

The glutamate story

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Supplementary Information

Contents: Eight figures showing the chemical structures of ligands that interact with glutamate receptors. References are given for reviews that contain further information on the pharmacology of these ligands.

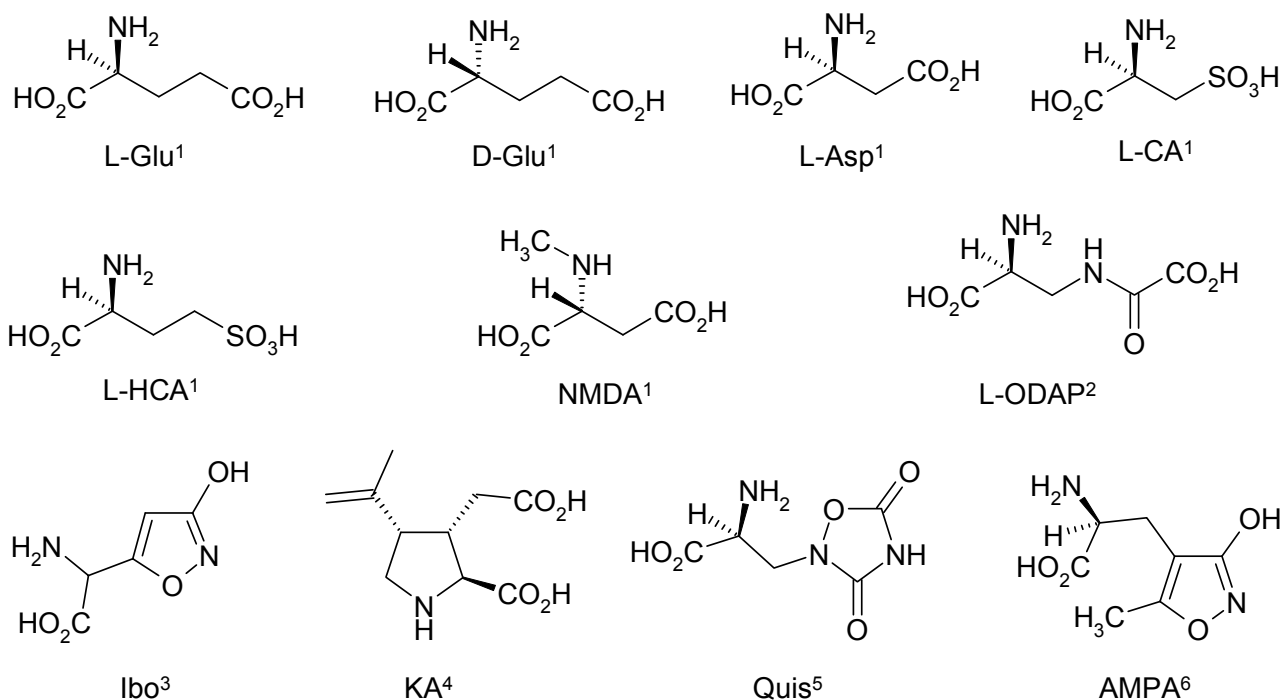


Fig 1. Structures of excitatory amino acids, with dates of first reports. 1, 1959-61; 2, 1965; 3, 1968; 4, 1970; 5, 1974; 6, 1980. See reviews by Curtis and Watkins, 1965; Curtis and Johnson, 1974; Watkins and Evans, 1981. Abbreviations: glu, glutamic acid; asp, aspartic acid; CA, cysteic acid; HCA, homocysteic acid; NMDA, N-methyl-D-aspartic acid; ODAP, β -N-oxalyl- α,β -diaminopropionic acid; ibo, ibotenic acid; KA, kainic acid; quis, quisqualic acid; AMPA, α -amino-3-hydroxy-5-methylisoxazole-4-propionic acid.

