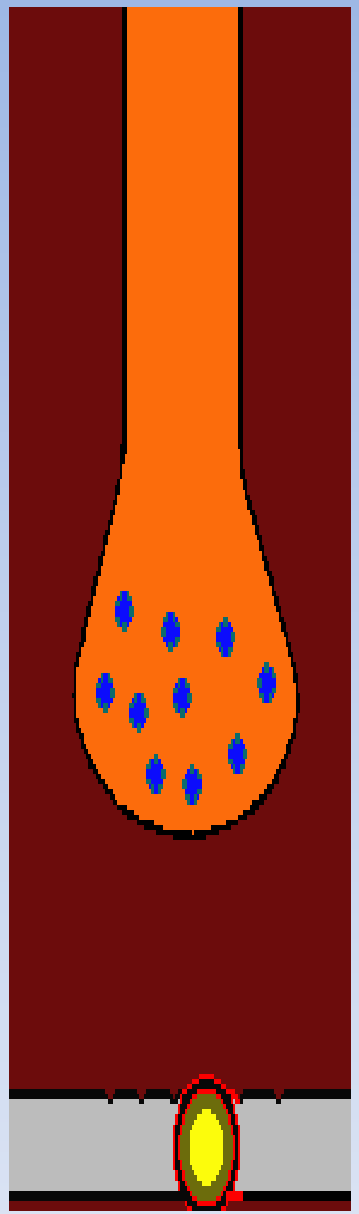
# serotonerjik receptors



Prof.Dr.Nuray Arı, 2018

# Serotonin Receptors & Functions

- Seven receptors, 5-$HT_1$- 5-$HT_7$ for serotonin are characterized, the first four have related functions
- All types are G-protein coupled receptor except 5-$HT_3$ receptors that are inotropic receptors

| Type | Distribution | Postulated Roles |
|---|---|---|
| 5-HT1 | Brain, instetinal nerves | Neuronal inhibition, behavioural effects, cerebral vasoconstriction |
| 5-HT2 | Brain, heart, lungs, smooth muscle control, GI system, blood vessels, platelets | Neuronal excitation, vasoconstriction, behavioural effects, depression, anxiety |
| 5-HT3 | Limbic system, ANS | Nausea, anxiety |
| 5-HT4 | CNS, smooth muscle | Neuronal excitation, GI |
| 5-HT5, 6, 7 | Brain | Not known |



