INDEX

Absorption pharmacokinetics
  nicotine dependence and withdrawal, 543–544
ABT431 compound
  schizophrenia dopamine hypothesis, 373
N-Acetyl aspartate (NAA)
  glutamate theory of schizophrenia
    pathological evidence, 292
  schizophrenia analysis, 256–257
  schizophrenia dopamine hypothesis, 289
N-Acetylcysteine (NAC)
  psychostimulant abuse and
cystine/glutamate transporter
  restoration, 576
Acoustic startle
  mouse anxiety models
    neurosteroid effects, 147
Acquired immunodeficiency syndrome
(AIDS)
  opiate addiction comorbidity with,
    691–694
Acute delivery systems
  nicotine dependence and withdrawal
    therapy, 547–548
Addictive disorders. See also Heroin
  addiction; specific disorders, e.g.
    Alcohol abuse
diagnostic criteria, 456–457
endocannabinoids, 675–676
γ-hydroxybutyric acid (GHB) and,
  635–636
hallucogens and, 639–640
nicotine dependence and withdrawal
  pharmacology, 536–545
  absorption pharmacokinetics,
    543–544
  bupropion, 549–550
  cannabinoid antagonists, 550
  distribution pharmacokinetics, 544
  metabolism and elimination
    pharmacokinetics, 544–545
  nicotine reinforcement
    neurosubstrates, 537–540
  nicotinic acetylcholine receptors,
    537
    functional adaptations, 540–541
  nicotinic antagonists, 548–549
  nicotinic partial agonists, 548
  nonnicotinic agents, 549–551
  opioid antagonists, 550–551
  overview, 545–546
  pharmacokinetics, 543–545
  public health policy and, 551–552
  replacement medications, 546–548
  tricyclic antidepressants, 550
  withdrawal neurosubstrates, 541–543
opiate addiction
  buprenorphine studies, 696–698
drug discovery survey, 699–700
epidemiology, 691–694
  future research issues, 698–699
treatment statistics, 694–696
AKT1 gene
dystrobrevin binding protein 1 (DTNBP1) schizophrenia susceptibility, 348–349
Alcohol
γ-hydroxybutyric acid (GHB) and, 634 neurosteroid effects and, 157–158
Alcohol abuse
animal models
neuroanatomical substrates, 466–467
behavioral paradigms, 467–470
central nervous system circuitry, 470–471
novel substrates, 471
dopamine neuronal systems and substrates, 471–486
bed nucleus of stria terminalis, 473–475
dopaminergic regulation, early research, 472–473
extracellular dopamine, 485–486
future research issues, 517–518
Adenosine receptors
anxiety neurobiology and deficits in, 29–30
Aδ fibers
pain pathways, 711–712
Adolescent patients
psychostimulant abuse chronic exposure and sensitization effects, 581–585
Adrenergic receptors
antipsychotic drugs mechanisms, 426–427 psychostimulant abuse, 575
Adrenocorticotropin hormone (ACTH) anxiety neurobiology and, 17 nicotine dependence and withdrawal, 539–540 psychostimulant abuse, 577–578 chronic exposure and sensitization effects, 580–585
Adult environmental effects
anxiety neurobiology, 35
Affective flattening in schizophrenia, 255–256
Agonist agents
psychostimulant abuse therapy, 586–587
systemic administration, 492–493, 503–504
ventral pallidum, 501–502
overview, 466
Alcohol-preferring rats (P rat line)
alcohol abuse studies
appropriate behavioral paradigms, 467–470
neuroanatomical controls, 469–470
reinforcer-specific controls, 469
central nervous system circuitry in, 470–471
characteristics of, 467
novel neuranatomical substrates, 471
AlloTHDOC
plasma levels, 137–140
Alogia
in schizophrenia, 255–256
z-Amino-3-hydroxy-5-methyl-isoxazole-4-propionic acid (AMPA)
benzodiazepine tolerance, 101
glutamate theory of schizophrenia
history of, 290–291
pathological evidence, 291–292
pharmacological evidence, 294–295
schizophrenia pharmacotherapy
drug development for, 392
Amino acid neurotransmission
anxiety disorder therapy, 72–75
anticonvulsants, 74–75
benzodiazepines, 73–74
Amino acid residues
benzodiazepines
GABA_A receptors, 106–108
D-Amino acid oxidase activator (DAO A)
schizophrenia candidate gene, 327
D-Amino acid oxidase (DAO)
schizophrenia candidate gene, 327
Amisulpiride
schizophrenia therapy
D_2/D_3 and D_4 receptor antagonism and regional specificity, 380
"AMPAkines"
glutamate theory of schizophrenia, 295
Amphetamine
chronic exposure and sensitization effects, 580–585
3,4-methylenedioxymethamphetamine reinforcement of, 615–616
monoamine neuropharmacology, 571–575
neuropeptide pharmacology and, 579
d-Amphetamine
alcohol abuse studies
dopaminergic receptor systems and substrates, 472–473
Amygdala. See also Extended amygdala (EA)
anxiety disorders and, 13–15
Anandamide
neuroactive steroid effects and, 158–159
Animal models. See also Mouse studies
alcohol-motivated behaviors
neuroanatomical substrates, 466–467
behavioral paradigms, 467–470
central nervous system circuitry, 470–471
novel substrates, 471
anxiety neurobiology
anxiety-like behavior in, 10–12
brain imaging studies, 14–15
early-life environmental effects, 33–34
rodent models, 6–9
3,4-methylenedioxyamphetamine neurotoxicity, 620–621
behavioral effects, 630–631
neurosteroid effects, 142–152
acoustic/fear-potentiated startle, 147
defensive burying behavior, 149–150
elevated-plus maze, 143–145
Geller/Seifter and Vogel conflict tests, 145–146
light-dark box, 146–147
mild mental stress models and social isolation, 151–152
mirrored chamber, 147–148
modified forced-swim test, 150–151
open-field activity, 148–149
separation-induced ultrasonic vocalizations, 150
obsessive-compulsive disorders (OCD), 224
psychostimulant abuse
chronic exposure and sensitization effects, 581–585
schizophrenia, 263–265
transient receptor potential V1 (TRPV1) receptors, 736
Anticonvulsants
anxiety disorder therapy, 74–75
migraine management, 766–767
\( \Delta^9 \)-tetrahydrocannabinol as, 672–673