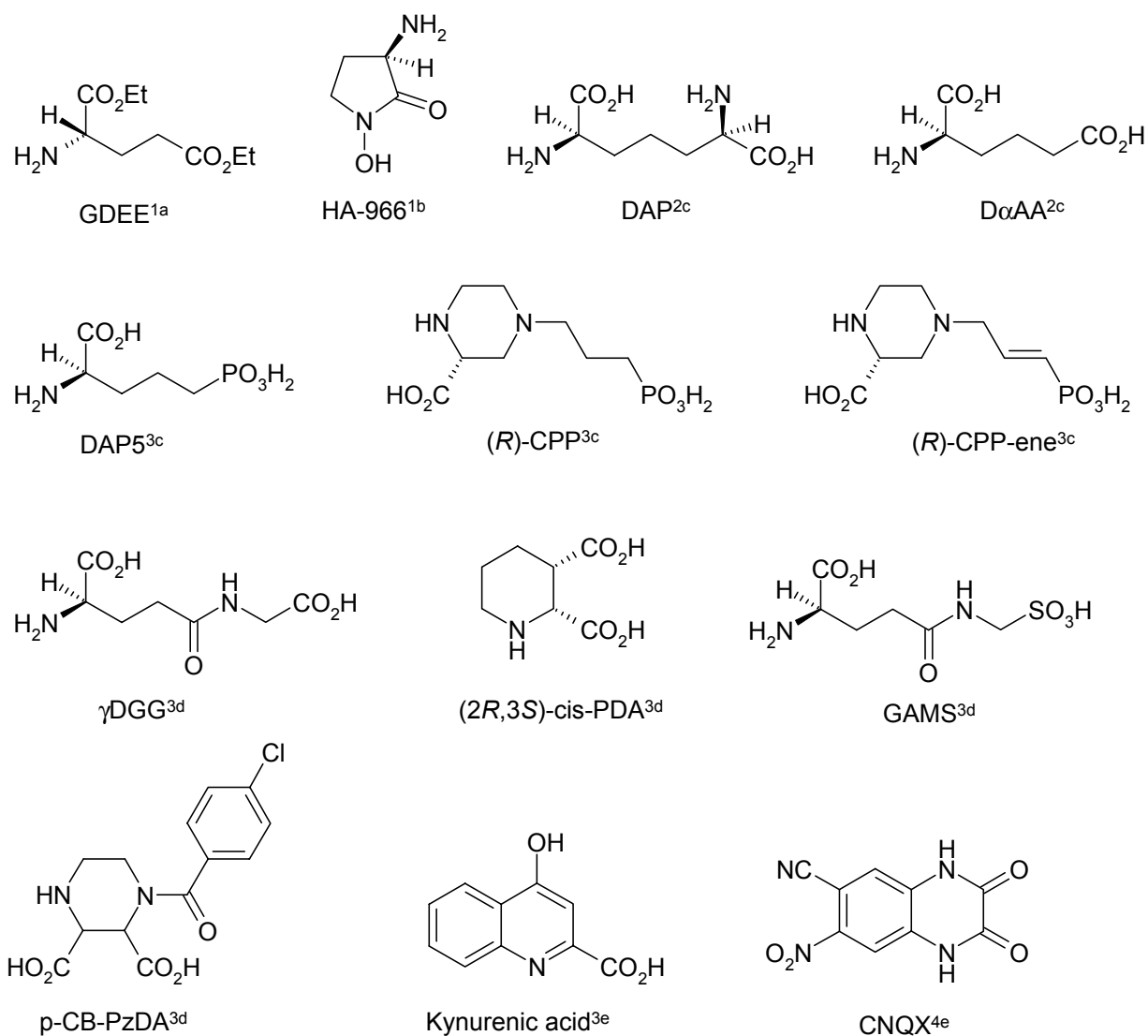
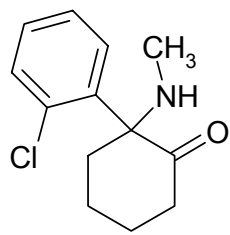
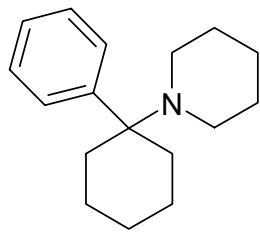


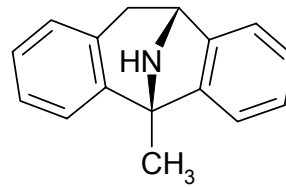
Fig 2. Structures of a range of early excitatory amino acid antagonists, with dates of first reports and receptor selectivities. 1, 1970-1; 2, 1976-7; 3, 1981-4; 4, 1988. a, quisqualate (AMPA); b, NMDA glycine site; c, NMDA glutamate site; d, NMDA glutamate site/quisqualate (AMPA)/kainate; e, NMDA glycine site/quisqualate(AMPA)/kainate. Reviewed by Watkins and Evans, 1981; Watkins, Krogsgaard-Larsen and Honoré, 1990; Jane et al., 1994.



