

Index

- 5HT. *See* serotonin
- ABC model of apathy, 536
- abstinence, 571–4
- acamprosate, 556
- acetyl coenzyme A, 505
- acetylcholine, 5, 505–10
 dopamine and, 166
- acetylcholinesterase, 505
- acetylcholinesterase inhibition, 509–18
- action potential, 67, 73
- active site, 45, 46
- acute pain, 379, 380
- addiction, 476, 539
 behavioral, 575
 dopamine theory of, 542–3
 substance addictions, 544–75
- adenosine, 440
- ADHD (attention deficit hyperactivity disorder), 34, 449, 485, 539
 comorbidities, 466, 480
 neurodevelopment, 463–5
 oppositional symptoms, 484
 prefrontal cortex tuning, 454–63
 symptoms and circuits, 449–53
 treatments, future, 484
 treatments, NET inhibitors, 480–4
 treatments, stimulants, 467–79
 treatments, symptoms and, 466–7
- advanced sleep phase disorder, 435, 437
- affective blunting, 142
- affective disorders, 244
- affective symptoms, 95
 positive and negative, 278, 280, 306
 schizophrenia, 145
- aggression, 145–7, 521, 577–8
- agitation, 145, 521–3
 dementia, 145, 157, 197
 glutamate target, 533
 neuronal networks of, 528–30
 treatment, 523–4
 treatment, multimodal monoamine, 530–2
- agomelatine, 306–8
- agonist spectrum, 37, 43, 45, 56–62, 184, 192
- agonists, 57, 58
 full, 37–41, 56, 192
 inverse, 42, 44–5, 61, 62, 240
 no agonist, 37
 partial. *See* partial agonists
- AIMS (Abnormal Involuntary Movement scale), 174
- akathisia, 166, 169
- alcohol, 377, 553–6
 abstinence, 573
 co-addictions, 553
 treatment of alcoholism, 556
- alcohol abuse, 378
- allodynia, 380
- allopregnanolone, 320, 322
- allosteric modulation, 64–6, 261, 262
- alogia, 142
- alpha-1 antagonism, 216, 225, 236, 327–8
- alpha-2 adrenergic agonists, 481–4
- alpha-2 antagonism, 309
- alpha-2 autoreceptors, 254, 256, 258
- alpha-2-delta ligands, 366, 377, 380
 pain alleviation, 398
 SNRI combinations, 399
- alpha pore, 69, 70
- alpha-synuclein, 493, 494
- alternative splicing, 26
- Alzheimer disease, 487–90. *See also*
 dementia
 agitation in, 521–4, 528–33
 delusions in, 157
 dementia stage 3, 502
 early detection, importance of, 497
 impulsivity, 539
 MCI stage 2, 500–2
 memory and cognition treatment, 509–18
 Parkinson's disease comorbidity, 494
 pathology, 488
 presymptomatic stage, 499–501
 psychosis in, 521–4
 targeting amyloid, 496–9
 vascular dementia comorbidity, 492
- amantadine, 169
- amisulpride, 205
- amotivational syndrome, 563
- AMPA receptors, 101, 104, 330, 331
- amphetamine, 337, 356, 441–2, 472–6, 569
 ADHD, 484
 formulations, 475
 isomers, 472
- amygdala, fear and, 364–5, 372, 374
- amyloid cascade hypothesis, 496–9
- amyloid plaques. *See* beta-amyloid
- amyloid precursor protein, 497–8
- amyotrophic lateral sclerosis, 353
- analgesia, 380
- anatomical basis of neurotransmission, 1–5
- anesthesia, dissociative, 570
- anhedonia, 142, 162
- antagonists, 41–3, 57, 58, 60, 62
 alpha-1, 216, 225, 236, 327–8
 alpha-2, 309
 silent, 41, 42, 45, 192
- anticholinergics, 166, 168, 215, 294
- anticonvulsants
 doubtful efficacy in bipolar disorder, 352–3
 insomnia treatment, 426
 mood stabilizers, 346
 proven efficacy in bipolar disorder, 347–51
- antidepressant actions, 195–234, 267, 283
- antihistamines, 161, 215, 295, 425–6
- antipsychotic actions, 161–2, 242
- antipsychotics. *See* drugs targeting
 serotonin receptors, drugs targeting
 dopamine D₂ receptors
- anxiety, 78, 145, 359
 OCD and, 576
- anxiety disorders, 196, 378
 ADHD and, 468
 comorbidity, 360
 core symptoms, 360
 definition, 360
 major depression and, 360–2
 MAOIs, 336
 noradrenergic hyperactivity in, 370–2
 overlapping symptoms of different, 362–3
 pain disorders and, 387
 psychotherapy, 359
 serotonin and, 368–70
 treatment of, 377–8, 421
- anxiety phenotype, 363
- anxiolytic actions, 196, 366
- apathy, 78, 536–7
- APOE4 gene, 497
- aripiprazole, 192, 229, 239, 326
- armodafinil, 442–4
- arousal, 457, 459
- arousal spectrum, 402
- asenapine, 220, 232
- asociality, 142
- asymptomatic amyloidosis, 499–501

