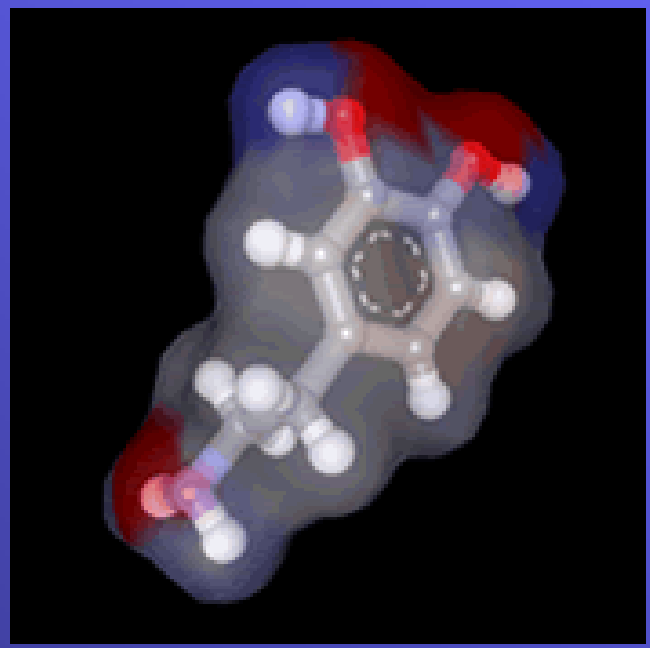
DOPAMINE RECEPTORS



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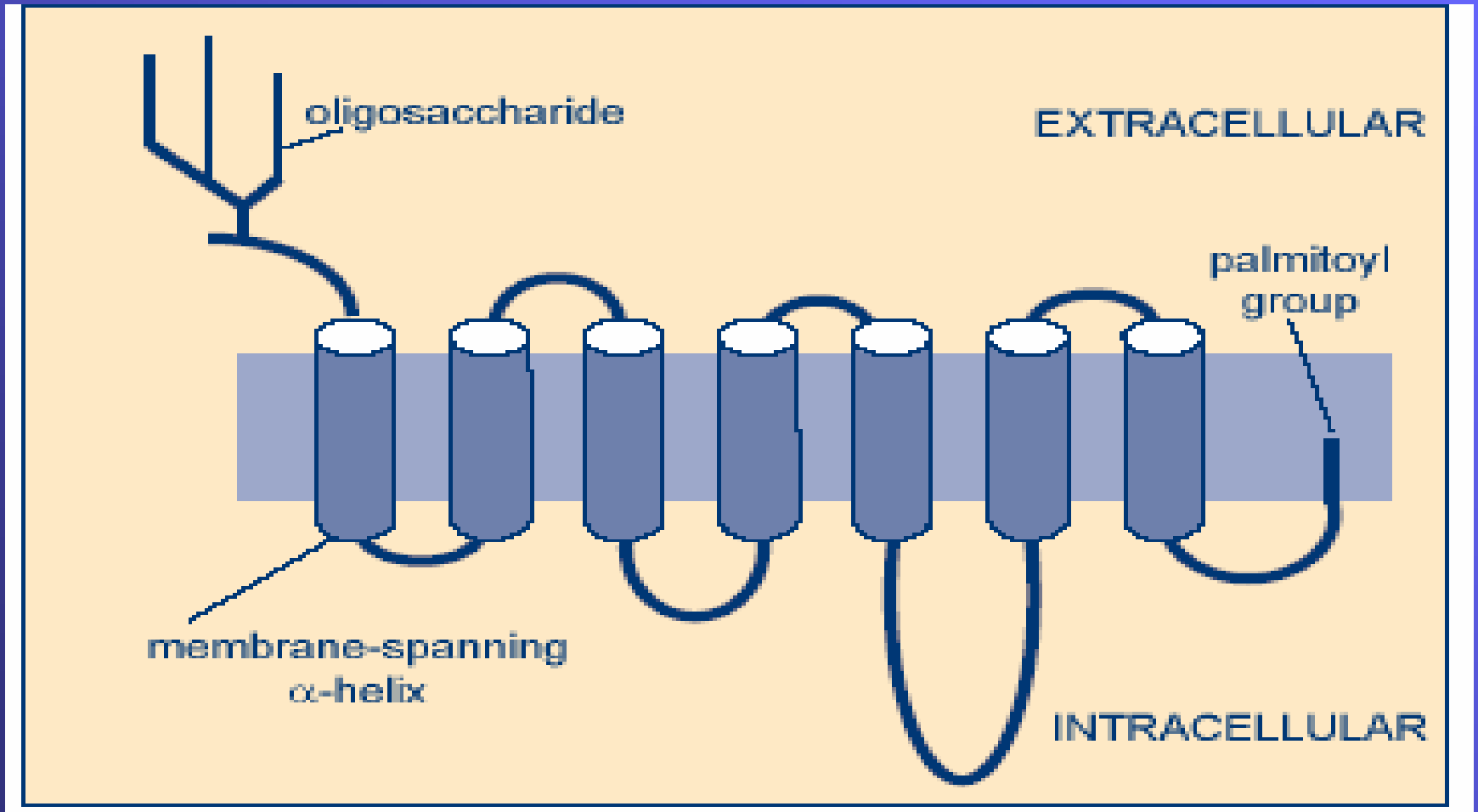
OUTLINE