Antidepressants
- anxiety disorder therapy, 64–70
  - beta blockers, 71
  - mirtazapine, 70
  - monoamine oxidase inhibitors, 70
  - selective serotonin reuptake inhibitors, 66–69
  - serotonin and noradrenaline reuptake inhibitors, 69
  - serotonin receptor agonists, 70–71
  - tricyclic antidepressants, 69–70

migraine management, 767

nicotine dependence and withdrawal therapy
- bupropion, 549–550
  - tricyclic

Antiemetics
migraine management, 765

Antihistamines
- anxiety disorder therapy, 75

Antinociception
- cannabinoid analgesics and, 668

Antipsychotics
- anxiety disorder therapy, 71–72
  - atypical agents, mechanisms of action
  - adrenergic mechanisms, 426–427
  - atypical antipsychotics
    - 5-HT\textsubscript{2A} receptor, 418–421
    - cholinergic mechanisms, 429–430
    - clozapine regimens
      - dopamine D\textsubscript{2} receptor blockade, 412–415
  - glutamatergic mechanisms, 427–429
  - neurogenesis, 430
  - neurokinin 3 receptors, 430
  - partial dopamine agonists, 416–417
  - serotonin receptor 5-HT\textsubscript{1A}-5-HT\textsubscript{2A} interactions, 424–425
  - serotonin receptor 5-HT\textsubscript{2A}-5-HT\textsubscript{2C} interactions, 422–424
  - serotonin receptor 5-HT\textsubscript{6}, 425–426
  - serotonin receptors, 417–418
  - serotonin release, 426
  - serotonin receptor 5-HT\textsubscript{2A} blockade
    - cortical dopamine efflux
    - and cognitive function, 421–422
    - extrapyramidal function, 422

substituted benzamides
- D\textsubscript{1}, D\textsubscript{3}, and D\textsubscript{4} receptors, 415–416
- table of drugs, 413
- typical vs. atypical drugs, 411–412
- metabolic syndrome with, 254
- obsessive-compulsive disorders
  - neuropharmacology, 229–234
  - symptom induction from, 234
- schizophrenia therapy
  - first-generation (conventional) agents, 383
  - glutamate theory of schizophrenia, 294–295
- history of, 370–371
- hypothesized mechanisms of action, 376–382
  - D\textsubscript{1} receptors, 380–381
  - D\textsubscript{2}/D\textsubscript{3} and D\textsubscript{4} antagonism and regional specificity, 380
  - D\textsubscript{2} occupancy thresholds and rapid dissociation, 378–380
  - D\textsubscript{2} receptor occupancy, 376–378
  - dopamine release, 381
  - NMDA receptor function, 381
  - synthesis reactions, 381–382
  - negative affect remediation, 255–256
  - psychosis management, 254
  - safety and tolerability, 387–388
  - second-generation (atypical) agents, 383–387

Anxiety and anxiety disorders
- alcohol abuse and \( \beta \)CCT/3PBC anxiety reduction efficacy, 510–511
- clinical management, 60–61
- corticotropin-releasing factor receptor antagonists
  - therapeutic potential of, 196–198
  - depression and pharmacotherapy, 80
- diagnostic criteria, 9–12, 61–62
- 3,4-methylenedioxymethamphetamine effects, 630–631
- neuroactive steroids
  - alcohol effects, 157–159
  - animal models, 142–152
  - behavioral effects, 142
  - brain and peripheral sources, 135–137
  - chemistry and pharmacology, 135–142
  - enantiomeric selectivity, 141–142
  - GABA\textsubscript{A} receptors and ligand-gated ion channels, 137–141
HPA axis function, 154–156
overview, 134–135
stress-induced behaviors, 154–155
neurobiology of
basic principles, 4
early-life environmental effects, 33–37
fear/anxiety circuits, 13–15
genetic susceptibility, 18–19
intracellular regulators, 30–33
knockout mice
neuronal messenger alterations, 24–26
neurotransmitter receptor deficits and
CRH proteins, 26–30
mouse genetics studies, 19–24
neurotransmitter systems and neuronal
messengers, 15–18
psychological traits
continuous expression of normal
personality, 9–10
genetic basis of, 4–6
mouse behavior extrapolation
studies, 6–9
pharmacotherapy
anxiolytic drugs, 62–75
amino acid neurotransmission, 72–75
anticonvulsants, 74–75
antidepressants, 64–70
antihistamines, 75
antipsychotics, 71–72
benzodiazepines, 73–74
beta-blockers, 71
lithium, 75
monoamine neurotransmission, 63–72
serotonin receptor agonists, 70–71
depressive disorders, 80
future research issues, 81
genetic basis of, 4–6
mouse behavior extrapolation
studies, 6–9
"Anxiety-related pathways"
anxiety neurobiology and, 36
Anxiolytic drugs
anxiety disorder pharmacotherapy, 62–75
amino acid neurotransmission, 72–75
anticonvulsants, 74–75
antidepressants, 64–70
antihistamines, 75
antipsychotics, 71–72
benzodiazepines, 73–74
beta-blockers, 71
lithium, 75
mirtazapine, 70
monoamine neurotransmission, 63–72
monoamine oxidase inhibitors, 70
selective serotonin reuptake inhibitors, 66–69
serotonin and noradrenaline reuptake
inhibitors, 69
serotonin receptor agonists, 70–71
tricyclic antidepressants, 69–70
corticotropin-releasing factor receptor
antagonists
future research issues, 198–199
nonpeptide ligands, 195–196
overview, 177–179
peptide ligand pharmacology, 185–195
ligand binding mechanisms, 190–195
receptor/ligand family structure,
179–185
ligand properties, 180–181
receptor subtypes and distribution,
181–185
therapeutic potential, 196–198
Appetite regulation
cannabinoid receptors and, 670–672
Arachidonic acid derivatives
diocannabionoid ligands, 663–664
transient receptor potential V1 (TRPV1)
receptor expression, 732–733
N-Arachidonoyl dopamine
diocannabionoid ligands, 663–664
Arachidonoyl ethanolamide
cannabinoid receptors and, 661–662
O-Arachidonoyl ethanolamide
diocannabionoid ligands, 663–664
Arousal
autonomic arousal
anxiety neurobiology, 4
animal anxiety-like behavior, 10–12
Asenapine
schizophrenia therapy, 389
Assembly mechanisms
GABA_A receptors
benzodiazepines, 108–110
Astressin
corticotropin-releasing factor receptor
antagonists
ligand binding mechanisms, 191–195
Attention-deficit hyperactivity disorder (ADHD)
obsessive-compulsive disorder comorbidity, 216
psychostimulant therapy, 568–569, 587
chronic exposure and sensitization effects, 581–585

Attention deficits
schizophrenia
animal models, 263–264

Augmentation strategies
obsessive-compulsive disorders
neuropharmacology, 225, 229–234

Autonomic arousal
anxiety neurobiology, 4
animal anxiety-like behavior, 10–12

Autoreceptors
partial dopamine agonists, 416–417

Avoidance behaviors
anxiety neurobiology, 4
animal anxiety-like behavior, 10–12

Avolition
in schizophrenia, 255–256

Baclofen
psychostimulant abuse therapy, 588

Basal ganglia-thalamic-frontal loops
obsessive-compulsive disorders
neuropharmacology, 221–222