http://slideplayer.com/slide/7766931/

# SEROTONIN RECEPTORS

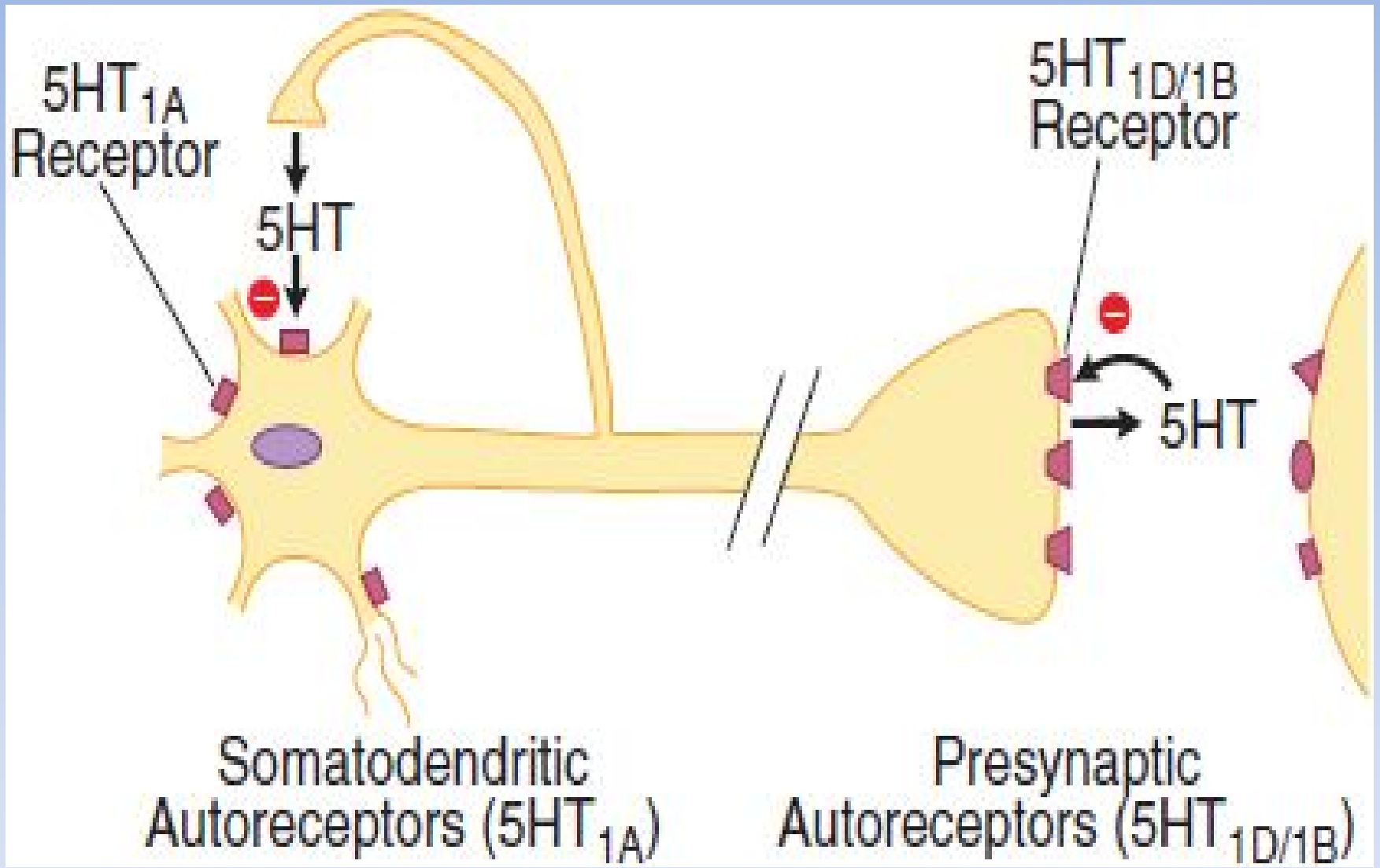
| Family | Type | Mechanism | Potential |
|---|---|---|---|
| $5\text{-}HT_1$ | G-protein coupled. | Decreasing cellular levels of cAMP. | Inhibitory |
| $5\text{-}HT_2$ | G protein coupled. | Increasing cellular levels of $IP_3$ and DAG. | Excitatory |
| $5\text{-}HT_3$ | Ligand-gated $Na^+$ and $K^+$ cation channel. | Depolarizing plasma membrane. | Excitatory |
| $5\text{-}HT_4$ | G-protein coupled. | Increasing cellular levels of cAMP. | Excitatory |
| $5\text{-}HT_5$ | G-protein coupled. | Decreasing cellular levels of cAMP. | Inhibitory |
| $5\text{-}HT_6$ | G-protein coupled. | Increasing cellular levels of cAMP. | Excitatory |
| $5\text{-}HT_7$ | G-protein coupled. | Increasing cellular levels of cAMP. | Excitatory |