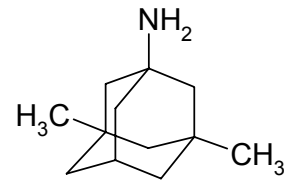
Ketamine¹



Phencyclidine (PCP)¹



MK-801²



Memantine³

Fig 3. Structures of some early NMDA receptor ion channel blockers, with dates of first reports. 1, 1982-3; 2, 1986; 3, 1992. Reviewed by Lodge et al., 1994; Kew and Kemp, 2005.

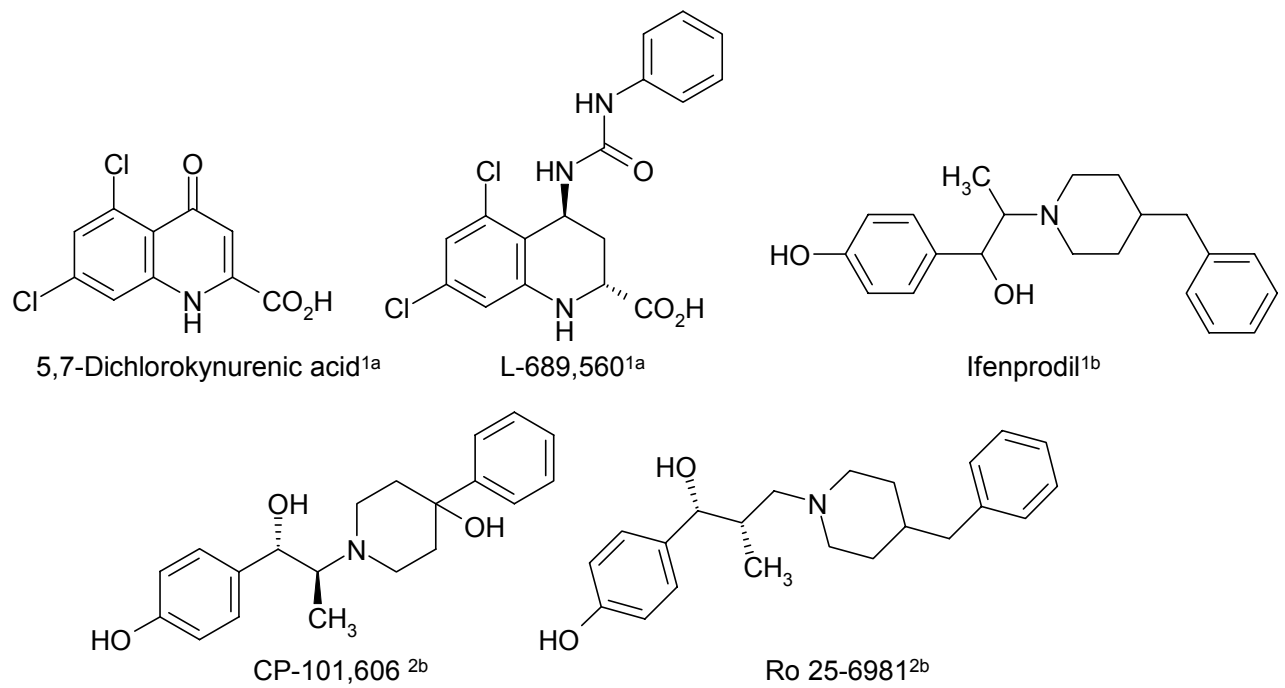


Fig 4. Structures of some NMDA receptor glycine (a) and polyamine site antagonists (b), with dates of first reports. 1, 1989-1992; 2, 1998. Reviews by Leeson and Iverson, 1994; Monaghan et al, 2004.