INDEX

- atomoxetine, 480–1
 auditory hallucinations, 113
 autoreceptors
 alpha-2, 254, 256, 258
 monoamine, 8
 avolition, 142
 axoaxonic synapses, 1, 3
 axodendritic synapses, 1, 3
 axosomatic synapses, 1, 3
- barbiturates, 556
 bath salts, 546
 BDNF (brain-derived neurotrophic factor), 266, 268, 329
 behavioral addictions, 575
 behavioral variant FTD, 494
 benzodiazepine-insensitive GABA_A receptors, 263–4
 benzodiazepines, 321, 366, 377
 caution with, 378
 insomnia treatment, 421–2
 benzodiazepine-sensitive GABA_A receptors, 259–62
 beta-amyloid, 488, 496–8, 502
 detection, 499, 501
 beta blockers, 375, 376
 beta subunits, 68
 bifeprunox, 192
 binge-eating disorder, 575
 bipolar depression, 244
 drug treatment, 236, 240
 family history of, 250
 first-line treatment, 342
 identifying, 250
 missed or delayed diagnosis, 250
 schizophrenia and, 249
 suicide rates, 251
 versus unipolar, 249–51
 bipolar disorder
 anticonvulsants with proven efficacy, 347–51
 anticonvulsants with uncertain efficacy, 352–3
 bipolar I, 247
 bipolar II, 244, 247
 combination treatments, 353
 drug treatment, 338–58
 blocking fear conditioning, 375–7
 blonanserin, 234, 241
 brexanolone, 320
 brexpiprazole, 192, 197, 230, 239, 327–8, 378, 530–2
 bright light therapy, 438, 440, 444
 buprenorphine, 560, 561, 562
 bupropion, 306–8, 353–4, 480, 533
 nicotine addiction, 551
 sertraline combination, 294
- buspirone, 333, 370
 butyrylcholinesterase, 505, 510
- caffeine, 440–1
 calcium channel blockers (L-type), 352
 cannabidiol (CBD), 563, 565, 567
 cannabis, 150, 563–7
 benefits and risks, 564
 side effects, 563
 therapeutic uses, 564
 carbamazepine, 350, 530
 cardiometabolic risk, 196, 224
 cardiometabolism, 198–201, 415
 cardiovascular disease, 156, 415, 432, 492, 524
 carfentanil, 560
 cariprazine, 192, 231, 240, 328, 343–5
 cataplexy, 434, 435, 446
 catechol-*O*-methyltransferase, 253
 central disorders of hypersomnolence, 432
 central pain, 379
 central sensitization, 395
 chemical neurotransmission, 1, 28
 anatomical versus, 1–5
 epigenetics, 23–6
 ion channels and, 73–6
 mood disorders, 252–64
 principles of, 5–9
 signal transduction cascades, 9–23, 28, 53
 triggering gene expression, 18
 ultradian sleep cycle, 414–16
 chemotherapy, side effects, 309
 child abuse, 370
 chlorpromazine, 161, 181, 201, 202
 choline, 505
 cholinergic agonists, 242
 cholinergic pathways, 509
 chromatin, 23
 chronic back pain, 388
 chronic pain, 379–400
 decreased gray matter, 387–90
 duloxetine treatment, 302–3
 milnacipran treatment, 303
 targeting sensitized circuits, 395–9
 treatment, 390–400
 circadian rhythm disorders, 430, 435–8
 depression, 271–5
 circadian rhythms, 307, 308
 setting of, 275
 circadian treatments, 438–40
 circadian wake drive, 409, 412
 citalopram, 295–6
 classic neurotransmission, 6
 clock genes, 271
 clomipramine, 335
 clonidine, 390, 482–3, 561
- closed state, 63
 clozapine, 217, 222–5
 cocaine, 544, 545
 codeine, 559
 cognition, Fab Four of, 317
 cognitive behavioral therapy, 374, 377, 576
 cognitive dysfunction
 ADHD, 455, 456, 458
 Alzheimer disease, 509–18
 chronic pain, 388
 depression, 273
 fibromyalgia, 390, 400
 Parkinson's disease, 493
 sleep disorders, 402
 sleep disturbance and, 414, 417
 vortioxetine treatment, 315–17
 cognitive symptoms, schizophrenia, 95, 144, 157
 competitive elimination, 151, 154
 compulsivity, 538–9, 571, 578
 impulsive–compulsive disorders, 539–43, 575
 OCD, 295, 360, 576–7
 conceptual disorganization, 78
 conditioned responses, 539
 conditioned stimuli, 539, 544
 consolidation, 375
 constitutive activity, 37, 57
 continuous positive airway pressure, 443
 controlled substance, 447
 cortico-brainstem glutamate pathways, 102
 cortico-cortical glutamate pathways, 105
 cortico-striatal glutamate pathways, 104
 cortico-striato-thalamo-cortical (CSTC) loops, 87, 362, 365–9
 cortico-thalamic glutamate pathway, 105
 CREB system, 15
 criminogenic behavior, 146, 147
 cytochrome P450 (CYP450), 49–50, 323
- daridorexant, 424
 DAT transporter. *See* dopamine transporters (DATs)
 date rape drugs, 447, 559
 delayed sleep phase disorder, 435, 437
 delirium, 569
 delusions, 77, 141, 524
 Alzheimer disease, 157
 dementia, 521
 Parkinson's disease psychosis, 157
 dementia, 486, 537. *See also* Alzheimer disease
 agitation in, 145, 157, 197
 apathy in, 536–7
 behavioral symptoms of, 521, 537
 definition, 487
 depression in, 534–5