BC1 RNA
anxiety neurobiology and, 32

Bed nucleus of stria terminalis (BST)
alcohol abuse studies
dopaminergic receptor systems and substrates, 473–475

Behavioral inhibition/activity
alcohol abuse
animal models
neuroanatomical substrates, 466–467
behavioral paradigms, 467–470
central nervous system circuitry, 470–471
novel substrates, 471
dopamine neuronal systems and substrates, 471–486
bed nucleus of stria terminalis, 473–475
dopaminergic regulation, early research, 472–473
extracellular dopamine, 485–486
future research issues, 517–518
GABAergic interactions with, 486 lateral hypothalamus, 481–485
ventral pallidum, 476–480
GABA$_A$ benzodiazepine receptor complex, molecular biology, 487–501
alcohol/modulator commonalities, 487–488
CA1/CA3 hippocampus, 511–516
efficacy of $\beta$CCT/3PBD modulation, GABA$_{A,1,2,3,5}$ receptors, 499–501
future research issues, 517–518
GABA-DA interaction hypothesis, 496–498
ligand selectivity with GABA$_{A_1}$ subunits, 498–499
microinjection studies, 505–506
naltrexone antagonist, 507–511
novel CNS GABAergic substrates, 498
probe applications, 488–493
site-specific microinjection, 493–496
subunit selectivity vs. intrinsic efficacy, 516–517
systemic administration, 492–493, 503–504
ventral pallidum, 501–502
overview, 466
anxiety neurobiology, 4
animal anxiety-like behavior, 10–12
3,4-methylenedioxymethamphetamine effects, 616–619
neurotoxic lesions and, 629–631
neurosteroids, 142
psychostimulant abuse
chronic exposure and sensitization effects, 580–585

Benzamides
D$_1$, D$_3$, and D$_4$ receptors, 415–416

Benzodiazepines (BZs). See also GABA$_A$ benzodiazepine receptor complex
anxiety disorder therapy, 73–74
flunitrazepam, 637
future research, 116–117

GABA$_A$ benzodiazepine receptor complex
alcohol abuse studies, 487–501
alcohol/modulator commonalities, 487–488
CA1/CA3 hippocampus, 511–516
efficacy of $\beta$CCT/3PBD modulation, GABA$_{A,1,2,3,5}$ receptors, 499–501
future research issues, 517–518
GABA-DA interaction hypothesis, 496–498

ligand selectivity with GABA_{A1} subunits, 498–499

microinjection studies, 505–506

naltrexone antagonist, 507–511

novel CNS GABAergic substrates, 498

oral administration, βCCT/3PBD

anxiety reduction, 510–511

vs. naltrexone, 507–511

site-specific microinjection, 493–496

site-specific microinjection techniques, 494–496

subunit selectivity vs. intrinsic efficacy, 516–517

systemic administration, 492–493, 503–504

ventral pallidum, 501–502

GABA_{A} receptors

assembly, clustering, and surface expression, 108–110

binding pocket, 105–108

brain function diversity, 110–112

functional diversity, knockout/knockin models, 112–114

single-cell response modulation, 99–100

structure and function, 93–96

subunit/subtype diversity, 103–104

3,4-methylenedioxymethamphetamine effects on, 628

receptor ligand pharmacology, 97–102

endogenous site, 98–99

metabolism functions, 101–102

single-cell GABA response modulation, 99–100

therapeutic action, 97–98

tolerance and dependence characteristics, 100–101

structure-activity relationships, 114–116

structure and function, 93–96

Beta-blockers

anxiety disorder therapy, 71

migraine management, 767

BIBN4096BS compound

calcitonin gene-related peptide sites and migraine therapy targeting, 762–764

Bicuculline

alcohol abuse studies

GABA_{A} benzodiazepine receptor complex, 487–488

site-specific microinjection techniques, 494–496

Bifeprunox

schizophrenia therapy, 389

Binding pocket structures

benzodiazepines

GABA_{A} receptors, 105–108

Biochemical markers

in schizophrenia, 260–262

Biochemistry

3,4-methylenedioxymethamphetamine effects, 616–619

Biogenesis of lysosome-related organelles complex-1 (BLOC1)
dystrobrevin binding protein 1 (DTNBP1)
molecular interactions, 353

Biological mechanisms

of schizophrenia, 256–263

Blood alcohol concentration (BAC) levels

alcohol abuse studies in alcohol-preferring rats, 468–470

Body temperature

3,4-methylenedioxymethamphetamine effects on, 617–618

neurotoxicity and, 624–625

Botulinum toxin (Botox)
migraine management, 768

Brain

anxiety disorder-related regions of, 13–15

benzodiazepine distribution, 110–112

3,4-methylenedioxymethamphetamine neurotoxicity biochemical and functional changes, 631–632

