

## Index

### a

- acetylcholine (ACh) 97, 121–124, 126, 132, 135, 138, 140–143, 145, 229, 238–239, 274–276, 325, 326, 328, 345
  - metabolism 238
- acetylcholine-binding protein (AChBP) 97, 330–331
- acetylcholine esterase (AChE) 122, 238, 239
- acetylcholinesterase (AChE) 123, 216, 276–280, 325, 327
- activation of potassium ion channels (GIRK) 45
- adenosine receptor 7
- adrenoreceptors
  - $\alpha$ 1-adrenoreceptors 43–48
  - $\alpha$ 2-adrenoreceptors 48–49
  - $\beta$ -adrenoreceptors 49–58
  - classification 43–44
  - effector mechanism 44–45
  - location 44
  - neurodisorders implication 45–46
  - structure considerations 44
- Ala322Asp 206
- alcohol dehydrogenase (ADH) 231
- $\alpha$ 1-adrenoreceptors 43–48
- $\alpha$ 2-adrenoreceptors 44, 46, 48–49
- $\alpha$ -Bgtx-insensitive receptors 124
- $\alpha$ -Bgtx-sensitive receptors 123
- $\alpha$ -Synuclein 232, 303, 313–316
- alprenolol 54
- Alzheimer's disease (AD)
  - acetylcholinesterase inhibitors 325–331
  - cause of 325
  - FDA-approved drugs for 326
  - GABAergic system 204
  - memantine 331
  - treatment 325
  - serotonin receptors 88
- amantadine 335, 344–345
- amine-based transmitter system 81
- amphetamines 23, 24, 64, 341
- amyloid  $\beta$  (A $\beta$ ) 304–307
- amyloid precursor protein (APP)
  - biological, biochemical, and neurochemical role of 305
  - crystal structures 305
  - C-terminus residues 305
  - iron export 304
  - isoform APP770 304
  - nuclear magnetic resonance (NMR) spectroscopy 305
  - proteolytic pathways 306
  - structure of 304
  - X-ray crystallography 309
- amyotrophic lateral sclerosis (ALS) 157, 275, 346–347
- antipsychotic drugs 9, 45, 325, 346
- apomorphine ((*R*)-enantiomer) 337
- aromatic amino acid decarboxylase (AADC) 230, 255–257

- astrocytes 157, 159, 201, 213, 216, 239, 240, 242, 281, 307
- attention-deficit hyperactivity disorder (ADHD) 3, 41, 253
- b**
- basolateral amygdala 121, 199
- $\beta$ -adrenoceptor kinase ( $\beta$ ARK) 51
- $\beta$ -adrenoceptors 44, 49–58
- $\beta_2$ -adrenoceptor 54
- $\beta_3$  homopentamer 207
- betaine transporter (BGT1) 201, 213, 216
- bisubstrate inhibitors 266–268, 345
- brainstem cholinergic system 121
- bromocriptine 335–337, 340
- bucindolol 51, 53
- c**
- calcium-dependent activator proteins 20
- carbidopa 256, 257, 333, 334, 343, 344
- carvedilol 51, 53
- catecholamine-O-methyl transferase (COMT) 43, 231, 233–236, 265–270, 333, 335, 343–345
- catecholamines metabolism
- dopamine 229–234
  - epinephrine 234–235
  - norepinephrine 234–235
- central nervous system (CNS) 5, 21, 42, 124, 155, 199, 258, 333
- central noradrenergic system (CNA) 41
- choline acetyltransferase (ChAT) 121, 122, 141, 238, 274–276
- cholinergic system
- acetylcholine 121
  - brainstem 121
  - choline transporter 141
  - dysfunction 121
  - magnocellular basal forebrain
    - cholinergic system 121–122
  - muscarinic receptors 123
  - nicotinic acetylcholine receptors 123
- choline transporter (ChT) 123
- high-affinity 143–145
  - vesicular acetylcholine transporter 141–143
- chorea and addiction 3
- chromaffin cells 257
- (S)-citalopram 104–107
- cortical GABAergic neurons 199
- cotransmission 41
- cotransmitters 41, 43, 58, 61
- cryo-EM 171, 172, 306, 309, 311–315
- d**
- diacylglycerol (DAG) 45, 87, 88, 133, 174
- diagonal band (DB) of Broca 121
- dihydrotanshinone I 279
- dihydroxyphenylalanine (DOPA) 3, 230, 249, 331, 333
- 3,4-dihydroxyphenylacetaldehyde (DOPAL) 231
- 3,4-dihydroxyphenylethanol (DOPET) 231
- 3,4-dihydroxyphenylacetic acid (DOPAC) 4, 5, 231
- 3,4-dihydroxyphenylglycol (DHPG) 42, 43, 234
- dihydroxyphenylalanine (DOPA) 3, 230, 249, 331, 333
- donepezil 279, 325–328, 346
- dopamine
- aminochrome-related redox reactions 233–234
  - biosynthesis of 230
  - conjugation reactions of 231, 232
  - degradation of 231
  - o*-quinones 232–233
  - production of 230
  - transformation of 231
- dopamine- $\beta$ -hydroxylase (DBH) 43, 233, 257–259
- dopamine receptors (DRs)
- amino acid sequence 6
  - biological aspects of 4
  - classification 5
  - D<sub>1</sub>-like receptors 6, 9–12
  - D<sub>2</sub>-like receptors 6, 12–18

