5. Het nicotine systeem, basics Richard

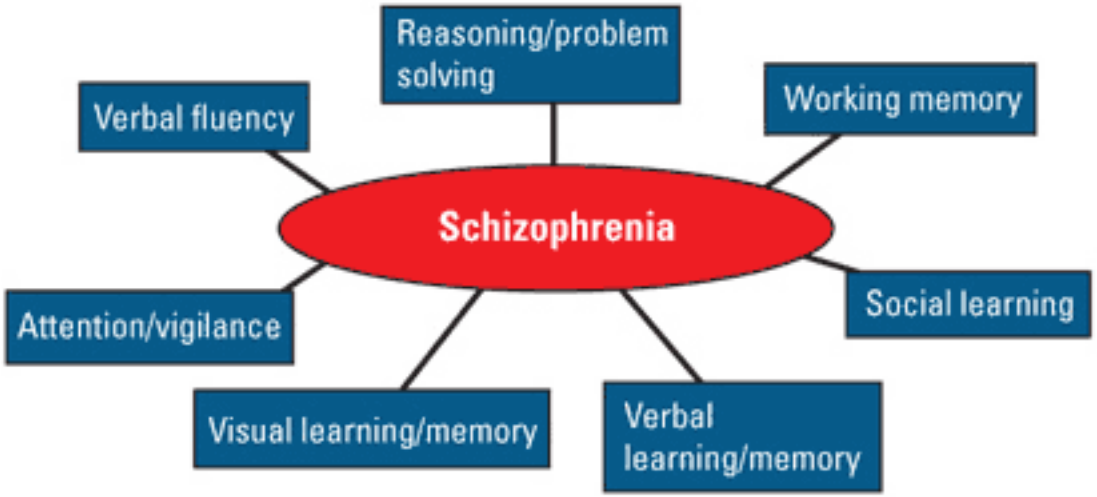
- Nicotine, Muscarine receptoren,
  - perifeer,
  - centraal,

- Wat voor soort receptoren zijn dit?
  - (langzaam? Snel? Ion-kanaal)

- geneesmiddelen die hier op inwerken.

MATRICS

Neuropsychological deficits in schizophrenia.[16]



The MATRICS group determined seven separable cognitive dimensions that are affected in schizophrenia.

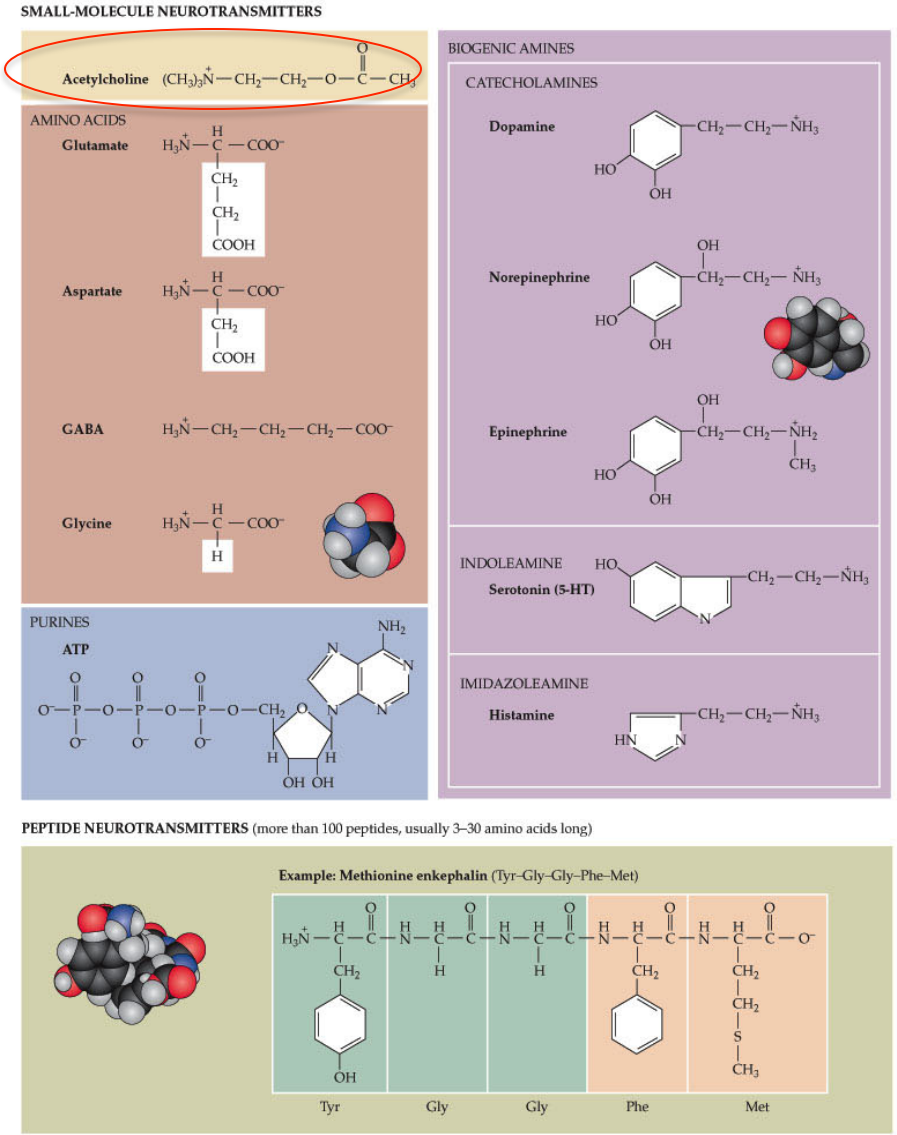
MATRICS=Measurement and Treatment Research to Improve Cognition in Schizophrenia.