neuroactive steroid sources, 135–137

neuroanatomical control regions

alcohol abuse studies in alcohol-preferring rats, 469–470

circuitry systems, 470–471

psychostimulant abuse, 574–575

Brain-derived neurotrophic factor (BDNF)
anxiety neurobiology, 4

genetic susceptibility studies, 18–19

knockout mice studies, 25–26

receptor deficits and, 29–30

schizophrenia therapy

serotonin receptor 5-HT_{2A} receptor and, 421–422

Brain imaging studies

obsessive-compulsive disorders, 217–222

animal models, 224
neuropharmacological implications, 220–222
schizophrenia, 256–260
Buprenorphine
opiate addiction therapy
comparative efficacy studies, 697–698
implementation issues and pilot studies, 698
regulatory approval studies, 696–697
Bupropion
nicotine dependence and withdrawal therapy, 549–550
Buspirone
anxiety disorder therapy, 70–71
opiate addiction therapy, 699
Butyrophenones
schizophrenia therapy
clinical profile, 383
CA1/CA3 hippocampal fields
alcohol abuse studies
GABA<sub>A5</sub> receptor probes, 511–516
Calcitonin gene-related peptide (CGRP)
migraine therapy, 759–763
injection techniques, 763
neurovascular model, 759–760
receptor antagonist therapeutic efficacy, 763–764
synthesis and actions, 760–761
targeted repression therapy, 768
trigeminovasculature sites, 761–763
pain management applications, 768–769
Calcitonin receptor-like receptor (CLR)
calcitonin gene-related peptide sites and migraine therapy targeting, 762
Calcium/calmodulin-dependent protein kinase II (CaMK II)
anxiety neurobiology and, 30–33
benzodiazepine tolerance, 101
Calcium channel blockers
migraine management, 767–768
vanilloid receptors and, 728–729
Calmodulin kinase II
transient receptor potential V1 (TRPV1) receptor sensitization, 735
cAMP response element binding (CREB) protein
psychostimulant abuse
chronic exposure and sensitization effects, 585
Cannabinoid hypothesis of schizophrenia pharmacotherapy, 394
Cannabinoid receptors. See also Marijuana analgesic properties, 666–668
cannabinoid<sub>1</sub> (CB-1) receptor
addictive disorders
modulator receptor and, 458–459
antagonist/agonist medication development, 700
anxiety neurobiology and deficits in, 29–30
appetite regulation, 670–672
cognition and, 669–670
convulsant effects, 672–673
emesis modulation, 673–675
identification of, 661–662
nicotine dependence and withdrawal therapy
antagonist agents, 550
pain management and, 667–668
prenatal development and, 664–665
signaling mechanisms, 662–663
cannabinoid<sub>2</sub> (CB-2) receptor
emesis modulation, 674–675
pain management and, 668–669
signaling mechanisms, 662–663
cognition and, 669–670
convulsant effects, 672–673
emesis modulation, 673–675
future research on, 676
reward, tolerance, and dependence, 675–676
in schizophrenia
animal model, 265
signaling mechanisms, 662–663
CAPON gene
schizophrenia molecular genetics, 328
Capsaicin
cloning of, 727–729
transient receptor potential V1 (TRPV1) receptor expression, 730–732
Carbamazepine
anxiety disorder therapy, 75
β-Carboline3-carboxylate-α,β-butyl ester
alcohol abuse studies
anxiety reduction with, 510–511
GABA<sub>A1,2,3,5</sub> receptor subunit modulation, 499–501
GABA<sub>A1</sub> receptor subunit selectivity, 498–499
microinjection techniques, 505–507
oral administration, 507–511
systemic administration, 503–504
β-Carboline antagonist ZK 93426
alcohol abuse studies
  GABA<sub>A</sub><sub>S</sub> receptor specificity, 514–516
  GABA<sub>A</sub> benzodiazepine receptor complex, 490–493
  GABAergic modification of dopamine agonists, 497
Cardiovascular system
  γ-hydroxybutyric acid (GHB) effects, 634
Caspase-1
  3,4-methylenedioxyamphetamine effects on, 628
Catechol-O-methyl transferase (COMT)
  anxiety neurobiology and knockout mice studies, 24–26
  obsessive-compulsive disorders metabolism studies, 223
schizophrenia
dopamine hypothesis, 373
  genetic evidence, 286–287
  genetics studies, 286–287
  imaging studies, 285–286
  molecular genetics
    chromosomal abnormalities, 328–329
    susceptibility gene identification, 347–348
    tolcapone targeting of, 389
Cell-cell interactions
  anxiety neurobiology
    neuronal deficits and, 30
Cell membrane-associated proteins
  anxiety neurobiology and mouse studies, 19, 21
Central nervous system (CNS)
alcohol abuse studies in alcohol-preferring rats
  circuitry systems, role of, 470–471
  control substrates, 469–470
  γ-hydroxybutyric acid (GHB) effects, 634
  pain pathways, 712–714
  schizophrenia and, 260–262
Cerebrospinal fluid (CSF)
corticotropin-releasing factor receptor antagonists
effects on, 177–179
  schizophrenia dopamine hypothesis and, 288–289
C fibers
  pain pathways, 711–712
  transient receptor potential V1 (TRPV1) receptor expression, 729
Chemotherapy
  emesis with cannabinoid modulation of, 674–675
Cholecystokinin
  anxiety neurobiology and, 17
  pain management and, 716–717
Cholinergic neurotransmitters
  atypical antipsychotic mechanisms, 429–430
  schizophrenia neurochemistry and, 261–262
  schizophrenia pharmacotherapy, 393–394
Chromosomal abnormalities
  schizophrenia molecular genetics, 328–331
catechol-O-methyltransferase, 328–329
  DISC1 gene, 330–331
  PRODH candidate gene, 329–330
  ZDHHC8 candidate gene, 330
Chromosome mapping
  anxiety neurobiology
    mouse studies, 19, 23
  schizophrenia
    susceptibility gene identification, 346–351
CL218,872
  alcohol abuse studies
    GABA<sub>A</sub><sub>1</sub> receptor subunit selectivity, 499
Clomipramine
  obsessive-compulsive disorder therapy, 69–70
Clonazepam
  obsessive-compulsive disorder therapy, 234
Clonidine
  schizophrenia pharmacotherapy, 393
Clozapine
dopamine D<sub>2</sub> receptor blockade, 412–415
  mechanisms of action
    cholinergic mechanisms, 429–430
    serotonin receptor 5-HT<sub>2A</sub>, 418–421, 420–421
    serotonin receptor 5-HT<sub>6</sub> and, 425–426
    serotonin receptor 5-HT/D<sub>2</sub> hypothesis, 417–418
  schizophrenia therapy
    brain-derived neurotrophic factor and, 421–422
    cholinergic receptor targeting, 393–394
  clinical profile, 387
  dopamine D<sub>2</sub> receptor blockade, 412–415
history of, 370
safety and tolerability, 388–389
schizophrenia-related psychosis, 254
Clusters
GABA<sub>A</sub> receptors
benzodiazepines, 108–110
Cocaine
abuse
3,4-methylenedioxymethamphetamine
reinforcement of, 615–616
monoamine neuropharmacology,
570–575
therapy developments for, 585–588
chronic exposure and sensitization effects,
580–585
neuropeptide pharmacology and, 578–579
Cocaine- and amphetamine-regulated
transcript (CART) peptides
psychostimulant abuse
chronic exposure and sensitization
effects, 585
Cognitive behavior therapy (CBT)
obsessive-compulsive disorders, 219–220
Cognitive function
cannabinoid receptors and, 669–670
3,4-methylenedioxymethamphetamine
and, 630–631
nicotine dependence and withdrawal
withdrawal neurosubstrates, 541–543
schizophrenia, 254–255
animal model, 263–264
 glutamatergic receptors, 428–429
neural network analysis, 259
serotonin receptor 5-HT<sub>2A</sub> receptor
enhancement, 421–422
Comorbid conditions
addictive disorders vulnerability with,
457–458
obsessive-compulsive disorders, 216
opiate addiction, 691–694
Compensatory mechanisms
dopamine hypothesis of schizophrenia,
284–285
Computed tomography (CT)
obsessive-compulsive disorders
brain imaging studies, 217–218
schizophrenia analysis, 256
Conditioned conflict tests
anxiety neurobiology
emotionality studies in mice, 8–9
Conditioned fear paradigms
emotionality studies in mice, 8–9
Continuous performance test (CPT)
schizophrenia
animal models, 263–264
Cortical dopamine
schizophrenia dopamine hypothesis and,
287–288
serotonin receptor 5-HT<sub>2A</sub> receptor
enhancement, 421–422
Corticosterone
psychostimulant abuse, 577–578
Corticostriatal-thalamic-cortical loops
integrated glutamate/dopamine
hypotheses of schizophrenia
neurochemistry and, 374–376
Corticotropin-releasing factor (CRF)
alcchol abuse studies
in alcohol-preferring rats, 471