- dimers and oligomers 6
  - effector mechanism 8–9
  - G-protein-coupled receptors 4
  - homo- and hetero-oligomerization 6
  - isoforms for 6
  - location 5
  - neurodisorders implication 9
  - posttranslational modifications 6
  - dopaminergic agonists 331, 335–340
  - dopaminergic neurons 3–5, 13, 21, 26, 125, 155, 232, 234, 250, 255, 331, 333, 335–337
  - dopaminergic presynaptic 5
  - dopaminergic system
    - dopamine transporter 21
    - definition 3
    - dopamine receptors 3
    - mesolimbic pathway 3
    - neurotransmitter dopamine 3
    - pathways of 3–4
    - vesicles by the monoamine transporter 18
  - dopamine synapse 5
  - dopamine transporter (DAT) 5
    - central nervous system 21
    - dysfunction of 21
    - molecular mechanism 24–26
    - quantitative assessment of 21
    - structural aspects 21–24
  - dorsal raphe nucleus projects 81, 252
  - Dravet syndrome 206
  - Drosophila* dopamine transporter (dDAT) 21, 65, 107
- e**
- electric eel 125
  - Electrophorus electricus* 125
  - entorhinal cortex 81
  - enzymes processing neurotransmitters
    - acetylcholinesterase 276–280
    - aromatic amino acid
      - decarboxylase 255–257
    - catecholamine-*O*-methyl transferase 265–270
    - choline acetyltransferase 274–276
    - dopamine  $\beta$ -hydroxylase 257–259
    - GABA transaminase 284–286
    - glutamic acid
      - decarboxylase 280–281
    - glutamine synthetase 281–284
    - 5-hydroxyindole-*O*-methyltransferase 272–274
    - monoamine oxidase 259–265
    - phenylethanolamine-*N*-methyl transferase 270–272
    - serotonin-*N*-acetyl transferase 274
    - tyrosine hydroxylase 249–252
  - epinephrine (EPI) 18, 43, 47–49, 54, 56, 229, 234–235, 249, 259, 270
  - Erwinia chrysanthemi* (ELIC) 331, 332
  - extracellular domains (ECD) 7, 10, 19, 22, 47, 49, 51, 52, 60, 62, 64, 89, 92, 96, 99, 100, 102, 126, 127, 129, 133, 142, 144, 163, 167, 170, 173, 177, 178, 186, 202, 207, 211–213, 215, 305, 330
- f**
- fasciculin-II (FAS) 277, 278
  - 3-fluoromethyl-7-(*N*-substituted aminosulfonyl)-1,2,3,4-tetrahydroisoquinolines 272
  - fragile X syndrome 162, 175, 176, 199
  - Friedreich's ataxia 346
- g**
- GABA<sub>A</sub> receptors
    - effector mechanisms 205
    - human subunits sequences 202
  - 5-HT<sub>3</sub> receptors 201
  - localization of 203
  - subunits structure 206
  - GABA<sub>B</sub> receptors
    - effector mechanisms 210–212
    - sequences of 210–211
    - structure of 212–213
  - GABA<sub>C</sub> receptors 201
  - GABAergic inhibition 199
  - GABAergic postsynaptic structures 5
  - GABA-releasing neurons 199
  - GABA transaminase (GABA-T) 200, 240, 284–286
  - galanin receptors 61
  - galantamine 328