Acetylcholine:

-Motoriek
-Aandacht
-Leren
-Geheugen

Target in Alzheimer en Parkinsonen
myasthenia gravis

Acetylcholine:



NEUROSCIENCE, Fourth Edition, Figure 6.1

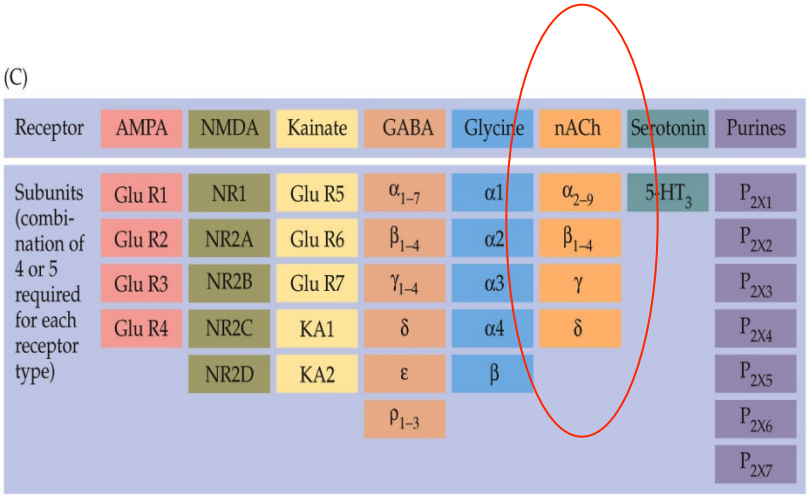
Acetylcholine

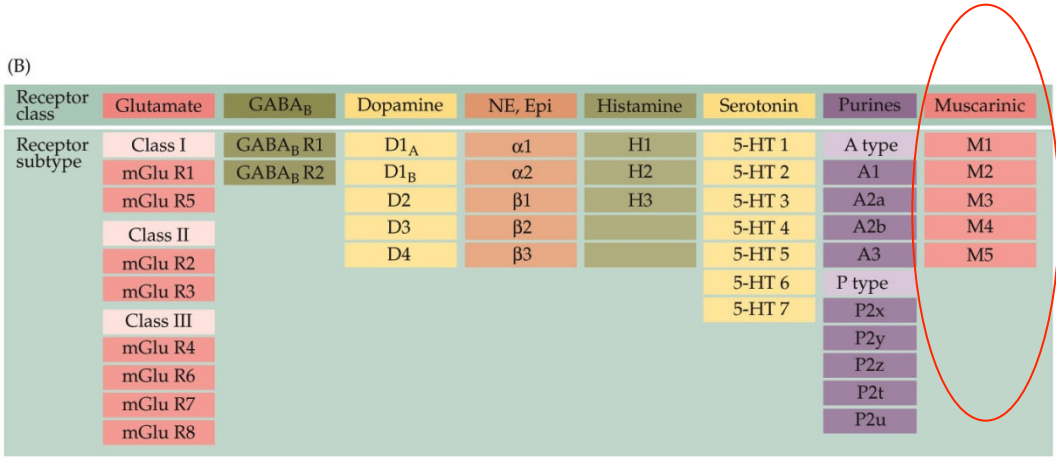
Muscarine Receptor

Nicotine Receptor

snel: ion kanaal receptoren (ionotropic)
snel

neuromodulatie: G-protein gekoppelde receptoren (metabotropic)
langzaam





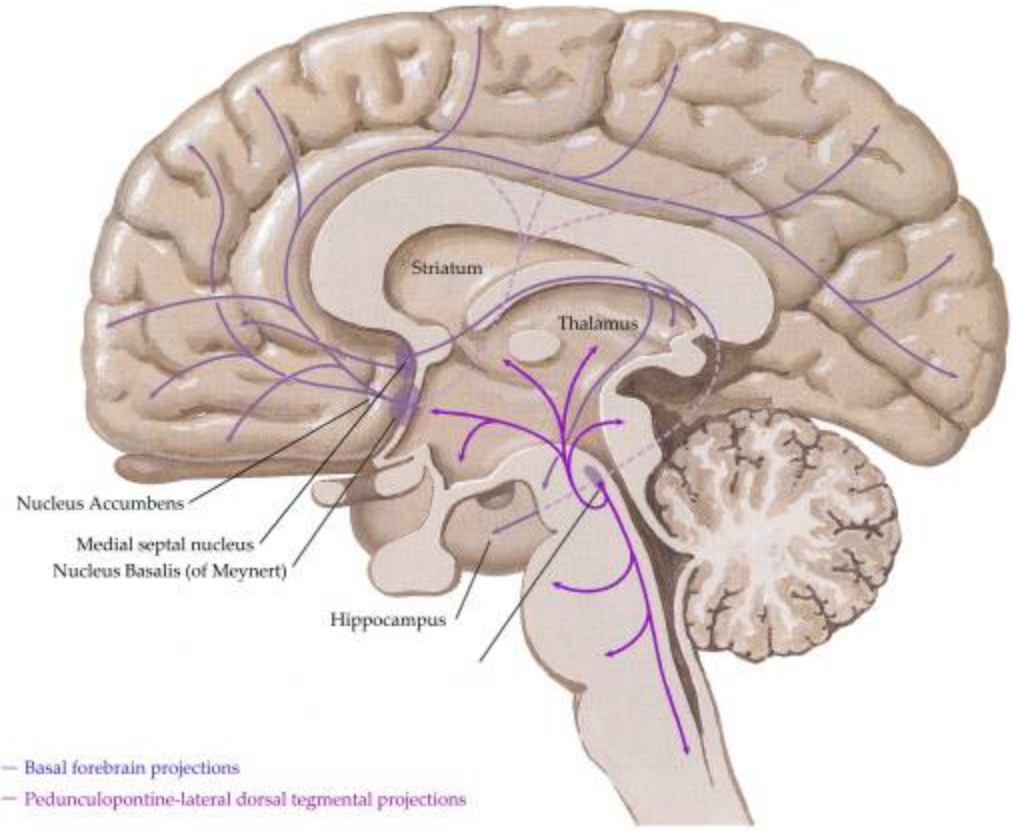
Spier
Neuronaal

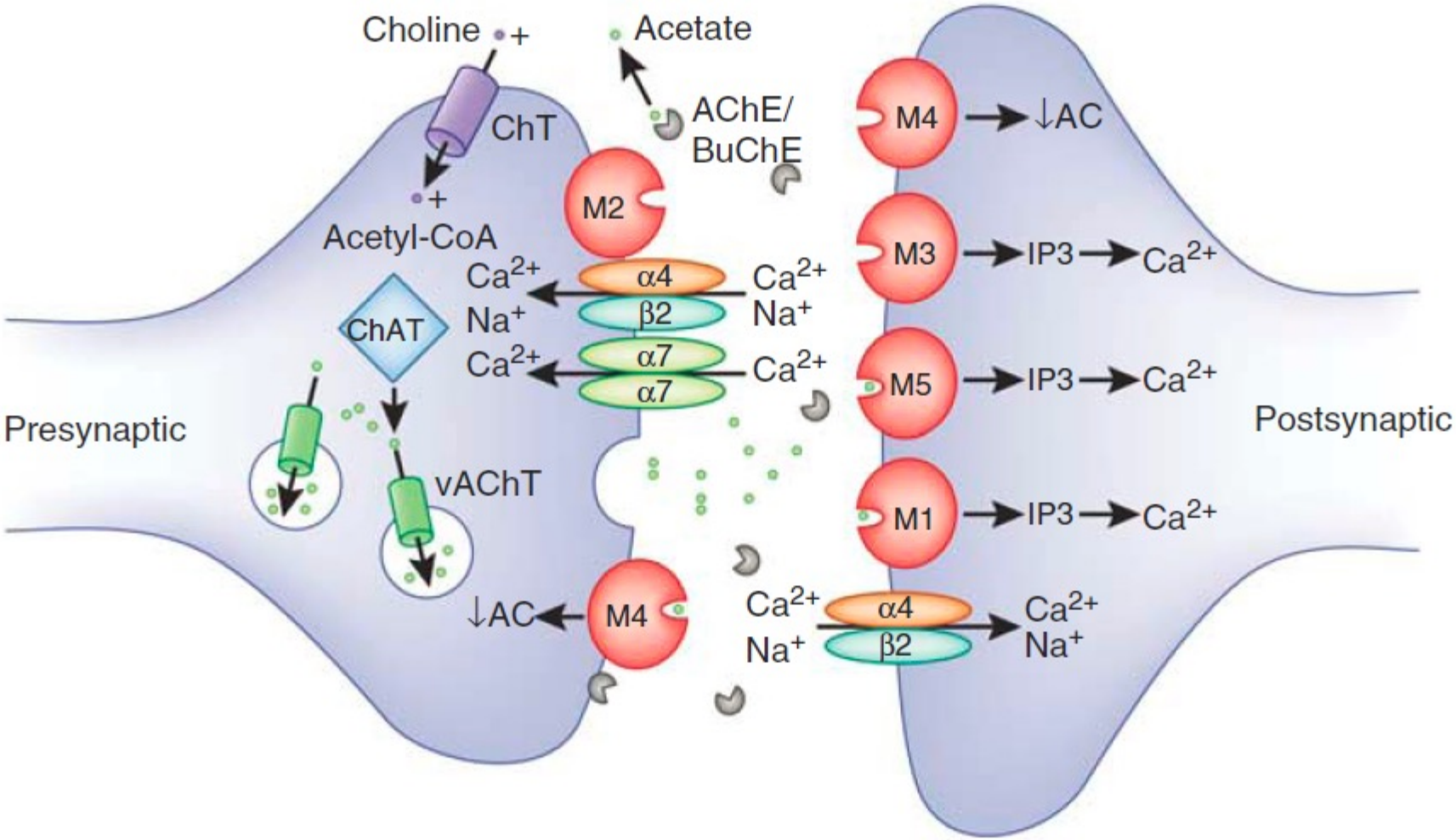
Nicotine Receptor

Rest & digest
Neuronaal

Muscarine Receptor

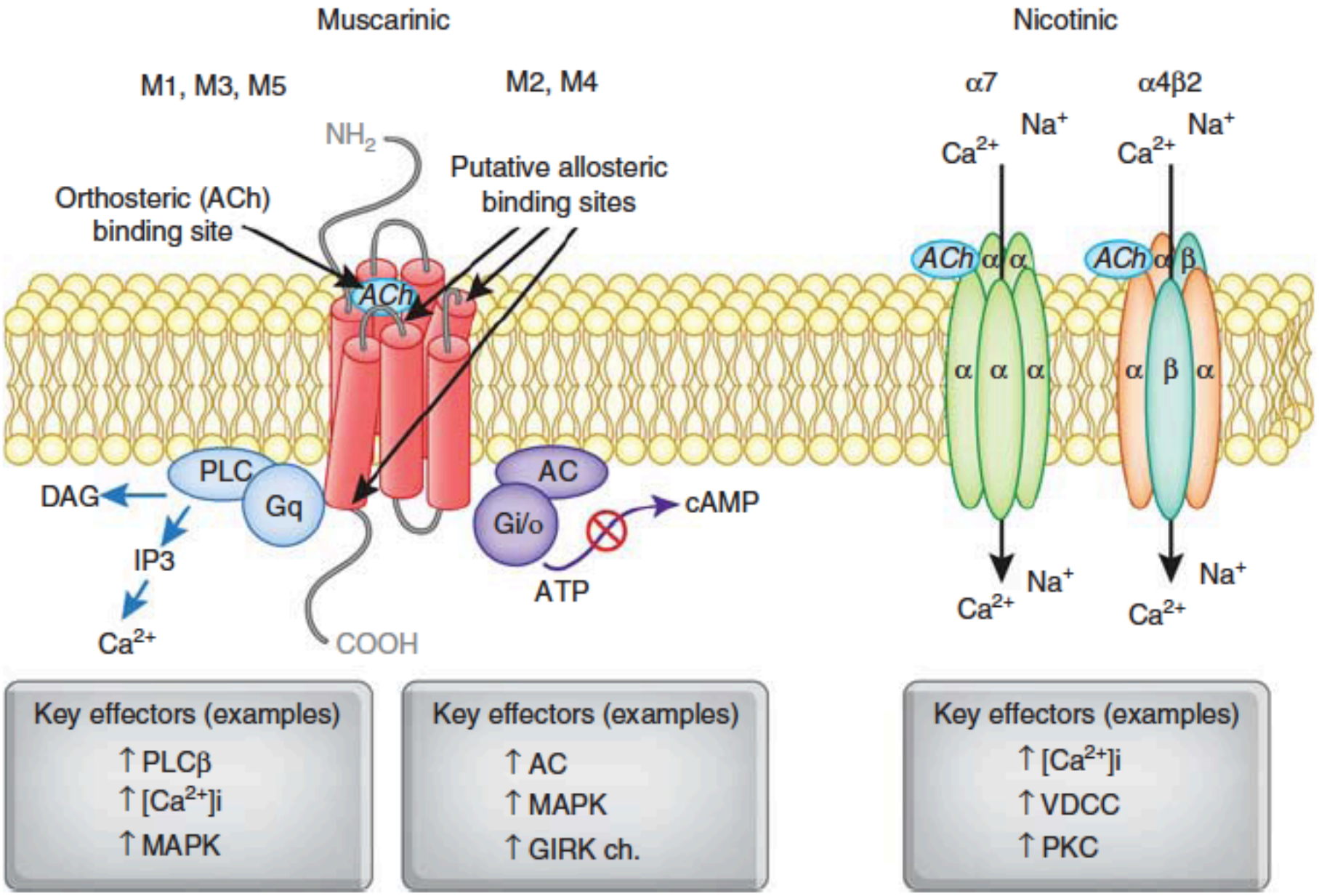
Projecties: - vanuit hersenstam