neurosteroid effects
acoustic/fear-potentiated startle, 147
nicotine dependence and withdrawal,
539–540
withdrawal substrate specificity, 543
opiate dependence therapy and, 699
psychostimulant abuse, 577–578
chronic exposure and sensitization
effects, 580–585
Corticotropin-releasing factor receptor
antagonists
anxiolytic applications
future research issues, 198–199
nonpeptide ligands, 195–196
overview, 177–179
peptide ligand pharmacology, 185–195
ligand binding mechanisms, 190–195
receptor/ligand family structure,
179–185
ligand properties, 180–181
receptor subtypes and distribution,
181–185
therapeutic potential, 196–198
Corticotropin-releasing hormone (CRH)
anxiety neurobiology and, 17
knockout mice studies, 25–26
receptor deficits, 28–30
Cortisol
nicotine dependence and withdrawal,
539–540
withdrawal substrate specificity, 543
Cotinine
nicotine dependence and withdrawal
metabolism and elimination
pharmacokinetics, 544–545
Countermodulation therapy
addictive disorders, 458–459
CP-154,526 antagonist
opiate dependence therapy and, 699
CRF$_1$ receptor
corticotropin-releasing factor receptor antagonists, 181–185
anxiety/depression therapeutic potential and, 196–198
ligand binding mechanisms, 190–195
nonpeptide ligands, 195–196
peptide ligand pharmacology, 185–195
CRF$_{2(a)}$ receptor
corticotropin-releasing factor receptor antagonists, 182–185
CRF$_{2(b)}$ receptor
corticotropin-releasing factor receptor antagonists, 182–185
CRF$_2$ receptor
corticotropin-releasing factor receptor antagonists, 182–185
ligand binding mechanisms, 190–195
peptide ligand pharmacology, 185–195
CX516 compound
schizophrenia pharmacotherapy, 392
Cyclic adenosine monophosphate (cAMP) corticotropin-releasing factor receptor antagonists
CRF receptor stimulation, 186–195
psychostimulant abuse
chronic exposure and sensitization effects, 584–585
Cyclic adenosine monophosphate (cAMP)-responsive nuclear factors
anxiety neurobiology and, 32
CYP1A2 enzyme
3,4-methylenedioxymethamphetamine neurotoxicity and, 622
CYP2A6 enzyme
nicotine dependence and withdrawal metabolism and elimination pharmacokinetics, 545
Cystine/glutamate transporters
psychostimulant abuse and, 576
Cytochrome P450 enzymes
benzodiazepine receptor ligand metabolism, 102
selective serotonin reuptake inhibitors, 68–69
Cytogenetic abnormalities
schizophrenia susceptibility gene identification, 346–351
Cytokines
anxiety neurobiology, 16–18
knockout mice studies, 26
3,4-methylenedioxymethamphetamine effects on, 627–628
D$_1$ receptor
alcohol abuse studies
bed nucleus of stria terminalis system, 475
lateral hypothalamus, dopaminergic regulation by, 481–485
ventral pallidum pathways, 477–480
psychostimulant abuse
monoamine neuropharmacology, 571–575
schizophrenia dopamine hypothesis
cortical vs. striatal dopamine, 288
history, 284–285
imaging evidence, 286–287
schizophrenia pharmacotherapy
antipsychotic agents, 380–381
schizophrenia therapy
agonist and antagonists, 390
substituted benzamides, 415–416
D$_2$/D$_3$ receptors
clozapine D$_2$ receptor blockade, 414–415
partial dopamine agonists, 416–417
psychostimulant abuse therapy, 586–587
selective antagonism
schizophrenia therapy, 380
substituted benzamides, 416
D$_2$ receptor
alcohol abuse studies
lateral hypothalamus, dopaminergic regulation by, 481–485
ventral pallidum pathways, 477–480
clozapine blockade, 412–415
psychostimulant abuse
chronic exposure and sensitization effects, 582–585
monoamine neuropharmacology, 571–575
schizophrenia dopamine hypothesis
cortical vs. striatal dopamine, 288
history, 284–285, 371–373
imaging evidence, 285–286
pathological evidence, 285
pharmacological evidence, 287
schizophrenia pharmacotherapy
  antipsychotic occupancy and effect,
  376–378
High 5-HT\textsubscript{2A} vs., 378
  occupancy thresholds and rapid
dissociation, 378–380
subtherapeutic occupancy time, 382
\textit{D}\textsubscript{3} receptor
  schizophrenia dopamine hypothesis
  genetic evidence, 286–287
  pathological evidence, 285
  pharmacological evidence, 287
  schizophrenia therapy
  antagonist development, 390
  substituted benzamides, 415–416
\textit{D}\textsubscript{4} receptor
  schizophrenia dopamine hypothesis
  pathological evidence, 285
  pharmacological evidence, 287
  schizophrenia therapy
  antagonism and regional specificity,
  380
  antagonist development, 390
  substituted benzamides, 415–416
  Deep brain stimulation (DBS)
  obsessive-compulsive disorders, 236–237
  Defensive burying behavior
  animal anxiety models
  neurosteroid effects, 149–150
  Dehydroepiandrosterone
  schizophrenia therapy, 394
  Dehydroepiandrosterone sulfate (DHEAS)
  in brain, 137
  schizophrenia therapy, 394
  Delta opioid receptors
  structure and function, 751
  Dependency risk
  endocannabinoids, 675–676
  Depolarization inactivation
  schizophrenia therapy
  \textit{D}_{2} receptor occupancy and effect,
  376–378
  Depression
  anxiety symptoms with
  pharmacotherapy, 80
corticotropin-releasing factor receptor
  antagonists
  therapeutic potential of, 196–198
  neuroactive steroid interactions,
  156–157
  stress-induced behavior
  neuroactive steroids, 156–157
  Desensitization
  transient receptor potential V1 (TRPV1)
  receptors, 735–736
  Designer drugs. See also specific drugs,
e.g. 3,4-Methylenedioxy-
  methamphetamine (MDMA)
  overview, 614
  Developmental genes
  obsessive-compulsive disorders, 223–224
  Diagnostic criteria
  anxiety disorders, 9–12, 61–62
  Diazepam binding inhibitor (DBI)
  benzodiazepine ligands, 98–99
3,4-Dihydroxyamphetamine (HHA)
  3,4-methylenedioxymethylamphetamine
  neurotoxicity and, 622
3,4-Dihydroxy-L-phenylalanine (DOPA)
  schizophrenia dopamine hypothesis,
  372–373
Dimerization
  opioid receptors, 752
  DISC1 gene
  schizophrenia molecular genetics, 330–331
  molecular interactions, 351–352
  susceptibility identification, 349–350
  Discontinuation syndrome
  selective serotonin reuptake inhibitors,
  67–69
  Distribution kinetics
  nicotine dependence and withdrawal, 544
  DOI
  hallucinogens and, 639
  schizophrenia therapy
  serotonin receptor 5-HT\textsubscript{2A}, 420–421
  Donepezil
  schizophrenia pharmacotherapy, 393–394
  Dopadecarboxylase
  schizophrenia dopamine hypothesis,
  372–373
  Dopamine agonist
  alcohol abuse studies
  GABAergic modification, 496–498
  partial agonists, 416–417
  psychostimulant abuse therapy, 586–587
  in schizophrenia
  animal models, 264
  Dopamine hypothesis of schizophrenia
  cortical vs. striatal dopamine, 287–289
  genetic evidence, 286–287
  glutamate theory consolidated with,
  295–296
  history, 284–285
imaging evidence, 285–286
neurochemistry and, 371–373
pathological evidence, 285
pharmacological evidence, 287
postmortem studies, 344
Dopamine neurotransmitters
addictive disorders
reward therapy and, 458–459
anxiety disorder therapy
antipsychotics, 71–72
anxiety neurobiology, 15–17
receptor deficits, 29–30
3,4-methylenedioxyamphetamine (MDMA)
receptor/transporter effects, 617
reinforcing properties, 614–616
nicotine dependence and withdrawal
withdrawal substrates, 542–543
obsessive-compulsive disorders, 223
psychostimulant abuse, 569–575
neuropeptide pharmacology, 579
neuropharmacology, 570–575
schizophrenia and, 260–262
COMT catabolism and, 328
drug targeting innovations, 389
Dopaminergic receptors
alcohol abuse studies
neuronal systems and substrates,
471–486
bed nucleus of stria terminalis,
473–475
dopaminergic regulation, early
research, 472–473
extracellular dopamine, 485–486
future research issues, 517–518
GABAergic interactions with, 486
lateral hypothalamus, 481–485
D2 dopaminergic regulation,
hypothesized mechanisms,
481–485
ventral pallidum, 476–480
hypothesized mechanisms, 478–480
alcohol abuse studies
in alcohol-preferring rats, 471
anxiety neurobiology and receptor
deficits, 29–30
nicotine dependence and withdrawal
nicotine reinforcement substrates,
538–540
psychostimulant abuse
chronic exposure and sensitization
effects, 582–585