- $G\alpha_i$ -coupled serotonin receptors 87  
 $G\alpha_{q/11}$ -coupled receptors 87  
 $G\alpha_s$ -coupled receptors 87  
 $\gamma$ -aminobutyric acid (GABA) receptors  
   betaine transporter 216  
   classification of 201  
   GABA<sub>A</sub> 204  
   GABA<sub>B</sub> 210  
   GABA<sub>C</sub> 201  
   location 201  
   metabolism 240  
   neurodegenerative disorders 204  
   sodium-and chloride-dependent  
     GABA transporters 216–218  
   system 199  
   vesicular GABA transporter 213,  
     216  
 GAT-1 213, 215–217  
 GAT-2 201, 216, 217  
 GAT-3 201, 213, 216–218  
 glutamate decarboxylase  
   (GD) 240–241  
 glutamate dehydrogenase  
   (GDH) 239  
 glutamate-glutamine cycle 281  
 glutamic acid decarboxylase  
   (GAD) 199, 201, 280–281  
 glutamic acid metabolism 239–272  
 glutamine synthetase (GLUL) 157,  
   239, 242, 281–284  
 glycosylation sites  
   kainate subunit 170  
   metabotropic receptors 178–184  
   *N*-methyl-*D*-aspartate subunit 206  
 G-protein coupled receptors (GPCR)  
   adrenoreceptors 43  
    $\alpha$ -helices characteristic of 14  
   crystals for 10  
   D<sub>1</sub>-like dopamine receptors 8  
   D<sub>2</sub>-like dopamine receptors 8  
   D<sub>4</sub> receptor 16  
   muscarinic receptors 123  
   rhodopsin 10  
   transmembrane proline residues 13  
 G-protein receptor kinase (GRK) 12, 44  
 G-protein signaling pathways 87
- h**  
 hetero-oligomers 6, 7  
 HierDock procedure 10, 12  
 high-affinity choline transporter  
   (ChT) 143–145  
 histofluorescence method 81  
 homo-oligomerization 6  
 homovanillic acid (HVA) 231  
 Huntington's disease (HD) 346  
 5-HT receptor 83  
 5-HT<sub>1A</sub> receptor 86, 93  
 5-HT<sub>1B</sub> autoreceptors 83  
 5-HT<sub>1B</sub> receptors 86  
 5-HT<sub>1D</sub> receptor 86  
 5-HT<sub>1E</sub> receptor 86  
 5-HT<sub>1</sub> receptor 89–92  
 5-HT<sub>2</sub> receptors 92–96  
 5-HT<sub>2A</sub> receptor 86, 93  
 5-HT<sub>2B</sub> receptor 86, 94–95  
 5-HT<sub>2C</sub> receptor 86, 92–93, 96  
 5-HT<sub>3</sub> receptors 96–98  
 5-HT<sub>3A</sub> subunit 86  
 5-HT<sub>3B</sub> subunit 86  
 5-HT<sub>4</sub> receptor 86, 88, 98  
 5-HT<sub>5</sub> receptor 98–100  
 5-HT<sub>5A</sub> receptor 86  
 5-HT<sub>6</sub> receptor 86, 100  
 5-HT<sub>7</sub> receptor 86, 101  
 hydrophobic transmembrane  
   domains 126  
 hydroxybenzyl isoproterenol  
   (HBI) 54  
 5-hydroxyindolacetic acid (5-  
   HIAA) 83  
 5-Hydroxyindole-*O*-methyltransferase  
   (HIOMT) 272  
 5-hydroxytryptophan (5-HTP) 83  
 hypoprolactinemia 3
- i**  
 immunohistochemical method 81  
 inositol triphosphate (IP3) 88  
 isoform APP770 304
- j**  
 Janus-activated kinase-2 (JAK2) 216