- major causes of, 488–96
- psychosis in, 110, 134, 157, 521–3
- psychosis in, treatment, 523–7
- symptomatic treatments, 503–5
- dendrites, 2
- depression, 145. *See also* bipolar
 - depression, unipolar depression
 - affective symptoms, 278, 280
 - circadian rhythm disorder in, 271–5
 - clinical effects of treatment, 284–5
 - dementia and, 534–5
 - drug side effects, 200
 - drug treatment, 229, 239
 - insomnia and, 418
 - major depressive disorder. *See* major depressive disorder
 - major depressive episode. *See* major depressive episode
 - mixed features of, 251
 - monoamine hypothesis of, 264–5, 290
 - monoamine receptor hypothesis of, 264–6, 267, 290
 - mood stabilizer treatment, 288
 - neuroplasticity and neuroprogression hypothesis of, 266–76
 - serotonin or dopamine blockers in, 342
 - symptom-based algorithm treatment, 280
 - time course of effects of drugs, 266
- depression with mixed features, 248, 342
- depressive psychosis, 78, 157
- descending spinal norepinephrine pathway, 390, 392
- descending spinal serotonergic pathway, 390, 394
- desensitization, 63, 64
- desvenlafaxine, 299, 302
- deuteration, 175, 177, 354
- dextromethadone, 355–8
- dextromethorphan, 306, 353–4, 533, 536
- diabetes, 198, 199, 415
- diabetic ketoacidosis, 199, 200
- Diagnostic and Statistical Manual of Mental Disorders (DSM-5)
 - ADHD, 463
 - insomnia, 420
 - major depressive episode, 245
 - manic episode, 245
 - mixed features, 248
- dietary tyramine interaction, 338
- diphenhydramine, 426
- direct (go) dopamine pathway, 89, 90
- disorganized/excited psychosis, 78
- disorientation, 78
- dissociation-assisted psychotherapy, 574
- dissociative anesthesia, 570
- dissociatives, 569–71
- disulfiram, 556
- DNA methylation, 24
- donepezil, 510
- DOPA decarboxylase, 253
- dopamine, 5
 - acetylcholine and, 166
 - conversion to norepinephrine, 253
 - increase in prefrontal cortex, 299–302
 - inefficient tuning of PFC by, 454–63
 - projections, 279
 - release, 5HT_{2A} regulation, 184–8
 - synthesis, 79, 80
 - volume neurotransmission, 8
- dopamine β -hydroxylase, 253
- dopamine blockers, 468
 - adverse effects, 524
 - bipolar disorder spectrum, 338–45
- dopamine D₁ receptors
 - drugs targeting, 204–41
- dopamine D₂ receptors. *See also* drugs targeting dopamine D₂ receptors
 - pre- and postsynaptic, 228
- dopamine D₃ receptors, 343–5
 - drugs targeting, 210, 240, 241
- dopamine deficiency syndrome, 306
- dopamine hypothesis of psychosis, 79–95, 110–14, 141
- dopamine neurotransmitter network, 79–91
 - classic pathways and key brain regions, 84
 - mesolimbic pathway, 89, 542–3
 - nigrostriatal pathway, 87–9
 - thalamic pathway, 85
 - tuberoinfundibular pathway, 85
- dopamine receptors, 81–5
- dopamine theory of addiction, 542–3
- dopamine transporters (DATs), 31, 80
 - ADHD treatment, 473–9
 - inhibition, 294, 333
- dopaminergic neurons, 79
- dorsal anterior cingulate cortex (dACC), 450, 451
- dorsal horn neurons, 382–4
- dorsal horn, descending spinal synapses in, 390–5
- dorsal root ganglia, 380, 381
- dorsolateral prefrontal cortex, 387, 400, 449
- doxepin, 425, 427
- drug abuse, 447, 539
 - DAT occupancy and, 476, 479
 - reversal of habit, 571–4
 - stimulants, 544–7
- drug-induced dystonia, 166, 169
- drug-induced parkinsonism, 165, 166–9, 181
- drugs targeting dopamine D₁ receptors, 204–41
- drugs targeting dopamine D₂ receptors, 159, 242
 - agitation in dementia, 197
 - antidepressant actions, 195–234
 - anxiolytic actions, 196
 - cardiometabolic actions, 198–201
 - first generation, 179–82, 201–3
 - individual properties, 204–41
 - mesocortical, 163
 - mesolimbic/mesostriatal, 161–3
 - nigrostriatal, 165–81
 - partial agonists, 189–92, 204–41
 - serotonin 2A and, 182–8
 - tuberoinfundibular, 164
- drugs targeting dopamine D₃ receptors, 210, 240, 241
- drugs targeting serotonin receptors, 159, 243
 - 1A receptors, 192–5, 207
 - 1B and 1D receptors, 214
 - 2A receptors, 182–8
 - 2C receptor, 211
 - 3 receptor, 212
 - 6 and 7 receptors, 213
 - agitation in dementia, 197
 - antidepressant actions, 195–234
 - anxiolytic actions, 196
 - cardiometabolic actions, 198–201
 - individual properties, 204–41
- DSST (digital symbol substitution test), 317
- dual orexin receptor antagonists (DORAs), 423–4, 430
- duloxetine, 299, 302–3, 535
- dynorphins, 390
- dyslipidemia, 198
- dystonia, drug-induced, 166, 169
- eating disorders, 293, 575
- Ecstasy, 357, 569
- empathogens, 569
- endocannabinoids, 6, 563, 564
- enkephalins, 390
- entactogens, 569
- enzyme inhibitors, 45
 - irreversible, 46
 - reversible, 47
- enzymes, 45–50
 - activity, 45
- epigenetics, 23–6
- Epworth Sleepiness Scale, 430
- escitalopram, 296
- esketamine, 331, 353, 571
- eslicarbazepine, 352
- euphoria, 560
- excessive daytime sleepiness. *See* hypersomnia
- excitation–secretion coupling, 6, 8–9, 73, 75