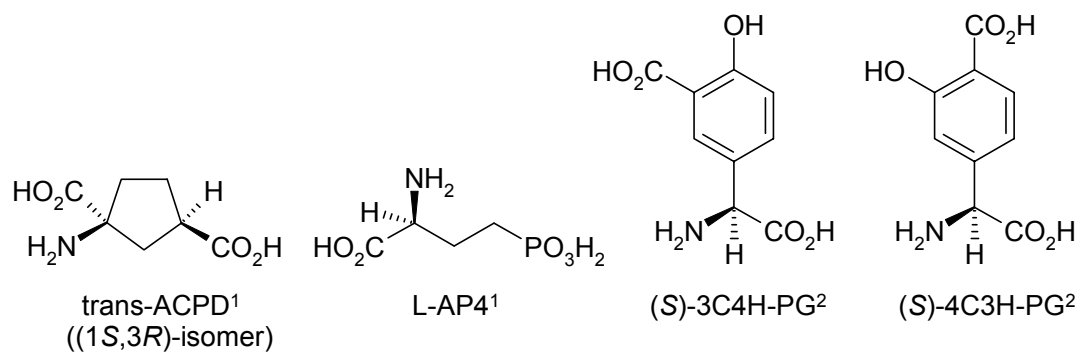
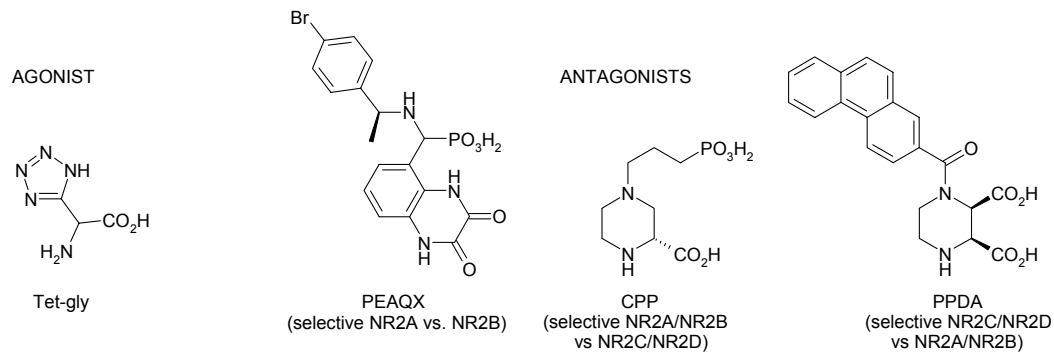
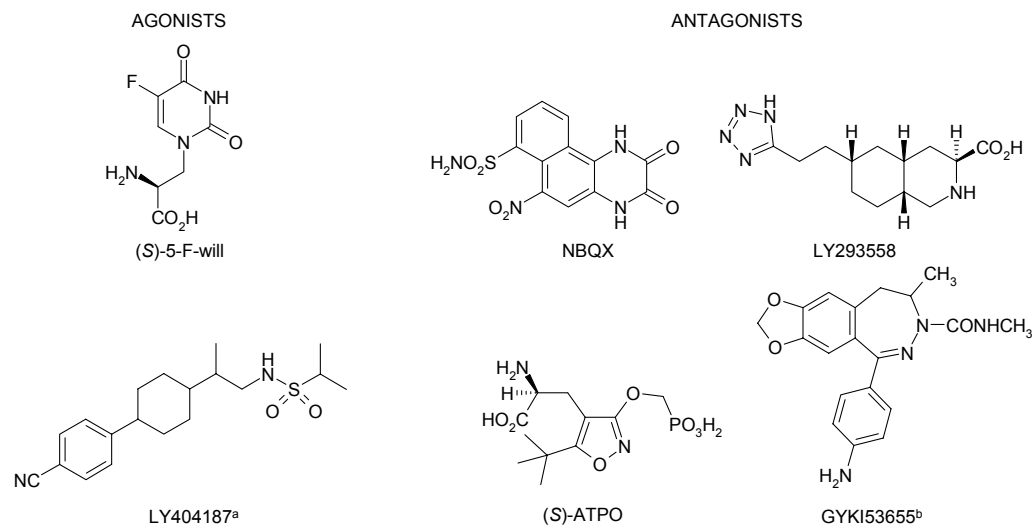


Fig 5. Structures of compounds useful in early identification of metabotropic glutamate receptors, with dates of first reports. 1, 1979-82; 2, 1987; 3, 1992. Reviewed by Monaghan et al., 1989; Watkins and Collingridge, 1994; Schoepp et al., 1999.