**k**

Krebs cycle 238, 242

**l**

laterodorsal pontine tegmentum  
(LDT) 121

L-DOPA induced dyskinesias  
(LID) 334

L-*erythro*-5,6,7,8-tetrahydrobiopterin  
(6R-BH4) 252

Leu146Met 206

Lewy body disease (LBD) 121,  
345–346

L-glutamic acid metabolism 240

ligand binding assays 123

**m**

M1 receptor 134

M2 receptor 135

M3 receptor 135–138

M4 muscarinic receptor 139–141

M5 receptor 141

magnocellular basal forebrain  
cholinergic system 121–122

mammalian target of rapamycin  
(mTOR) 101, 176, 336

MAO-B inhibitors, pd  
safinamide 340–343  
selegiline 340–341  
rasagiline 340–342

marine ray 125

median raphe nucleus projects 81

melatonin 236, 237, 272, 274

memantine 325, 331, 332

MembStruk procedure 10, 12, 13

mesocortical pathway 3, 4

mesocorticolimbic pathways 3

mesolimbic pathway 3

3-methoxy-4-hydroxyphenylglycol  
(MHPG) 43

Michaelis complex 266, 267

misfolded proteins  
 $\alpha$ -Synuclein 313–316  
amyloid  $\beta$  (A $\beta$ ) 304–307  
neurodegenerative  
disorders 303–304

tau ( $\tau$ ) protein 307–313

mitochondrial monoamine oxidase  
(MAO) 43

mitogen-activated protein kinases  
(MPK) 8, 45, 87, 133, 134, 161,  
174

monoamine oxidase (MAO)  
flavin-dependent enzyme 259

MAO-A

amino acid sequences of 260  
catecholaminergic neurons 260  
clorgyline 260  
crystal forms of 263  
Cys406 260  
cysteines 260  
deficiency of 261  
isoform of 260  
noradrenergic cell bodies 260  
Ser383 260  
serotonergic neurons and glial  
cells 260  
serotonin and  
norepinephrine 260  
substrate/inhibitor cavity 263  
tyramine and dopamine 260

MAO-B

amino acid sequences of 260  
crystal structures of 261  
Cys397 260  
cysteines 260  
deprenyl 260  
isoform of 260  
phenylethylamines 260  
serotonergic cell bodies 260  
structure of 262  
tyramine and dopamine 260  
X-ray structure of 261

movement disorders 3

murine D<sub>3</sub> receptor 14

muscarinic receptors (mAChRs)

effector mechanisms 133  
gene family 132–133  
G-protein coupled receptors 123  
location 124–125  
M1–M5 subtypes 124  
M1 receptor 134