INDEX

- excitatory amino acid transporter, 96, 99
excitement, 78
executive dysfunction, 144, 449–50
exposure therapy, 374, 378, 574, 576, 577
extinction
 fear, 373, 374–5, 574
 pharmacological, 573
extrapyramidal symptoms, 166
- F17464, 241
FDG PET, 490, 492, 502
fear, 363–6
 neurobiology of, 364–5
 noradrenergic hyperactivity, 371
fear conditioning, 370–4
 blocking, 375–7
fear extinction, 373, 374–5, 574
fentanyl, 559
fibro-fog, 390, 400
fibromyalgia, 303, 387–9
 cognitive dysfunction, 388, 400
 targeting ancillary symptoms,
 399–400
 treatment, 448
fight or flight response, 359, 364
first messengers, 11, 13
flashbacks, 568
flumazenil, 263
fluoxetine, 293–4
 olanzapine combination, 293, 326,
 343
fluphenazine, 202, 203
fluvoxamine, 295
forensic hospitals, 146, 147, 156
frontotemporal dementias, 494–6
frontotemporal lobar degeneration, 494
full agonists, 37–41, 56, 192
- G protein, 14
G-protein-linked receptors, 36–45, 50
 agonist spectrum, 37, 43, 45
 agonists, 37–41
 antagonists, 41–3
 inverse agonists, 42, 44–5
 no agonist, 37
 partial agonists, 41, 43–4
 structure and function, 36
G-protein-linked systems, 11, 12, 13
GABA (γ -aminobutyric acid), 5, 257–64,
 349
 action termination, 258
 synthesis, 255
GABA interneurons
 5HT receptors on, 121, 125, 130
 prefrontal cortex, 105–10
GABA receptors, 258–64
 GABA_A, 321, 366, 421–3
 GABA_A receptor subtypes, 258–61
 GABA_B, benzodiazepine-insensitive,
 263–4
 GABA_B, benzodiazepine-sensitive,
 259–62
GABA transaminase (GABA-T), 258
GABA transporter (GAT), 34, 258
GABAergic drugs, 276
gabapentin, 352, 366, 395, 426
galanthamine, 514
gambling disorder, 575
gamma-hydroxybutyrate (GHB), 400,
 446–8, 559
gene activation, 18, 19, 24, 25
gene expression
 epigenetics, 23–6
 molecular mechanism, 18–23
 neurotransmission triggering, 18
 phosphoprotein triggering cascades,
 15–18
gene silencing, 24, 25
generalized anxiety disorder, 361, 377
genetic testing, 323–5
genetics
 ADHD, 463
 schizophrenia, 148–50
genotyping, 50
ghrelin, 415
glucose metabolism, 490
glutamate, 5, 96
 agitation in Alzheimer disease, 533
 Alzheimer disease target, 515–18
 key pathways in the brain, 102
 synthesis, 96–7
 synthesis of GABA from, 255
glutamate hypothesis of psychosis,
 95–114
glutamate neurotransmitter network,
 96–106
glutamate receptors, 99–105
 ionotropic, 54
 metabotropic, 100, 103
 NMDA. *See* NMDA glutamate
 receptors
glutamate transporters, 34
glutamic acid decarboxylase, 255
glycine transporters, 34
glycine, synthesis, 97–9
Goldilocks solution, 43, 60, 191, 227,
 428
grandiose expansiveness, 78
gray matter, chronic pain, 387–90
GSK-3 (glycogen synthase kinase), 48
guanfacine, 482–3
- habit circuit, 544, 561, 571, 572
habits, 538, 539, 576
hallucinations, 77, 113, 141, 435, 568
 dementia, 521
 Parkinson's disease psychosis, 157
 visual, 113, 524
hallucinogen-assisted psychotherapy,
 355–8, 376
hallucinogens, 135, 138, 567–9
haloperidol, 181, 202, 204
heroin, 559, 561, 573
heteroreceptors, 125
hippocampal-accumbens glutamate
 pathway, 104
hippocampus, 372, 374
histamine, 35, 402–6, 409
histamine 1 antagonism, 425–6, 427
histamine receptors, 406
histones, methylation, 23
homeostatic sleep drive, 408, 412
hormone-linked systems, 11, 12
hostile belligerence, 78
HPA (hypothalamic-pituitary-adrenal)
 axis, 266, 270
human genome, 18
Huntington's disease, 28, 175
hydrocodone (Vicodin), 559
hyperactivity, 452, 454, 463
hyperalgesia, 380
hyperarousal, 418
hyperdopaminergia, 90, 92, 93
hyperglycemic hyperosmolar syndrome,
 199, 200
hyperprolactinemia, 165, 187, 192
hypersomnia, 402, 430–40
 causes of, 431–5
 treatment of, 440–8
hypervigilance, 402
hypnotic actions, 311
 insomnia treatment, 421–30
hypnotics, sedative, 556
hypocretins, 406–11
hypodopaminergia, 95
hypomania, 248
hypothalamic neurons, 407
- idiopathic hypersomnia, 432, 433
illusions, 568
iloperidone, 225, 236
immediate early genes, 19, 20
impulse control disorders, 577–8
impulsive–compulsive disorders, 539
 binge eating, 575
 neurocircuitry of, 539–43
impulsive violence, 147, 577
impulsivity, 452, 454, 463, 538–9, 571, 578
inactivation state, 61, 63
inattention, 449, 450, 451, 463
indirect (stop) dopamine pathway, 89, 90
inhalants, 547
inherited disease, classic theory of, 148
insomnia, 311, 402, 418–20

- behavioral treatments, 430
- diagnosis and comorbidities, 418–20
- treatment, 421–31
- insulin resistance, 197, 198, 200
- internet addiction, 575
- interneurons, 380
- inverse agonists, 42, 44–5, 61, 62, 240
- ion-channel-linked systems, 11, 12
- ion channels, 76
 - ligand-gated. *See* ligand-gated ion channels
 - neurotransmission and, 73–6
 - voltage-sensitive. *See* voltage-sensitive ion channels
- ionotropic glutamate receptors, 54
- iproniazid, 336
- irreversible enzyme inhibitors, 46

- kainate receptors, 101, 104
- ketamine, 106, 328–32, 353, 376, 569–71
- ketamine-assisted psychotherapy, 574
- kinase, third messenger, 14, 16