A. NMDA receptor

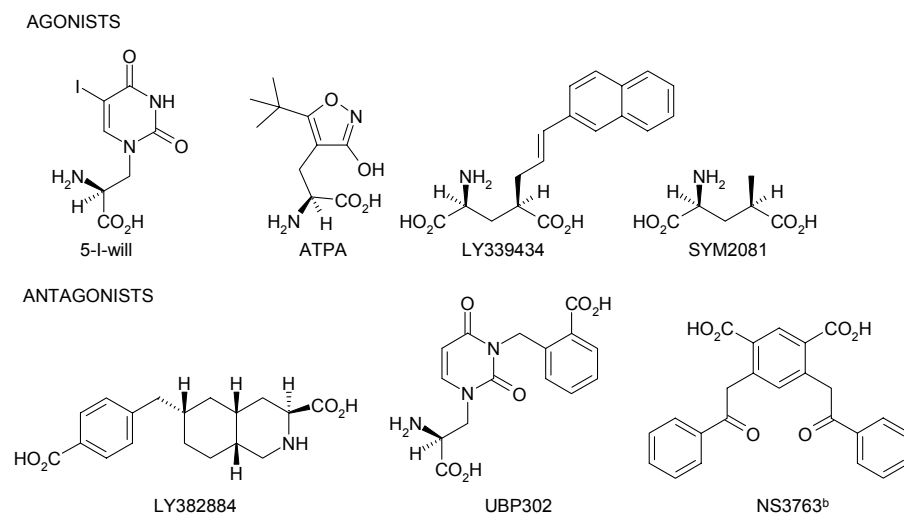


B. AMPA receptor



^a Positive allosteric modulator ^b Negative allosteric modulator

C. Kainate receptor

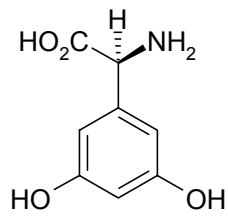


^b Negative allosteric modulator

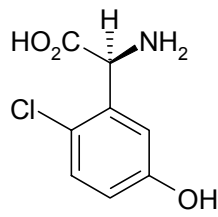
Fig 6. Selective agonists and antagonists for NMDA, AMPA, and kainate ionotropic glutamate receptors.

GROUP I mGlu receptors

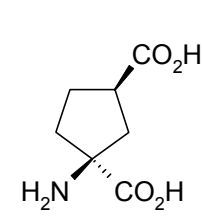
AGONISTS



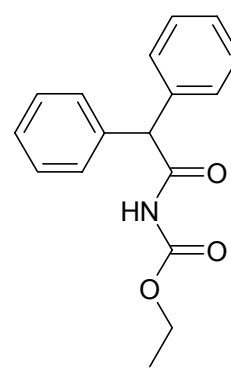
(S)-DHPG



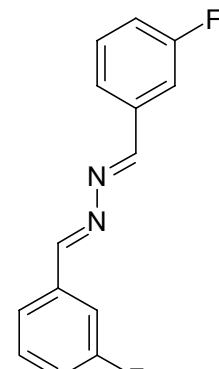
CHPG
(mGlu5)



(1S,3R)-ACPD



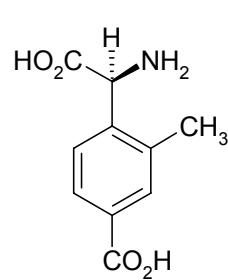
Ro 01-6128^a
(mGlu1)



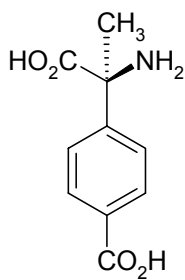
DFB^a
(mGlu5)

^a Positive allosteric modulator

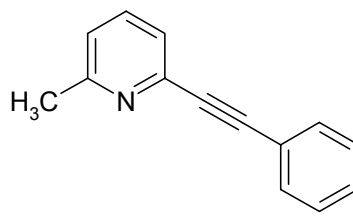
ANTAGONISTS



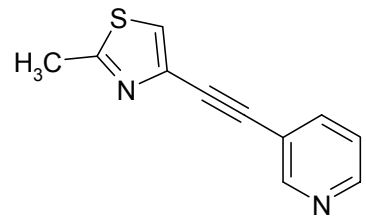
LY367385 (mGlu1)



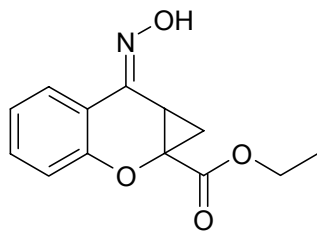
(S)-MCPG



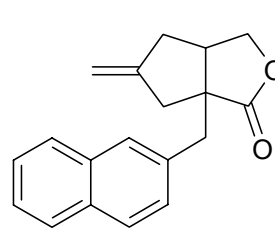
MPEP^b
(mGlu5)