- muscarinic receptors (*contd.*)  
 M2 receptor 135  
 M3 receptor 135–138  
 M4 receptor 139–141  
 M5 receptor 141  
 neurodisorders implication 134  
 transmembrane regions 132  
 X-ray structures 132
- muscle-type nicotinic receptors 123
- n**
- N*-acetylserotonin (NAS) 237, 272
- neurodegenerative disorders  
 Alzheimer's disease (AD)  
 acetylcholinesterase  
 inhibitors 325–331  
 cause of 325  
 FDA-approved drugs for 326  
 memantine 331  
 treatment 325
- amyotrophic lateral  
 sclerosis 346–347
- Friedreich's ataxia 346
- Huntington's disease 346
- Lewy body disease 345–346
- Parkinson's disease  
 amantadine 344–345  
 catecholamine-O-methyl  
 transferase inhibitors 343–344  
 dopaminergic agonists 335–340  
 L-DOPA 331, 333–335  
 MAO-B inhibitors 340–343  
 treatment of 331, 333
- spinal muscular atrophy 347
- neurodevelopmental disorders 126, 199
- neuronal calcium sensor-1 (NCS-1) 13
- neuronal nicotinic receptors 123–126
- neuropeptides receptors 58–63
- neuropeptide Y (NPY) 58–60
- neuropsychiatric symptoms 326, 337
- neurotransmitters 229  
 acetylcholine metabolism 238–239  
 catecholamines  
 metabolism 229–235  
 GABA 240–242  
 glutamic acid 239–242  
 serotonin metabolism 235–238
- nicotinic acetylcholine receptors  
 (nAChRs) 124–126, 328
- nicotinic receptors (nAChRs)  
 $\alpha_4\beta_2$  receptor complex 132  
 $\alpha$ -Bgtx-insensitive receptors 124  
 $\alpha$ -Bgtx-sensitive receptors 123  
 effector mechanisms 125–126  
 electric organs 125  
 ganglionic 123  
 ligand-gated ion channels 123, 125  
 location 124–125  
 neurodisorders implication 126  
 neuromuscular 123–124  
 pentameric arrangement of 130  
 structure and function of 125  
 subunit combinations for 130  
 subunits structure 126
- nigrostriatal pathway 3, 4, 230, 337, 341
- norepinephrine (NE) 18, 41–45, 49–51,  
 57, 61, 63–65, 102, 229, 234–236,  
 249, 257, 259, 260, 265, 270–272
- noradrenaline 41, 234–236, 270, 340
- noradrenergic system  
 adrenoceptors 43–58  
 autoregulation 43  
 central 41  
 norepinephrine transporter 63–65  
 neuropeptides receptors 58–63  
 noradrenaline 41  
 norepinephrine 41–45  
 peripheral 41
- norepinephrine transporter (NET) 42,  
 43, 63–65
- nucleus basalis magnocellularis  
 (nBM) 121
- o**
- 3-*O*-methyldopa (3-OMD) 333, 343
- organophosphorus (OP)  
 compounds 277
- oxyanion hole 279
- p**
- paired helical (PHF) 311, 312
- 1-palmitoyl-2-oleoyl-*sn*-glycero-3-  
 phosphocholine (POPC) 89
- paraventricular nucleus (PVN) 44

- Parkinson's disease (PD)
- aromatic amino acid
    - decarboxylase 255–257
  - amantadine 344–345
  - catecholamine-O-methyl transferase
    - inhibitors 343–345
  - dopamine- $\beta$ -hydroxylase 257–259
  - cholinergic activity 121
  - dopaminergic agonists 335–340
  - dopaminergic neurons 3–5
  - GABAergic system 204
  - L-DOPA 333–335
  - MAO-B inhibitors 340–343
  - treatment of 331
  - tyrosine hydroxylase 249–252
- pedunculopontine tegmental nucleus (PPT) 121
- phenylethanolamine-*N*-methyl transferase (PNMT) 270–272
- phospholipase C (PLC) 8, 45, 84, 87, 88, 133, 174
- phospholipase D 45, 174
- phosphorylation sites
- kainate subunit 170
  - metabotropic receptors 178–184
  - N*-methyl-*D*-aspartate subunit 325
- pirenzepine insensitive 124
- pirenzepine sensitive 124
- piribedil 335, 336
- polymorphism 12, 14, 16, 49, 51, 53, 54, 56, 64, 101, 103, 126, 144, 176, 249, 265
- pramipexole 335–337
- preNAC steric zipper 316
- protein aggregation 303, 306
- protein kinase A (PKA) 8, 44, 45, 87, 102, 133, 134
- protein kinase C (PKC) 8, 45, 87, 102, 133, 134, 174, 274
- pteridine-binding enzymes 252
- pyridoxal-5'-phosphate (PLP) 255, 333
- pyridoxal-5'-phosphate (PLP)-dependent enzyme 280, 284
- r**
- raphe nucleus 81, 252, 260
- rasagiline 261, 263, 264, 340–342
- rivastigmine inhibits 328
- ropinirole 335–337
- rotigotine 335–337
- S**
- S*-adenosylhomocysteine (SAH) 265
- S*-adenosyl-L-methionine (SAM) 265
- safinamide 340–343
- schizophrenia 3, 4, 6, 9, 12, 14, 16, 18, 46, 57, 58, 65, 81, 88, 93, 101, 103, 121, 126, 134, 157, 162, 176, 199, 204, 206, 249, 258, 265, 266, 275, 281
- selegiline (L-deprenyl) 340
- serotonergic neurons 82, 83, 100, 104, 255, 257, 260
- serotonergic system
- complex anatomy of 81
  - dysfunction of 81
  - pathways of 81–82
  - serotonin 82–83
  - serotonin reuptake
    - transporter 102–107
  - topography and morphology of 81
- serotonin metabolism 235–238
- serotonin-*N*-acetyl transferase (SNAT) 274
- serotonin receptors
- classification of 83–86
  - CNS and periphery 86
  - effector mechanism 87–88
  - 5-HT<sub>1</sub> 89–92
  - 5-HT<sub>2</sub> 92–96
  - 5-HT<sub>3</sub> 96–98
  - 5-HT<sub>4</sub> 98
  - 5-HT<sub>5</sub> 98–100
  - 5-HT<sub>6</sub> 100–101
  - 5-HT<sub>7</sub> 101–102
  - neurodisorders implications 88–89
  - structure and function of 86–87
- serotonin reuptake transporters (SERTs) 83, 102–107
- serotonin transporter (SERT) 65, 82, 100, 102, 104, 107
- seven transmembrane (7TM) 6, 10–12, 44, 58, 62, 86, 87, 90, 98, 100, 101, 132, 134, 176, 177