- lamotrigine, 350–1
- late genes, 20, 22
- lemborexant, 423
- leptin, 415
- leucine zippers, 19, 20, 21
- levodopa, 170
- levomilnacipran, 300, 303
- Lewy bodies, 157
- Lewy body dementias, 492–5
- licarbazepine, 352
- ligand-gated ion channels, 51–66, 76
 - agonist spectrum, 56–62
 - allosteric modulation, 64–6
 - different states of, 61–4
 - gatekeeper, 52
 - pentameric subtypes, 53
 - structure and function, 53
 - tetrameric subtypes, 54–5
- lisdexamfetamine, 473, 575
- lithium, 48, 332, 345–6
- local anesthesia, 380
- lofexidine, 561
- long-term potentiation, 151
- LSD, 357, 568
- lumateperone, 227, 237–9
- lurasidone, 226, 236, 343

- magic mushrooms, 357
- magnesium, 104
- magnetic resonance imaging, 491
- major depressive disorder, 246, 252
 - anxiety disorder and, 360–2
 - core symptoms, 360
- major depressive episode, 248, 277
 - symptoms and circuits, 277

- mania
 - anticonvulsant treatment, 346
 - carbamazepine treatment, 350
 - drug treatment, 195
 - lithium treatment, 345
 - mixed features of, 248, 251
 - mood stabilizer treatment, 288
 - serotonin and dopamine blockers in, 338, 342
 - valproate treatment, 349
- manic episodes, 245, 277, 278
- MAOIs. *See* monoamine oxidase inhibitors
- mazindol, 485
- MDMA, 356, 376, 378, 569–71
 - assisted psychotherapy, 574
- MDPV, 546
- medication-assisted therapy, 561
- melatonergic agents, 439, 440
- melatonin, 275, 439, 440
- melatonin receptors, 306
- memantine, 520, 521–4, 533
- memory difficulties, 316
 - Alzheimer disease, 509–18
- memory, traumatic, 356, 366, 375, 574
- mesocortical dopamine pathway, 95
- mesocortical hypodopaminergia, 95
- mesolimbic dopamine pathway, 89, 542–3
- mesolimbic hyperdopaminergia, 90
- mesostriatal hyperdopaminergia, 93
- messenger RNA (mRNA), 26
- metabolic highway, 198, 199, 201
- metabolic monitoring, 196, 199
- metabolic toolkit, 201
- metabotropic glutamate receptors, 100, 103
- metformin, 201
- methadone, 355, 559, 560, 561, 562
- methylation, 23, 24
- methylphenidate, 441–2, 469–72, 484
 - formulations, 470
- mianserin, 309
- microRNA (miRNA), 27
- migrants, 150
- mild cognitive impairment, 487, 490, 493, 500–2
- milnacipran, 300, 303
- mirtazapine, 232, 308–13, 333
- mixed dementia, 495
- mixed features, 248, 251–2
- modafinil, 333, 442–4
- Molly, 357, 569
- monoamine autoreceptors, 8
- monoamine hypothesis of depression, 264–5, 290
- monoamine oxidase (MAO), 253

- monoamine oxidase inhibitors (MAOIs), 336–7, 377
 - bipolar depression, 342
 - dietary tyramine interaction, 338
 - drug–drug interactions, 338
 - subtypes, 337–41
- monoamine projections, 279
- monoamine receptor hypothesis of depression, 264–6, 267, 290
- monoamine transporters, 30, 31–4, 208
- unipolar depression, 285–8
- mood disorders, 244, 282, *See also* mania, depression
 - description of, 244–52
 - future treatments for, 353–8
 - mixed features of, 248, 251–2
 - neurobiology of, 252–76
 - pain disorders and, 387
 - symptom-based treatments, 279–82
 - symptoms and circuits in, 277–82
- mood episodes, 246
- mood related psychosis, 157
- mood spectrum, 244–9
- mood-stabilizers, 288, 345–6
- mood-stabilizing action, 283
- morphine, 559, 561
- motivation, lack of, 536
- motor disturbances, 78
- motor side effects, 165–81
 - partial agonists, 192
- mu-opioid receptors, 390, 556
- multimodal monoamines, 530–2
- Multiple Sleep Latency Test, 431
- muscarinic receptors, 506–7

- nalmefene, 556, 573
- naloxone, 560
- naltrexone, 306, 556, 561, 563, 573, 575
- NAMs (negative allosteric modulators), 64–6
- narcolepsy, 407, 430, 433, 435, 443, 444, 446
- nausea and vomiting, 309
- n*-back test, 449, 451
- nefazodone, 311
- negative affect, 278, 280
- negative feedback regulatory signal, 255
- negative symptoms, 95, 142–4, 156
 - secondary, 162–3
- NET transporters. *See* norepinephrine transporters (NETs)
- neuroactive steroids, 320–5
- neurobiology
 - mood disorders, 252–76
 - sleep and wakefulness, 402–15
- neurodevelopment, 151, 152
 - ADHD, 463–5
 - schizophrenia, 151–3

