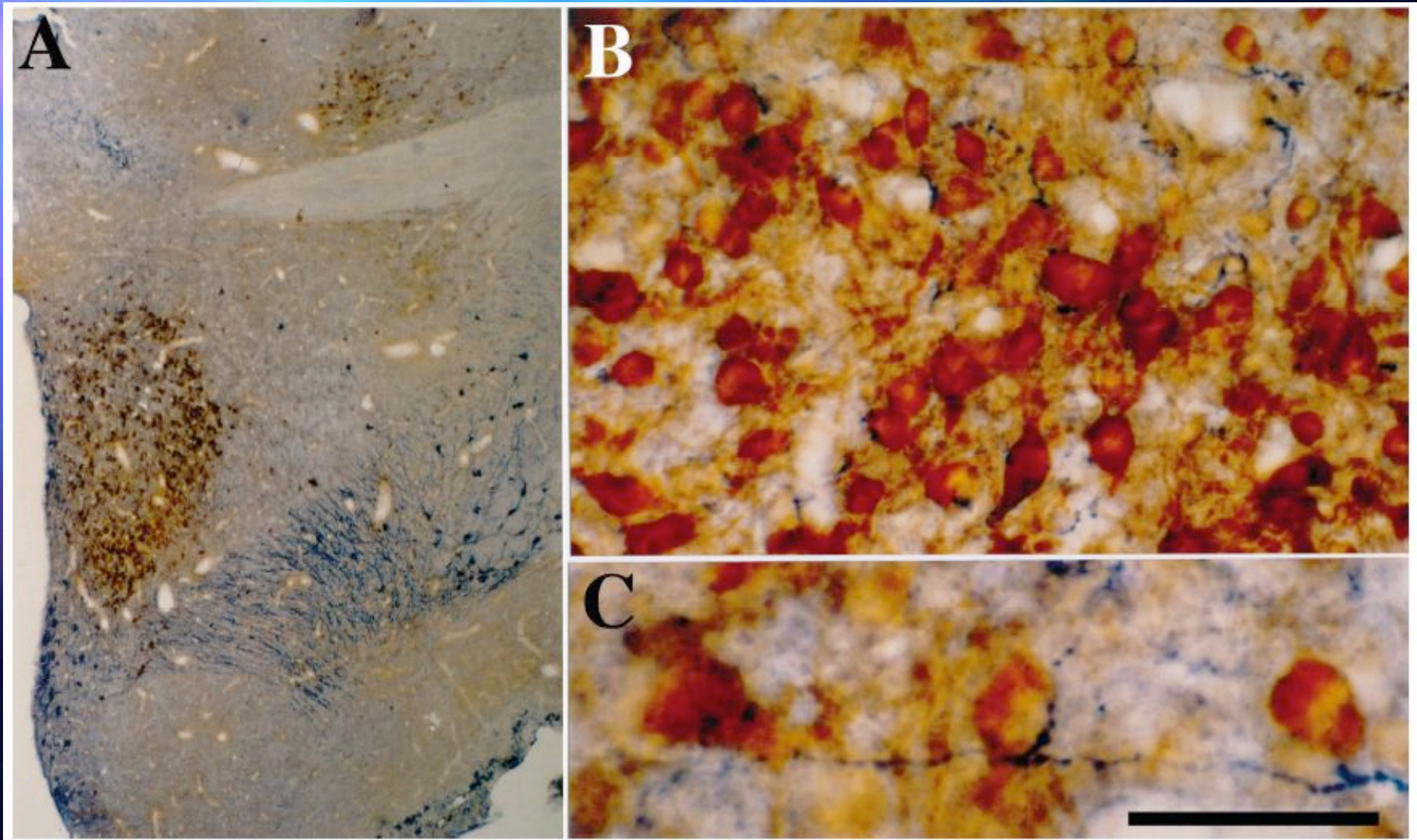
ARO-ir si trova nei terminali presinaptici