| SUBTYPE | SIGNALING EFFECTOR | LOCALIZATION | FUNCTION | SELECTIVE AGONIST | SELECTIVE ANTAGONIST |
|---|---|---|---|---|---|
| $5HT_{1A}$ | ↓ AC | Raphe nuclei, cortex, hippocampus | Autoreceptor | 8-OH-DPAT | WAY 100135 |
| $5HT_{1B}$[a] | ↓ AC | Subiculum, globus pallidus, substantia nigra | Autoreceptor | — | — |
| $5HT_{1D}$ | ↓ AC | Cranial vessels, globus pallidus, substantia nigra | Vasoconstriction | Sumatriptan | — |
| $5HT_{1E}$ | ↓ AC | Cortex, striatum | — | — | — |
| $5HV_{1F}$[b] | ↓ AC | Brain and periphery | — | — | — |
| $5HT_{2A}$[c] | ↑ PLC, $PLA_2$ | Platelets, smooth muscle, cerebral cortex | Aggregation, contraction, neuronal excitation | α-$CH_3$-5HT, DOI, MCPP | Ketanserin, LY53857 |
| $5HT_{2B}$ | ↑ PLC | Stomach fundus | Contraction | α-$CH_3$-5HT, DOI | LY53857 |
| $5HT_{2C}$ | ↑ PLC, $PLA_2$ | Choroid plexus, hypothalamus | CSF production, neuronal excitation | α-$CH_3$-5HT, DOI | LY53857, Mesulergine |
| $5HT_3$[d] | cations | Parasympathetic nerves, solitary tract, area postrema | Neuronal excitation | 2-$CH_3$-5HT | Ondansetron, tropisetron |
| $5HT_4$ | ↑ AC | Hippocampus, GI tract | Neuronal excitation | Renzapride | GR 113808 |
| $5HT_{5A}$ | ↓ AC | Hippocampus | Unknown | — | — |
| $5HT_{5B}$ | Unknown | — | Pseudogene | — | — |
| $5HT_6$ | ↑ AC | Hippocampus, striatum, nucleus accumbens | Neuronal excitation | — | SB 271046 |
| $5HT_7$ | ↑ AC | Hypothalamus, hippocampus, GI tract | Unknown | 5-CAT | |

*AC, adenylyl cyclase; PLC, phospholipase C; $PLA_2$; phospholipase $A_2$; 8-OH-DPAT, 8-hydroxy-(2-N,N-dipropylamino)-tetraline; DOI, 1-(2,5-dimethoxy-4-iodophenyl) isopropylamine; MCPP, metachlorphenylpiperazine; MK212; 5-CAT, 5-carboxamino-tryptamine.*

*[a]Also referred to as $5HT_{1Dβ}$. [b]Also referred to as $5HT_{1Fβ}$. [c]Aka the D receptor. [d]a 5HT-gated ion channel, aka the M receptor.*