Dopamine transporter
catechol-O-methyl transferase
as schizophrenia susceptibility gene,
347–348
inhibitors
psychostimulant therapy targeting,
587–588
obsessive-compulsive disorders
abnormalities, 219–220
psychostimulant abuse
monoamine neuropharmacology,
573–575
schizophrenia
dopamine hypothesis and, 285
Dorsolateral prefrontal cortex (DLPFC)
schizophrenia dopamine hypothesis, 373
DRD2/DRD3 receptors
schizophrenia molecular genetics, 331–332
catechol-O-methyl transferase
susceptibility gene, 347–348
Drug abuse
dopaminergic receptor systems and
substrates
bed nucleus of stria terminalis system,
474–475
rewarding/reinforcing effects in, 459
stress-induced response
neuroactive steroid effects and,
159–160
Dyadic encounters
schizophrenia
animal models, 264
Dynorphins
structure and classification, 747
Dysbindin
dystrobrevin binding protein 1 (DTNBP1)
molecular interactions, 353
schizophrenia candidate gene, 326,
348–349
Dystrobrevin binding protein 1 (DTNBP1)
schizophrenia candidate gene, 325–326
chromosome mapping, 346
chromosome identification of, 348–349
functional implications, 332–333
molecular interactions, 352–353
Dystrophin-associated glycoprotein
complex (DCG)
dystrobrevin binding protein 1
identification
schizophrenia candidate gene, 348–349

Electroencephalography (EEG)
schizophrenia analysis, 256

Elevated-plus maze (EPM)
animal anxiety-like behavior and, 12
neurosteroid effects, 143–145
emotionality studies in mice, 7–9

Elevated-zero maze (EZM)
emotionality studies in mice, 8–9

Elimination mechanisms
nicotine dependence and withdrawal, 544–545

Emesis
antiemetics
migraine management, 765
cannabinoid receptors modulation of, 673–675

Emotionality studies
anxiety neurobiology
rodent models, 6–9

Enantiomeric selectivity
neuroactive steroids, 141–142

Endocannabinoid system, 662–665
cannabinoid receptors and signaling, 662–663
physiology and pharmacology, 665–675
prenatal developmental effects, 664–665
reward, tolerance and dependence mechanisms, 675–676
synthesis and metabolism, 663–664

Endogenous opioids
classification, 746–748

Endogenous sites
benzodiazepine ligands, 98–99
β-Endorphins
structure and classification, 747–748

Enkephalin neurons
nicotine dependence and withdrawal, 540

Enkephalins
structure and function, 746–747

Enthoprotin
schizophrenia molecular genetics, 328

Environmental factors
addictive disorders vulnerability, 457–458
anxiety neurobiology
early-life experience, 33–34

Epilepsy
endocannabinoids and, 672–673

Erβ3 gene
NRG1 molecular interaction, 353–355
regulator of G-protein signaling 4
schizophrenia candidate gene, 328

Ergots
migraine management, 765

Ethanol
neuroactive steroid effects and, 158–159

Eticlopride
alcohol abuse studies
lateral hypothalamus, effects on, 481–485
ventral pallidum receptor blockade, 478

Excitatory amino acid transporters (EAATs)
glutamate theory of schizophrenia
pathological evidence, 292

schizophrenia genetics
GRM3 gene, 349

Extended amygdala (EA)
alcohol abuse studies
dopaminergic receptor systems and substrates, 473–474
GABA_A benzodiazepine receptor complex manipulation
site-specific microinjection studies, 493–496

Extracellular dopamine
alcohol abuse studies
dopaminergic regulation mechanisms, 485–486

Extrapyramidal symptoms (EPS)
atypical antipsychotics drugs, 411–412
clozapine D2 receptor blockade, 412–415

schizophrenia therapy
antipsychotics and, 370–371
D2 receptor occupancy and effect, 376–378
D2 receptor occupancy thresholds and rapid dissociation, 379–380
first-generation antipsychotics, 383
second-generation antipsychotics, 383–388
serotonin receptor 5-HT2A blockade, 422