INDEX

- neurofibrillary tangles, 488, 502, 503
neuroinflammation, 270
neuroleptic-induced deficit syndrome, 162
neuroleptic malignant syndrome, 169
neuroleptics, 162
neuronal cell loss, 488, 490, 491
neurons, 1, 2
 general structure, 2
neuropathic pain, 380, 382–90, *See also* fibromyalgia
 central mechanisms, 382–6
 peripheral mechanisms, 382
neuropathic pain syndromes, 380
neuropeptides, 35
neuroplasticity and neuroprogression
 hypothesis of depression, 266–76
neurotransmission, 1, *See also* chemical neurotransmission
 anatomical basis of, 1–5
neurotransmitters, 5–6
 enzymes as. *See* enzymes
 psychosis pathways, 79
 transporters. *See* transporters
neurotrophic factors, loss of, 266, 268
neurotrophin-linked systems, 11, 12
neutropenia, 224
NGF (nerve growth factor), 6
nicotine, 63, 466, 547–53
 alternative forms of delivery, 551
 treatment of addiction, 548–53
nicotinic receptors, 506, 507–9, 548
nigrostriatal dopamine pathway, 87–9
nitric oxide, 6
nitric oxide synthase, 295
NMDA antagonism, 328, 330, 355
NMDA glutamate hypofunction
 hypothesis of psychosis, 105–14
NMDA glutamate receptors, 97–101, 104
 histamine at, 406
 hypofunction, 111, 114
NMDA receptor activation, 375
nociception, 380, 381
 pain pathways, 396
nociceptive nerve fibers, activation, 381
nociceptive pathway, 381
 from the spinal cord to the brain, 382–4
 to the spinal cord, 381–2
non-24-hour sleep–wake disorder, 437, 438
non-REM sleep, 413, 414
noradrenaline. *See* norepinephrine
noradrenergic hyperactivity, 370–2
norepinephrine, 5, 252–6, 370
 action termination, 253
 inefficient tuning of prefrontal cortex by, 454–63
 projections, 279
 synthesis, 252
norepinephrine–dopamine reuptake inhibitors (NDRIs), 303–6, 333
norepinephrine receptors, 254–6, 258
norepinephrine transporters (NETs), 31, 254
norepinephrine transporter (NET)
 inhibition, 294, 298–303, 370
 ADHD, 480–4
norquetiapine, 227
NRX101, 237
NSAIDs (nonsteroidal anti-inflammatory drugs), 382
nucleosomes, 23
nucleus accumbens, 162
obesity, 198, 415, 575
obsessive–compulsive disorder (OCD), 295, 360, 576–7
obstructive sleep apnea, 430, 431, 434, 443
olanzapine, 218, 225
 fluoxetine combination, 293, 326, 343
ondansetron, 556
OPC4392, 193
open state, 63
opiates, 559
opioid use disorder, 355
opioids, 375, 390, 556, 559
 abstinence, 573
 addiction, 559–60
 addiction, treatment of, 560–2
 endogenous neurotransmitter system, 559
orbital frontal cortex, 454
orexin, 409, 435
 dual orexin receptor antagonists, 423–4, 430
 orexin receptors, 407
 orexins, 406–11
oxcarbazepine, 352
oxycodone (OxyContin), 559
pain, 379–84, *See also* chronic pain
 definition, 380
 in dementia, 537
 mood and anxiety disorders and, 387
paliperidone, 223, 235
PAMs (positive allosteric modulators), 64–6, 421–3
panic attacks, 361, 377, 569
panic disorder, 361, 372, 377
paralytic ileus, 167, 183
paranoid psychosis, 78
parkinsonism, drug-induced, 165, 166–9, 181
Parkinson's disease, 338
 Alzheimer disease comorbidity, 494
 cognitive dysfunction, 493
 Parkinson's disease dementia, 492–5
 Parkinson's disease psychosis, 78, 133, 136, 139, 157, 524
paroxetine, 294, 295
partial agonists, 41, 43–4, 57–61, 189–95, 204–41
Pavlov's dogs, 370
pentameric ligand-gated ion channels, 53
perceptual distortions, 78
periaqueductal gray, 390
peripheral pain, 379
perospirone, 233, 241
PET scans
 beta-amyloid, 499, 501
 FDG PET, 490, 492, 502
pharmacodynamics, 49
pharmacokinetics, 49
 hypnotic actions, 426–30
pharmacological extinction, 573
phasic dopamine system, 455
phasic inhibition, 259
phenacyclidine, 106, 569–71
phosphatase, third messenger, 15, 16
phosphoprotein cascades, 15–18
phosphoprotein messenger, 13–15
pimavanserin, 231, 240, 526
pitolisant, 444
plasma membrane transporters, 30
polygenic risk score, 150
polysomnography, 420, 431
positive affect, 278, 280, 306
positive symptoms, 90, 141, 156
 psychosis, 92–3
postsynaptic dopamine receptors, 81
posttraumatic stress disorder (PTSD), 360, 362
 drug treatment, 196
 fear conditioning, 372
 treatments for, 377, 568, 574
prazosin, 370
predementia AD, 500–2
prefrontal cortex
 disorder of the, 449–53, 463
 dopamine neurotransmission, 8
 dorsolateral, 387, 400, 449
 GABA interneurons, 105–10
 increased dopamine in, 299–302
 inefficient tuning of, 454–63
 ventromedial, 372, 374
pregabalin, 352, 366, 395, 426
presymptomatic stage of Alzheimer disease, 499–501
presynaptic dopamine receptors, 81, 82
primary afferent neurons, 380, 381
primary transcript, 26
prisons, 146, 156