https://basicmedicalkey.com/5-hydroxytryptamine-serotonin-and-dopamine

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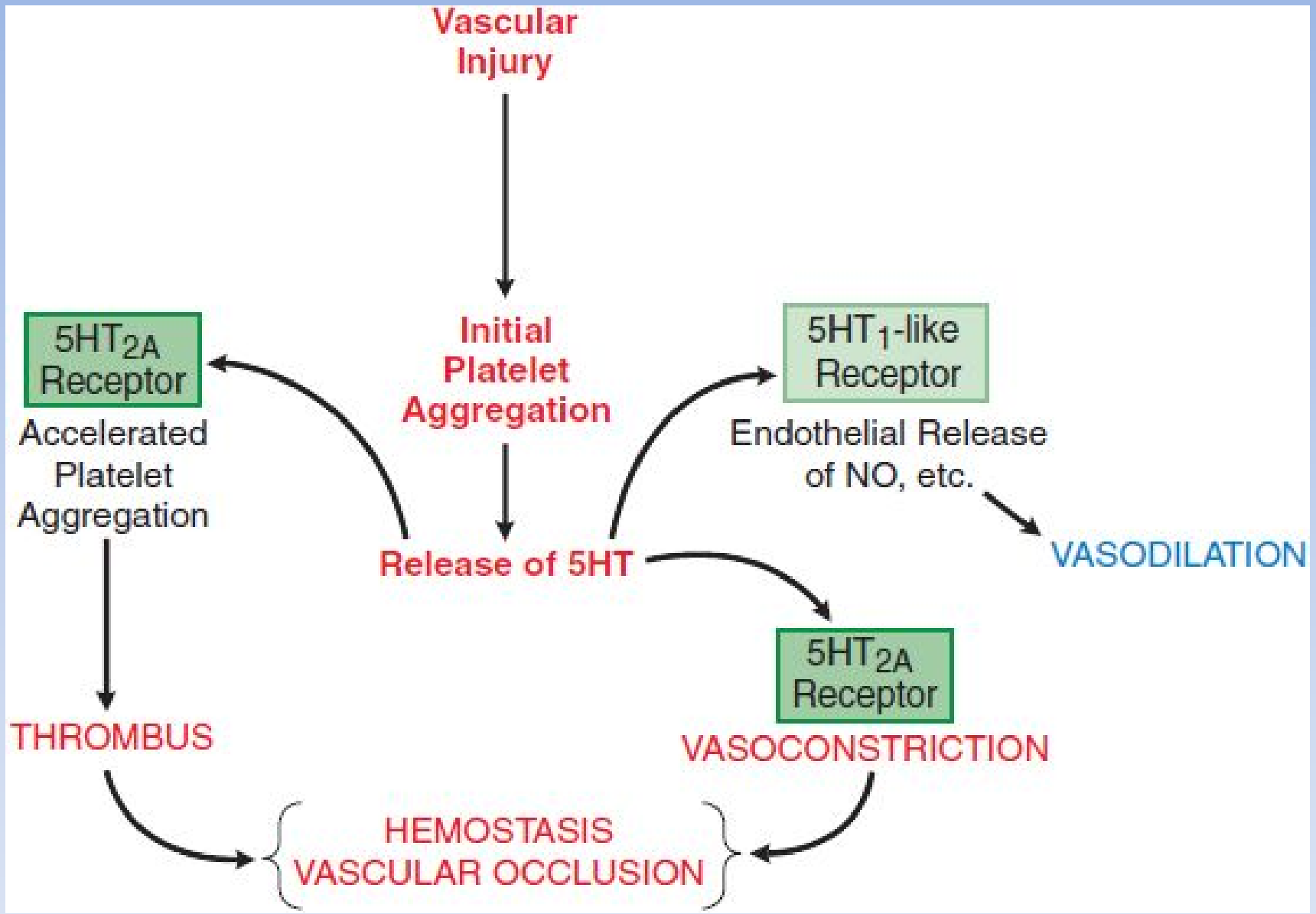


https://basicmedicalkey.com/5-hydroxytryptamine-serotonin-and-dopamine

| SITE | RESPONSE | RECEPTOR |
|---|---|---|
| Enterochromaffin cells | Release of 5HT | $5HT_3$ |
| | Inhibition of 5HT release | $5HT_4$ |
| Enteric ganglion cells | Release of ACh | $5HT_4$ |
| (presynaptic) | Inhibition of ACh release | $5HT_{1P}$, $5HT_{1A}$ |
| Enteric ganglion cells | Fast depolarization | $5HT_3$ |
| (postsynaptic) | Slow depolarization | $5HT_{1P}$ |
| Smooth muscle, intestinal | Contraction | $5HT_{2A}$ |
| Smooth muscle, stomach fundus | Contraction | $5HT_{2B}$ |
| Smooth muscle, esophagus | Contraction | $5HT_4$ |

*ACh, acetylcholine.*

https://basicmedicalkey.com/5-hydroxytryptamine-serotonin-and-dopamine

| RECEPTOR | ACTION | DRUG EXAMPLES | CLINICAL DISORDER |
|---|---|---|---|
| $5HT_{1A}$ | Partial agonist | Buspirone, ipsaperone | Anxiety, depression |
| $5HT_{1D}$ | Agonist | Sumatriptan | Migraine |
| $5HT_{2A/2C}$ | Antagonist | Methysergide, risperidone, ketanserin | Migraine, depression, schizophrenia |
| $5HT_3$ | Antagonist | Ondansetron | Chemotherapy-induced emesis |
| $5HT_4$ | Agonist | Cisapride | GI disorders |
| SERT (5HT transporter) | Inhibitor | Fluoxetine, sertraline | Depression, obsessive-compulsive disorder, panic disorder, social phobia, posttraumatic stress disorder |

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