MTEP^b
(mGlu5)



CPCCOEt^b
(mGlu1)

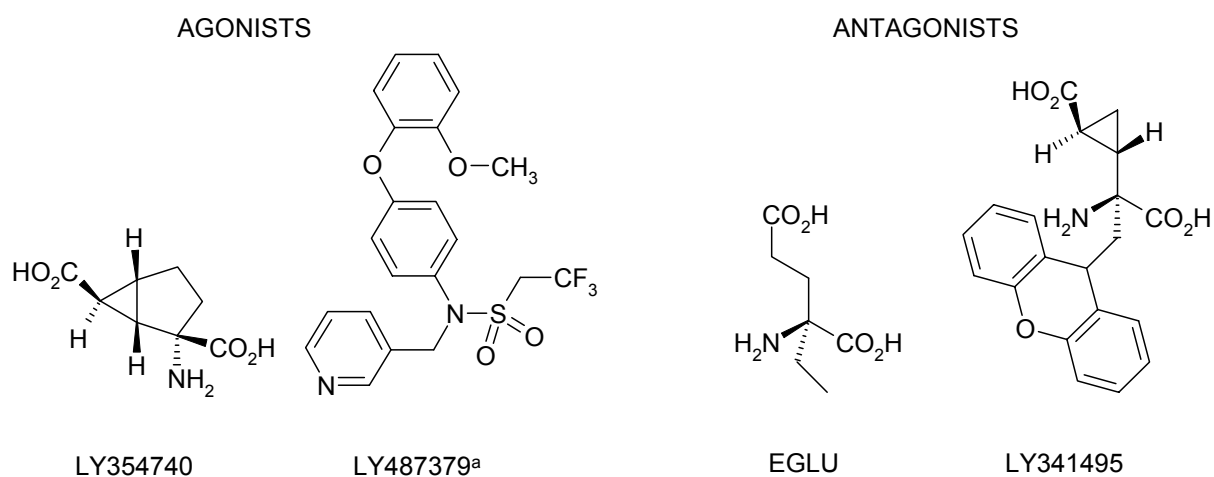


BAY36-7620^b
(mGlu1)

^b negative allosteric modulator

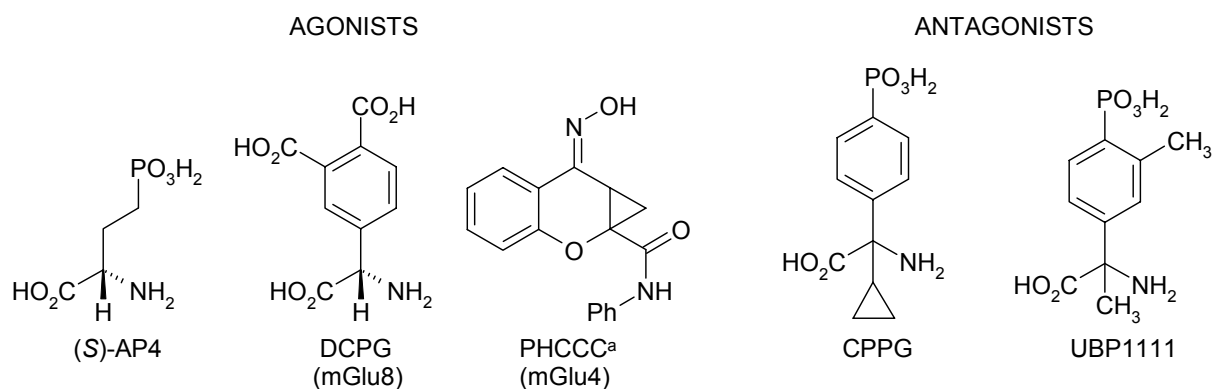
Fig 7. Selective agonists and antagonists for group I metabotropic glutamate receptors.

GROUP II mGlu receptors



^a Positive allosteric modulator

GROUP III mGlu receptors



^a Positive allosteric modulator of mGlu4 and negative allosteric modulator of mGlu1

Fig 8. Selective agonists and antagonists for group II and III metabotropic glutamate receptors.

References

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