- vanuit basale kernen Meynert
- interneuronen in striatum





Jones et al 2012

Problemen vinden specifieke compounds…



Cholinerge hypothese psychose (1975)

Postmortem studies:

-verlaagde muscarine en nicotine receptoren in patienten met SCZ
-verlaagde ChAT in patienten met SCZ

Challenge studies:
-mACh en nAch receptor antagonist verergeren positieve/cognitieve symptomen in patienten met SCZ en induceren deze in gezonde vrijwilligers

-mACh en nACh agonist en AChEI kunnen symptoomverlichting geven

TABLE 2.
Location and Function of Muscarinic Receptors[18-21,23,24,35-44]

	Location	***Cellular Function***	***Systemic Function***	***Changes in Schizophrenia***
M_1	Striatum, cortex, hippocampus	Gq; Postsynaptic, modulate fast transmission and metabotropic function	Learning, memory, possible role in some types of epilepsy, cleave amyloid precursor protein, IL-2 production	Down in hippocampus, stratum, PFC, NAc
M_2	Basal forebrain, thalamus, heart, brainstem, pupil, exocrine glands, spinal cord	Gi; Presynaptic inhibitory auto/heteroreceptor	Salivation, akinesia, bradycardia, smooth muscle contractility, bronchoconstriction, tremor, hypothermia, analgesia, axonal growth	Down in striatum
M_3	Brain (evenly distributed), pupil, hypothalamus, exocrine glands, peripheral arteries	Like M_1	Salivation, smooth muscle contractility, vasorelaxation, NO release, appetite	Unknown
M_4	Striatum, cortex, hippocampus, spinal cord	Like M_2 plus inhibitory postsynaptic	Regulate striatal DA release, modulate PPI, analgesia, keratinocyte migration	Down in hippocampus, stratum, PFC, NAc
M_5	DA neurons, basal ganglia, brain vasculature	Like M_1	Cerebral arterial vasorelaxation	Unknown

M=muscaranic; Gq=G protein that activates phospholipase C; Gi=inhibitory G protein; PFC=prefrontal cortex; DA=dopaminergic; NAc=nucleus accumbens; PPI=pre-pulse inhibition.

Sellin AK, Shad M, Tamminga C. *CNS Spectr*. Vol 13, No 11. 2008.