- processing speed, 317
 prodromal negative symptoms, 143
 proinflammatory molecules, 270
 projection neurons, 380
 prolactin levels, 164, 187, 193
 pseudobulbar affect, 535
 psilocin, 568
 psilocybin, 357, 376, 568, 569
 assisted psychotherapy,
 psychedelic experience, 568
 psychiatric vital sign, 381, 399, 401
 psychic pain, 302
 psychomotor retardation, 78
 psychopathic violence, 147, 577
 psychosis, 77, 158, *See also* schizophrenia
 cannabis and, 563
 dementia, prevalence in, 521
 dementia-related, 110, 134, 157, 521–3
 dementia-related, treatment of, 523–7
 depressive, 78, 157
 dopamine hypothesis of, 79–95,
 110–14, 141
 drug treatment. *See* drugs targeting
 serotonin receptors, drugs targeting
 dopamine D₂ receptors
 glutamate hypothesis of, 95–114
 mood-related, 157
 neurotransmitter pathways, 79
 other psychotic disorders, 156–8
 paranoid, 78
 Parkinson's disease. *See* Parkinson's
 disease psychosis
 positive symptoms of, 90, 92–3
 serotonin hyperfunction hypothesis
 of, 131–41
 serotonin hypothesis of, 111–41
 symptoms of, 77–8
 psychotherapy
 anxiety disorders, 359
 cognitive behavioral therapy, 374,
 377, 576
 dissociation-assisted, 574
 hallucinogen-assisted, 355–8, 376
 ketamine-assisted, 574
 MDMA-assisted, 574
 psilocybin-assisted, 574
 PTSD, 378
 psychotic violence, 146, 577
 psychotomimetic experience, 569
 psychotropic drugs
 enzymes as targets of, 45–50
 G-protein-linked receptors as targets,
 36–45, 50
 ion channels as targets of, 51–76
 molecular targets, 29
 nomenclature, 29
 transporters as targets, 29–35, 50
- PTSD. *See* posttraumatic stress disorder
 (PTSD)
- quetiapine, 219, 220, 227–32, 326, 343
 quinidine, 353–4, 534, 536
- radafaxine, 304
 ramelteon, 439
 rasagiline, 338
 rashes, 352
 receptor tyrosine kinases, 48
 reconsolidation, 374, 375, 376, 574
 recurrence in depression, 284
 reduced positive affect, 280, 306
 relapse, 571
 in depression, 284, 286
 REM sleep, 413, 414, 435
 remission in depression, 284, 286
 repetitive transcranial magnetic
 stimulation (rTMS), 577
 reserpine, 174
 response in depression, 284
 resting state, 57, 61, 63
 retrograde neurotransmission, 6–7
 reuptake pumps, 174, *See also*
 transporters
 reversible enzyme inhibitors, 47
 reward, 542, 544
 reward conditioning, 545
 reward pathway, 572
 rheostat analogy, 43
 ribosomal RNA (rRNA), 27
 riluzole, 352
 risperidone, 222, 234, 235
 rivastigmine, 510–16
 RNA, 26–7
 RNA interference, 26
 roluperidone, 235, 241
- safinamide, 338
 SAGE-217, 322
 salivation, excessive, 224
 samidorphan, 201
 schizoaffective disorder, 249
 schizophrenia, 141, 156, *See also*
 psychosis
 affective symptoms, 95, 145
 aggressive symptoms, 145–7
 bipolar disorder and, 249
 cognitive symptoms, 95, 144, 157
 dopamine hypothesis of psychosis in,
 92–5
 drug treatment. *See* drugs targeting
 serotonin receptors, drugs targeting
 dopamine D₂ receptors
 future drug treatment, 241–2
 genetics and, 148–50
 life expectancy, 156
- nature and nurture of, 149
 negative symptoms, 95, 142–4, 156
 neurodegeneration and, 154–6
 neurodevelopment and, 151–3
 NMDA receptor hypofunction, 111, 114
 positive symptoms, 141, 156
 positive symptoms of psychosis in, 92–3
 second messenger
 forming, 11–14
 to phosphoprotein cascades, 15–18
 to phosphoprotein messenger, 13–15
 secondary negative symptoms, 162–3
 sedation, 197, 202
 sedative hypnotics, 556
 segmental central sensitization, 384
 selegiline, 337, 338
 SEP-363856, 242
 serine, synthesis, 97–9
 serious mental illness (SMI), 156
 serotonergic hypnotics, 424–5
 serotonin, 5, 113
 anxiety and, 368–70
 dementia-related psychosis, 524–7
 neuronal network, 121
 projections, 279
 synthesis and termination of action,
 114–15
 serotonin antagonist/reuptake inhibitors
 (SARIs), 311–16
 serotonin blockers
 bipolar disorder spectrum, 338–45
 serotonin hyperfunction hypothesis of
 psychosis, 131–41
 serotonin hypothesis of psychosis,
 111–41
 serotonin network, 113–33
 constructing, 119–21
 serotonin partial agonist reuptake
 inhibitor (SPARI), 296–9
 serotonin receptors. *See also* drugs
 targeting serotonin receptors
 5HT_{1A}, 116, 118, 121, 296–9, 317
 5HT_{1B}, 125, 318
 5HT_{1B/D}, 118, 119, 318
 5HT_{2A}, 125
 5HT_{2A}, dopamine release regulation,
 184–8
 5HT_{2A}, hyperactivity/imbalance,
 111–41
 5HT_{2B}, 117, 119
 5HT_{2C}, 125, 293–4
 5HT₃, 125–9, 309–13, 318
 5HT₆, 130
 5HT₇, 130–3, 318–24
 overview, 114
 serotonin transporters (SERTs), 31, 33
 inhibition of, 289, 296, 317, 318–24
 sertindole, 232, 240