Extroversion vs. introversion (E trait)
anxiety neurobiology, 5–6

Face validity
animal anxiety-like behavior and, 12
Fatty acid amide hydrolase (FAAH)
convulsant effects of, 672–673
emesis modulation, 674–675
INDEX

793

endocannabinoid ligands, 664
endocannabinoid physiology and, 666
Fear/anxiety circuits
anxiety neurobiology, 13–15
Fear-potentiated startle mouse anxiety models neurosteroid effects, 147
Feverfew
migraine management, 768
FEZ1 protein
DISC1 schizophrenia candidate gene molecular interactions, 351–352
First-generation antipsychotics (FGAs)
schizophrenia therapy clinical profiles, 383
D₂ receptor occupancy and effect, 376–378
history of, 370–371
NMDA receptor antagonists, 381
second-generation antipsychotic comparisons, 384–387
Fixed-ratio (FR) schedule
alcohol abuse studies in alcohol-preferring rats, 469
Flumazenil
alcohol abuse studies
GABA_A5 receptor specificity, 512–516
GABA_A benzodiazepine receptor complex, 490–493
endogenous ligand sites, 98–99
Flunitrazepam
overview, 637
Fluorodeoxyglucose (FDG) studies
schizophrenia analysis, 257
Fluoxetine
3,4-methylenedioxymethamphetamine effects on, 616, 627
nicotine dependence and withdrawal withdrawal substrate specificity, 542–543
Fluphenazine
adrenergic receptor mechanisms, 427
Free-radical formation
3,4-methylenedioxymethamphetamine neurotoxicity, 624
Frontal cortex abnormalities
glutamate theory of schizophrenia pathological evidence, 292
Functional candidate genes
schizophrenia molecular genetics, 331–332
Functional imaging studies
obsessive-compulsive disorders, 219–220
schizophrenia analysis, 257–260
Fyn tyrosine kinase
anxiety neurobiology and, 31
GABA_A-benzodiazepine receptor complex
alcohol abuse studies, 487–501
alcohol/modulator commonalities, 487–488
CA1/CA3 hippocampus, 511–516
efficacy of βCCT/3PBD modulation, GABA_A1,2,3,5 receptors, 499–501
future research issues, 517–518
GABA-DA interaction hypothesis, 496–498
ligand selectivity with GABA_A1 subunits, 498–499
microinjection studies, 505–506
naltrexone antagonist, 507–511
novel CNS GABAergic substrates, 498
oral administration, βCCT/3PBD anxiety reduction, 510–511
vs. naltrexone, 507–511
probe applications, 488–493
site-specific microinjection, 493–496
subunit selectivity vs. intrinsic efficacy, 516–517
systemic administration, 492–493, 503–504
ventral pallidum, 501–502
GABAergic neurons
alcohol abuse studies
in alcohol-preferring rats, 471
bed nucleus of stria terminalis system, 474
dopamine agonist modification, 496–498
GABA_A5 receptor specificity, 512–516
novel substrates, 498
ventral pallidum dopaminergic regulation and, 479–480
cannabinoid₁ (CB-1) receptors and, 672–673
integrated glutamate/dopamine hypotheses of schizophrenia, 375–376
psychostimulant abuse, 574–575
chronic exposure and sensitization effects, 583–585
γ-aminobutyric acid (GABA) receptors and, 576–577
novel therapeutic developments, 588
Gabapentin
  anxiety disorder therapy
  amino acid neurotransmission, 75
  migraine management, 766–767
GA-BARAP
  GABA_A receptors
  benzodiazepines, 109–110
"GABA shift" assay
  alcohol abuse studies
    GABA_A benzodiazepine receptor complex
    subunit selectivity vs. intrinsic efficacy, 517
Galantamine
  schizophrenia pharmacotherapy, 393–394
γ-aminobutyric acid (GABA) receptors
  addictive disorders
    modulator therapy and, 458–459
  anxiety disorder therapy
    amino acid neurotransmission, 72–75
    anxiety neurobiology and, 15–17
    knockout mice deficit studies, 26–30
  cannabinoid receptors and neurotoxicity effects, 673
GABA_A receptors
  alcohol abuse studies
    novel substrates, 498
    ventral pallidum dopaminergic regulation and, 479–480
  benzodiazepines
    assembly, clustering, and surface expression, 108–110
    binding pocket, 105–108
    brain function diversity, 110–112
    functional diversity, knockout/knockin models, 112–114
    single-cell response modulation, 99–100
    subunit/subtype diversity, 103–104
GABA_A1 subunit
  alcohol abuse studies, 498–501
  microinjection techniques, 505–507
  ventral pallidum selectivity, 501–503
GABA_A5 subunit
  as alcohol substrate probes, 511–516
  neuroactive steroids, 137–141
GABA_B receptors
  alcohol abuse studies
    ventral pallidum dopaminergic regulation and, 479–480
  γ-hydroxybutyric acid (GHB)
    mechanisms and, 634–635
    migraine management with anticonvulsants, 766–767
  neuroactive steroids
    enantiomeric selectivity, 141–142
    nicotine dependence and withdrawal nicotine reinforcement substrates, 538–540
  NRG1 molecular interaction, 354–355
  psychostimulant abuse and, 576–577
  schizophrenia neurochemistry and, 261–262
γ-hydroxybutyric acid (GHB)
  addiction risk, 635–636
  mechanism of action, 634–635
  overview, 632–633
  pharmacological effects, 633–634
"Gate control" theory
  classification of, 713–714
Geller-Seifter test
  mouse models of anxiety, 8–9
  neurosteroid effects, 145–146
Gene expression
  psychostimulant abuse
    chronic exposure and sensitization effects, 584–585
Gene linkage studies
  schizophrenia, 323–324
  future research issues, 355–356
  susceptibility gene identification, 344–351
Generalized anxiety disorder (GAD)
  buspirone therapy, 71
  pharmacotherapy, 77
  serotonin/noradrenaline reuptake inhibitors, 69
  tricyclic antidepressants, 69–70
Genetic studies. See also Gene linkage studies; Molecular genetics
  addictive disorders vulnerability, 457–458
  anxiety neurobiology, 4–6
  environmental effects and, 34–35
  susceptibility studies, 18–19
  glutamate theory of schizophrenia, 293–294
  obsessive-compulsive disorders, 222–224
  developmental genes, 223–224
  dopamine, 223
  glutamate, 223
  neurotransmitter metabolism, 223
  serotonin, 222–224
schizophrenia, 262–263
animal models, 264
dopamine hypothesis, 286–287
epidemiology, pathophysiology, and neurobiology, 323
Gepirone
anxiety disorder therapy, 71
Glia-derived protein
GABA_A receptors
benzodiazepines, 108–110
Glucocorticoid receptor (GR)
stress-induced behaviors
neuroactive steroids, 153–154
Glucocorticoid receptor (GR) transcription factor
anxiety neurobiology and, 31
Glucocorticoids
anxiety neurobiology and, 17
Glucocorticoid hormones
psychostimulant abuse, 577–578
Glucose utilization
schizophrenia psychosis
neural network analysis, 257–258
Glutamate neurotransmitters
anxiety disorder therapy
amino acid neurotransmission, 72–75
nicotine dependence and withdrawal withdrawal substrates, 542–543
obsessive-compulsive disorders, 223
pain management and, 717
psychostimulant abuse and, 575–576
schizophrenia neurochemistry and, 261–262
targeted drug development for, 391–392
Glutamate reuptake inhibitors
schizophrenia pharmacotherapy, 391–392
Glutamatergic system
addictive disorders
modulator therapy and, 458–459
atypical antipsychotics, 427–428
nicotine dependence and withdrawal nicotine reinforcement substrates, 538–540
psychostimulant abuse, 569–576
chronic exposure and sensitization effects, 583–585
novel therapeutic developments, 588
in schizophrenia, 264
molecular genetics
functional candidate genes, 331–332
pharmacotherapy
 glutamate reuptake inhibitors, 391–392
Glutamate theory of schizophrenia
dopamine hypothesis and, 295–296
 genetic evidence for, 293–294
history, 289–291
 imaging evidence for, 292–293
 neurochemistry of, 373–374
 pathological evidence for, 291–292
 pharmacological evidence for, 294–295
Glutamic acid decarboxylase (GAD)
anxiety neurobiology and knockout mice studies, 24–26
schizophrenia susceptibility genetics, 350–351
Glutathione conjugates
3,4-methylenedioxymethamphetamine neurotoxicity and, 622
Glycine
schizophrenia pharmacotherapy
NMDA targeting with, 391–392
Glycine transporter 1 (GlyT1)
glutamate theory of schizophrenia pharmacological evidence, 294–295
Glycine transporter inhibitors
schizophrenia pharmacotherapy
NMDA targeting with, 391–392
G-protein coupled receptors (GPCRs)
corticotropin-releasing factor receptor antagonists
ligand binding mechanisms, 192–195
delta opioid receptors, 751
kappa opioid receptors, 751–752
mu opioid receptors and, 748–751
regulator of G-protein signaling 4
schizophrenia candidate gene, 328
G-protein-gated inwardly rectifying K^+ (GIRK) channels
anxiety neurobiology and receptor deficits and, 29–30
G proteins
cannabinoid receptors and, 662–663
psychostimulant abuse chronic exposure and sensitization effects, 584–585
GRM3 gene
 schizophrenia molecular genetics, 331–332
 susceptibility identification, 349
Group A beta-hemolytic streptococcus (GABHS) infection
obsessive-compulsive disorders and, 235
Guanfacine
schizophrenia pharmacotherapy, 393