- **Functions of Dopamine**
- **Dopamine Receptors structure**
- **Dopamine Receptors**
  - D1 & D2 Family
- **Regulation of Dopamine**

Roles of Dopamine

- Role in movement
- Role in pleasure and motivation
- Controls the flow of information from other areas of the brain

Structure of Dopamine Receptors

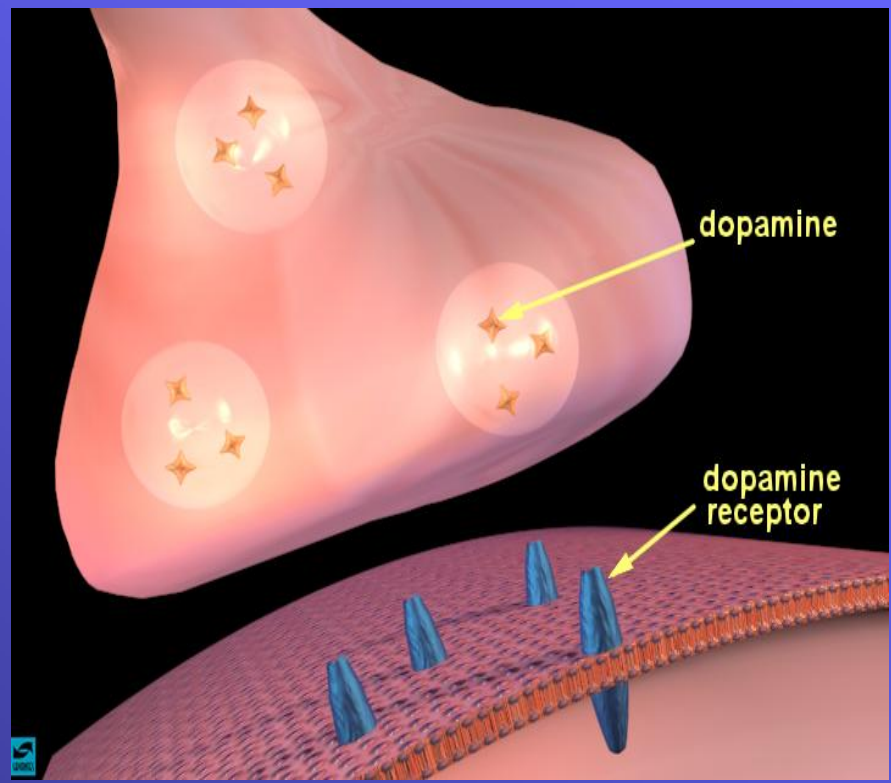


Dopamine Receptors

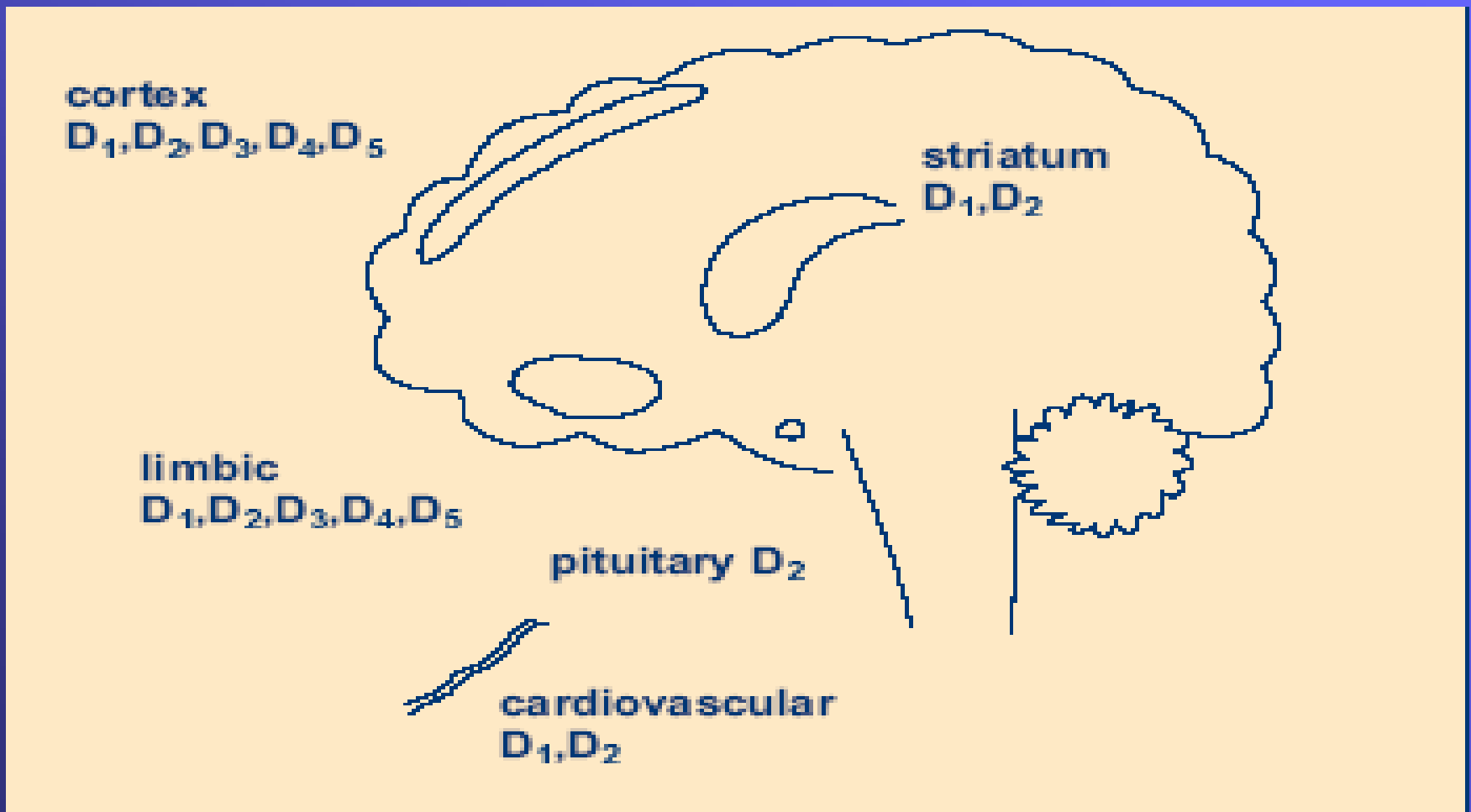
- There are five types of dopamine receptors.D1,D2,D3,D4,D5.
- We can catogorize dopamine receptors in two two main subtypes:
- **D1 like receptor family:** the Gs protein is involved and adenylyl cyclase would be activated. The action of the enzyme causes the conversion of adenosine triphosphate to cyclic adenosine monophosphate (cAMP).
- **D2 like receptor family**: which is the receptor combining with the Gi protein and its activated alpha-subunit then inhibits adenylyl cyclase so that the concentration of cAMP is reduced.

Dopamine Receptors

- Five subtypes of dopamine receptor have been cloned. The D1 and D5 receptors are closely related, and couple to Gs alpha and stimulate adenylyl cyclase activity. In contrast, the D2, D3 and D4 receptors couple to Gi alpha and inhibit the formation of cAMP.