INDEX

- sertraline, 294, 378
 setiptiline, 309
 shift work disorder, 435, 436, 444
 sigma-1 binding, 294, 295
 signal propagation, 74
 signal transduction cascades, 9–23, 28, 53
 four important types of, 11, 12
 second messenger, forming, 11–14
 second messenger, to phosphoprotein cascades, 15–18
 second messenger, to phosphoprotein messenger, 13–15
 time course, 11
 silent antagonists, 41, 42, 45, 192
 Sinclair method, 573
 SLC1 gene family, 31, 35
 SLC17 gene family, 31, 35
 SLC18 gene family, 31, 35
 SLC32 gene family, 31, 35
 SLC6 gene family, 30, 31–5
 sleep
 neurobiology of, 402–15
 purpose of, 414–15
 REM and non-REM, 413, 414, 435
 sleepiness, 430–4
 sleep/wake cycle, 412–13
 disturbance of, 414, 416
 small interfering RNA (siRNA), 27
 small nuclear RNA (snRNA), 27
 smoking, 476. *See also* nicotine
 cessation, 306, 573
 snare proteins, 73
 SNRIs (serotonin–norepinephrine reuptake inhibitors), 298–303
 $\alpha_2\delta$ ligand combinations, 399
 anxiety disorders, 368
 arousal combo, 333
 mirtazapine combination, 333
 pain treatment, 380
 triple action combo, 333
 social anxiety disorder, 362, 372, 377
 sodium oxybate, 446–8
 sodium potassium ATPase (sodium pump), 32, 33
 sodium valproate, 347–50
 solriamfetol, 444
 soma, 2
 somatic pain, 302
 somatosensory cortex, 380
 specific neutral amino acid transporters (SNATs), 96
 spinobulbar tracts, 380
 spinothalamic tract, 380
 SSRIs (selective serotonin reuptake inhibitors), 289–96
 anxiety disorders, 368
 clinical uses of, 289
 common features of six drugs, 289–92
 depression in dementia, 534
 OCD, 577
 triple-action combo, 333
 unique properties of six drugs, 292–3
 stabilizers. *See* partial agonists
 steroids, neuroactive, 320–5
 Stevens Johnson syndrome, 352
 stigma, 145
 stimulants, 467–79, 544–7
 atypical, 546
 slow release vs. fast release, 478–9
 targeting DATs, 473–8
 treatment of addiction, 547
 stimulus-response conditioning, 571
 strengthening, synapse, 151, 154
 stress, ADHD, 467, 469, 480
 stroke, 492, 524
 Stroop test, 450, 451
 subjective memory complaints, 487, 488
 sublingual formulation, 232
 substance addictions, 544–75
 substrates, 45, 46
 suicide, 145, 156
 clozapine treatment, 223
 depressed patients, 251
 mixed feature patients, 251
 prevention, 346
 suicide inhibitors, 46
 sulpiride, 202, 205
 supersensitivity, 170, 171
 suprachiasmatic nucleus, 275, 307
 suprasegmental central sensitization, 384, 390
 suvorexant, 423
 synapses, 1, 3
 enlarged, 5
 synaptic neurotransmission, 4
 synaptogenesis, 151, 154
 tardive dyskinesia (TD), 166
 pathophysiology, 170–4
 treatment, 174–81
 tasimelteon, 439
 tau protein, 488, 494, 502, 503
 tetrabenazine, 175–6
 tetrahydrocannabinol (THC), 563, 565, 567
 tetrameric ligand-gated ion channels, 54–5
 thalamic dopamine pathway, 85
 thalamo-cortical glutamate pathway, 104
 third-messenger kinase, 14, 16
 third-messenger phosphatase, 15, 16
 thyroid, 333
 tonic inhibition, 259, 263
 topiramate, 201, 352, 556, 575
 trace amines, 241–38
 tradozone, 311–15, 424–5
 transduction, 381
 transfer RNA (tRNA), 27
 transporters, 29–35, 50
 classification and structure, 29–31
 histamine and neuropeptides, 35
 monoamine, 30, 31–4, 208
 SLC1 gene family, 31
 vesicular, 32, 35
 tranlycypromine, 337
 traumatic memories, 356, 366, 375, 574
 trazodone, 535
 treatment responsiveness, 155
 tricyclic antidepressants (TCAs), 333–7
 triglyceride levels, 197, 198, 199
 tryptophan, 114
 tuberoinfundibular dopamine pathway, 85
 tuberomammillary nucleus, 406, 408
 type 2 diabetes, 415
 tyramine, 338
 tyrosine, 80, 252
 tyrosine hydroxylase, 253
 ultradian sleep cycle, 413–16
 unipolar depression, 34, 244
 augmenting strategies for, 325–35
 drugs for, 289–325
 monoamine reuptake blockers, 285–8
 or bipolar, 249–51
 second-line monotherapies, 333–8
 treatment resistance in, 323–38
 valbenazine, 177
 valproic acid (valproate), 347–50
 varenicline, 551, 552, 573
 vascular dementia, 491–2, 534
 VEGF (vascular endothelial growth factor), 329
 venlafaxine, 299, 302
 ventromedial prefrontal cortex, 372, 374
 vesicular transporter for glutamate, 99
 vesicular transporters, 31, 32, 35
 VIAATs (vesicular inhibitory amino acid transporters), 255
 vilazodone, 296–9
 viloxazine, 485
 violence, 145–7, 575, 577–8
 visual hallucinations, 113, 524
 vital sign, 381, 399, 401
 VMAT1, 174
 VMAT2 inhibition, 174–81
 VMAT2 transporter, 31, 81, 254
 VMATs (vesicular monoamine transporters), 35

- voltage-sensitive calcium channels (VSCCs), 70–3, 366, 395
- voltage-sensitive ion channels, 66–73, 76
 - structure and function, 66
- voltage-sensitive sodium channels (VSSCs), 67–70, 347, 350, 351, 381
- volume neurotransmission, 6–9
- vortioxetine, 311, 315–20, 535
- wake-promoting agents, 440–8
- wakefulness, neurobiology of, 402–15
- weight gain, 198, 224
- widespread pain index (WPI), 387
- withdrawal syndrome, 546, 560
- worry, 362, 363
 - neurobiology of, 365–9
 - noradrenergic hyperactivity, 372
- xanomeline, 242
- Z drugs, 425–6
- ziprasidone, 224, 236
- zolpidem, 423
- zopiclone, 423
- zotepine, 221, 233