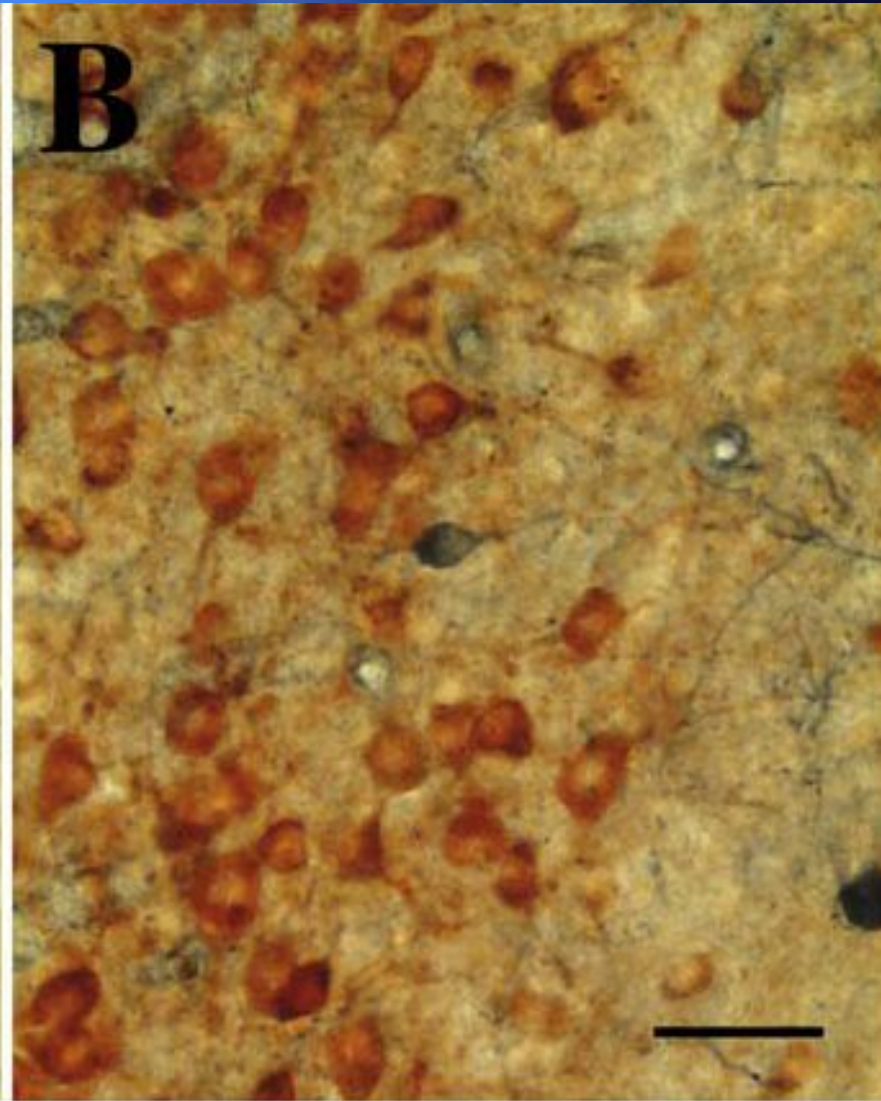
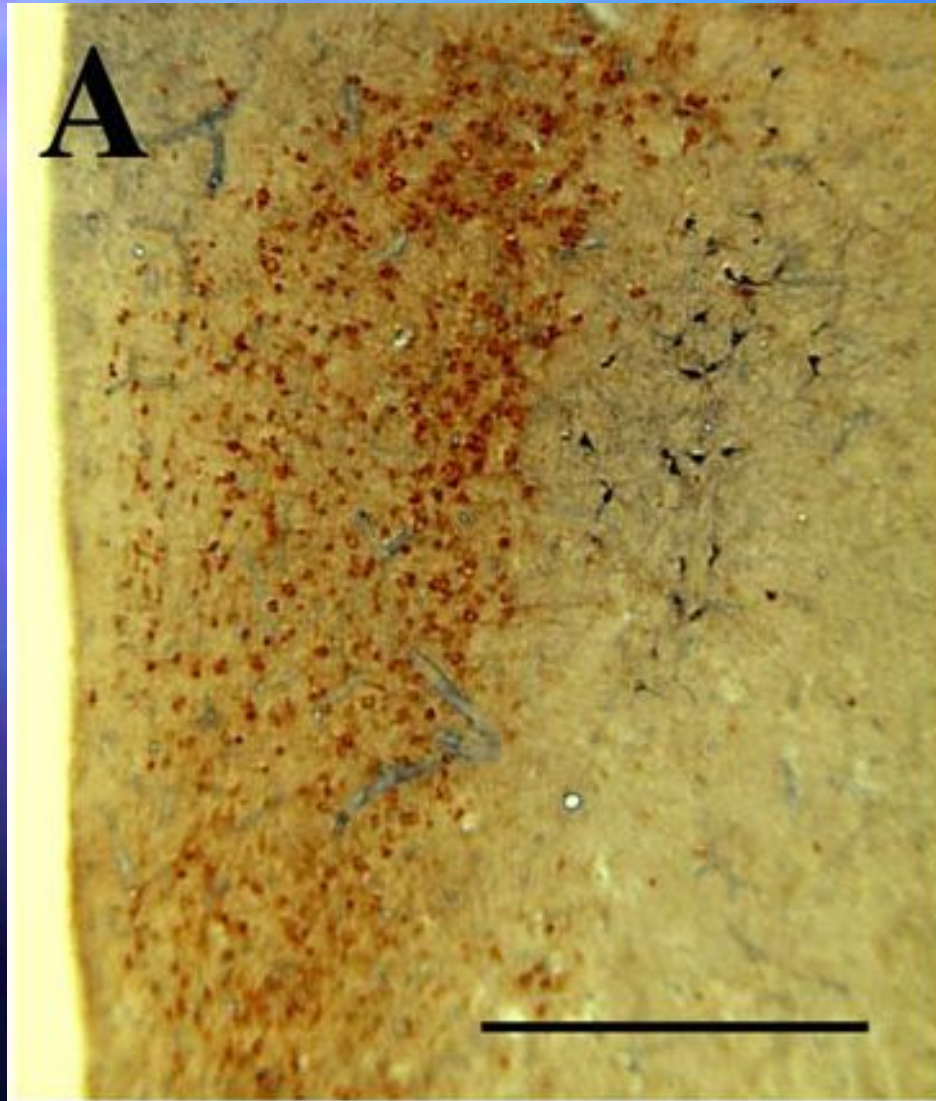
Innervazione catecolaminergica dei neuroni ARO-ir



I neuroni ARO-ir sono innervati da fibre a VT



Innervazione da parte di fibre NOS-ir



Afferenze e steroidi sessuali

- Le fibre catecolaminergiche provengono dall'Area Ventrale ed in particolare da cellule che presentano recettori per gli estrogeni
- Le fibre a VT sono sessualmente dimorfiche e provengono dal BST ove sono molto numerosi i recettori per gli estrogeni e gli androgeni
- L'espressione della NOS è a sua volta estrogeno-dipendente.

