GLUTAMATE RECEPTORS

SUBMITTED BY

ÖZGE ŞENYURT
MİNE NUYAN
ERTAN ÖZERTAN
M. EMRE ÖZDEMİR
Glutamate is the major excitatory neurotransmitter in the mammalian CNS, acting through both ligand gated ion channels (ionotopic receptors) and G-protein coupled (metabotopic) receptors.

Glutamate receptors play a vital role in the mediation of excitatory synaptic transmission.
Glutamate acts on:

- **NMDA-receptor family**
  - NMDAR1
  - NMDAR2A, ...

- **AMPA-receptor family**
  - GluR1
  - GluR2
  - GluR3
  - ...
  - GluR6

- **Kainate-receptor family**

**Receptor subunits**

- **Metabotropic receptors**
  - **Group I** (Phospholipase C activation)
    - mGlu1A
    - mGlu5A
  - **Group II** (Adenylyl cyclase inhibition)
    - mGlu2
    - mGlu3
  - **Group III** (Adenylyl cyclase inhibition)
    - mGlu4, mGlu8
    - mGlu6, mGlu6
Figure 2. General structure of an ionotropic glutamate receptor subunit. Ionotropic glutamate receptor subunits follow the same basic structural pattern with an extracellular N-terminus and large loop that together form the ligand binding domain. The C-terminus is intracellular and is often the site of splice variation and interaction sites with intracellular proteins.
Fig. 6a. Non-NMDA receptors are selectively agonized by kainate, AMPA and quisqualate. The associated ion channels are more permeable to Na+ and K+ ions than Ca+2 (from Kandel et al., 1991).

Fig. 6b. NMDA receptors are structurally complex, with separate binding sites for glutamate, glycine MG+2, Zn+2 and polyamines. NMDA-gated channels are more permeable to Ca+2 than Na+ ions (from Kandel et al., 1991).
NON-NMDA RECEPTORS

- Give immediate response upon binding of glutamate
- More permeable to Na\(^+\) & K\(^+\) than Ca\(^+\)
- Influx of Na\(^+\) causes depolarization of the membrane which is the major factor for activating NMDA type receptors
Unlike non NMDA receptors, they require a co-agonist GLYCINE.
Because, as long as the membrane remains polarised, the pore of the channel is blocked by physiological, extracellular concentration of Mg$^{2+}$. 
Metabotropic Glutamate (mGlu) Receptors

- Metabotropic glutamate (mGlu) receptors are G-protein coupled receptors (GPCRs).

**Fig. 5a.** Ionotropic receptors and their associated ion channels form one complex (top). Each iGluR is formed from the co-assembly of multiple (4-5) subunits (From Kandel et al., 1991).

**Fig. 5b.** Metabotropic receptors are coupled to their associated ion channels by a second messenger cascade (top). Each mGluR is composed of one polypeptide, which is coupled to a G-protein (from Kandel et al., 1991).
They are not co-assembled from multiple subunits, but are one polypeptide with common 7 transmembrane domain.
They have been subdivided into three groups, based on

- sequence similarity,
- pharmacology
- intracellular signalling mechanisms
Figure 7. Classification of the metabotropic glutamate receptors.
Metabotropic glutamate receptor groups (from Pin and Duvoisin, 1995).

<table>
<thead>
<tr>
<th>group</th>
<th>mGluR</th>
<th>agonist(s)</th>
<th>intracellular pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>mGluR1, mGluR5</td>
<td>quisqualate, ACPD</td>
<td>increase phospholipase C activity, increase cAMP levels, increase protein kinase A activity</td>
</tr>
<tr>
<td>II</td>
<td>mGluR2, mGluR3</td>
<td>L-CCG-1, ACPD</td>
<td>decrease cAMP levels</td>
</tr>
<tr>
<td>III</td>
<td>mGluR4, mGluR6, mGluR7, mGluR8</td>
<td>L-AP4 (APB)</td>
<td>decrease cAMP or cGMP levels</td>
</tr>
</tbody>
</table>
REFERENCES

http://www.webvision.med.utah.edu/GLU.html

http://www.bris.ac.uk/Depts/Synaptic/info/glutamate.html
THANK YOU FOR YOUR ATTENTION