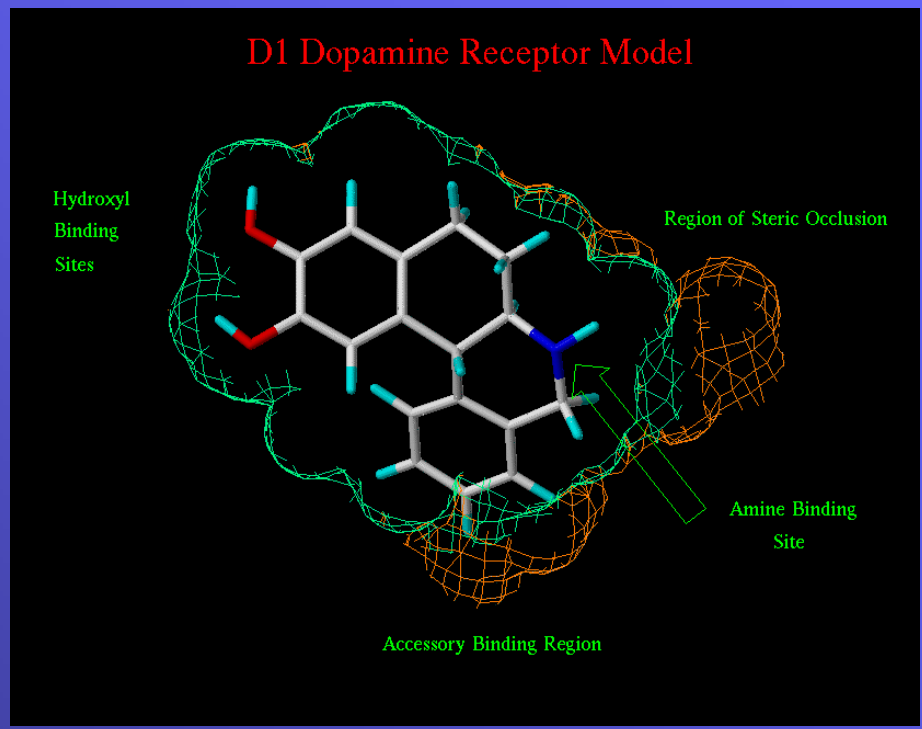


Distribution of Dopamine Receptors



D1 receptors

- Most abundant receptor in the central nervous system
- Lack of introns
- 446 aa
- Higly expressed in basal ganglia
- Chromosome 5
- Stimulate AC



D5

- Intronless
- 477aa
- 50% homology with D1
- Chromosome 4
- Very striking gene control pseudogene that %90 homology with D5
- Expression in nucleus of thalamus ;suggesting that role in pain stimuli
- Stimulate AC

D2

- 7 introns
- Third cytoplasmic domain is long and the carboxyl terminus is short
- Chromosome 11
- Inhibtit AC,phospoinositide turnover
- Activation of potassium channel,potentiation of arachidonic acid release

- Two isoforms;D2L and D2s by alternative splicing.
- Similar profiles in terms of affinity but different in regulation.
- Higly expressed in basal ganglia,nucleus accumbes septi,ventral tegmental area

D3

- Five introne s
- 446aa
- Chromosome 3
- As a functional receptor remains uncertain
- Similarity to D2 and the expression areas may give qlue
- Recent study shows it might mediate positive regulatory influences of Da on production of neurotension.

D4

- 4 introns
- 387 aa
- Homology with D2 and D3 41% and 39%
- Chromosome 11
- Hippocampu and frontal cerebral cortex

Dopamine 1 (DA1) Receptor agonists

- Fenoldopam
- Piribedil
- Ibopamine
- SKF 3893
- Apomorphine

Therapeutic uses of DA1 Receptor Agonists

- Decreases peripheral resistance
- Inducing lowering of arteriel blood pressure-increases in heart rate and increases in sympathetic tone
- Increases in activity of the renin aldosterone system

Dopamine 2 (DA 2) Receptor Agonists

- Bromocriptine
- Pergolid
- Lisuride
- Guinpirole
- Carmoxirole

Theraputic uses of DA2 receptor agonists

- Used for treating Parkinson's disease
- Inhibits protactin release (which decreases tumor size)

DA 1 Receptor Antagonists

- SCH23390
- Clozapine (used for treating schizophrenia

DA 2 Receptor Antagonists

- Metoclopramid
- Domperidone
- Sulpiride
- Haloperidol

- Gastric Motility Disorders