- sodium-and chloride-dependent GABA transporters (GAT1-3) 213–218
- spinal muscular atrophy (SMA) 347
- straight filaments (SF) 311, 312
- suprachiasmatic nucleus (SCN) 86
- t**
- tau ( $\tau$ ) protein 303, 307–313
- territrem B 279
- tetrahydrobiopterin 230, 251, 252
- Tetronarce californica* 328
- thalamic pathway 3, 44, 203, 204
- Torpedo californica* 125, 277
- transmembrane domains (TMD) 5–7, 16, 18, 19, 22, 44, 47, 49, 52, 60, 62, 64, 86, 89, 91, 92, 96, 98–102, 126, 127, 129, 130, 132, 133, 141–144, 159, 160, 163, 167, 170, 173, 178, 186, 202, 205, 207, 211, 215, 216, 258, 260, 264, 265, 305
- transmembrane segment 3 (TM3) 10
- traumatic brain injury (TBI) 51
- tryptophan-5-monooxygenase (TPH) 252–255
- tryptophan hydroxylase 82, 235, 249, 252–255
- tuberoinfundibular pathway 3
- tyrosine hydroxylase (TH)
- catecholamines 249
  - crystal structure of 250
  - deficiency 249
  - Fe<sup>2+</sup> and BH<sub>4</sub> 249
  - ferrous iron 249
  - iron-containing 252
  - isoforms 249
  - micromolar affinity of 251
  - neurodisorders 249
  - NMR solution structure of 251
  - phosphorylation 251
  - rate-limiting enzyme 249
  - tryptophan hydroxylase 252
  - unstructured *N*-terminal region 250
  - X-ray structure of 251
- v**
- Val-Gln-Ile-Ile-Asn-Lys segment 308
- ventral tegmental area (VTA) 21, 81, 86, 155, 199
- vesamicol 143
- vesicles by the monoamine transporter (VMAT) 83
- vesicular acetylcholine transporter (VACHT) 122, 123, 141–143, 216
- vesicular GABA transporter (VGAT) 200, 201, 213, 216
- vesicular inhibitory amino acid transporter (VIAAT) 213, 215
- vesicular monoamine transporter (VMAT) 4, 5, 18–21, 42, 82, 143, 216, 231
- voltage-dependent calcium channels (VDCCs) 8, 45, 174, 210, 212
- voltage-gated calcium channel (VGCC) 82, 83, 122, 156, 200