Hallucinogens
LSD, 637–640
addiction, 639–640
mechanism of action, 638–639
pharmacology, 638

Haloperidol
serotonin receptor 5-HT6 and, 425–426
Hamilton depression and anxiety scales
corticotropic-releasing factor receptor antagonists
anxiety/depression therapeutic potential, 197–198

Heat exposure
transient receptor potential V1 (TRPV1) receptor expression, 730–732

Hepatitis C
opiate addiction comorbidity with, 691–694

Heroin addiction
incidence and prevalence, 692–694
neuropeptide pharmacology and, 578–579
pharmacotherapy
history of, 451–457
treatment statistics, 694–696

High 5-HT2A
schizophrenia therapy
D2 affinity vs., 378

High alcohol drinking (HAD) rats
alcohol abuse studies
characteristics of, 467

Hippocampus
alcohol abuse studies
CA1/CA3 fields
GABA_A5 receptor probes, 511–516
anxiety disorders and, 13–15
3,4-methylenedioxymethamphetamine effects on
long-term neurochemical effects, 619–620

Homeobox genes
obsessive-compulsive disorders, 223–224

HTR2A receptor
schizophrenia molecular genetics, 331–332

Human immunodeficiency virus
opiate addiction and exposure to, 691–694

Hydroxyl radicals
3,4-methylenedioxymethamphetamine neurotoxicity and, 627

Hydroxyzine
anxiety disorder therapy, 75

Hyperdopaminergic state
schizophrenia dopamine hypothesis and evidence for, 287

Hyperthermia
3,4-methylenedioxymethamphetamine neurotoxicity and, 624–625

Hypodopaminergia
schizophrenia dopamine hypothesis, 288–289

Hypothalamic-pituitary-adrenal (HPA) axis
anxiety neurobiology and, 17
corticotropic-releasing factor receptor antagonists, 177–179
nicotine dependence and withdrawal
nicotine reinforcement substrates, 539–540
withdrawal substrate specificity, 543
psychostimulant abuse, 577–578
chronic exposure and sensitization effects, 580–585
stress-induced behaviors
neuroactive steroids, 153–159

Idazoxan
adrenergic receptor mechanisms, 427

Iloperidone
schizophrenia therapy, 389

Imaging studies
brain regions
anxiety disorders and, 13–15
glutamate theory of schizophrenia, 292–293

Imidazobenzodiazepines
alcohol abuse studies
GABA_A5 receptor specificity, 512–516

Immediate early genes
psychostimulant abuse
chronic exposure and sensitization effects, 585

Immune response
3,4-methylenedioxymethamphetamine effects on, 618

Immunoglobulin therapy
obsessive-compulsive disorders, 235

Immunomodulatory therapy
obsessive-compulsive disorders, 235

Indole agents
serotonin receptor 5-HT2A, 418–421
INDEX 797

Indolealkylamines, 637–640
   addiction, 639–640
   mechanism of action, 638–639
   pharmacology, 638

Infection
   obsessive-compulsive disorders and, 235

Inflammation
   transient receptor potential V1 (TRPV1) receptor expression, 729

Integrated glutamate/dopamine hypotheses of schizophrenia
   basic principles, 295–297
   pharmacotherapy and, 374–376

Interleukin-1β converting enzyme (ICE)
   3,4-methylenedioxymethamphetamine effects on, 628

Interleukin-1β release
   3,4-methylenedioxymethamphetamine effects on, 628

Intracellular signaling molecules
   anxiety neurobiology and mouse studies, 19, 22
   phenotype analysis, 30–33
   psychostimulant abuse
      chronic exposure and sensitization effects, 584–585
      schizophrenia therapy, 394–395

Intrinsic efficacy
   alcohol abuse studies
      GABA<sub>A</sub> benzodiazepine receptor complex
      subunit selectivity vs., 516–517

Ionotropic glutamate receptors
   atypical antipsychotics, 427–429

J-domain fragments
   corticotropin-releasing factor receptor antagonists
      ligand binding mechanisms, 192–195

Kainate receptors
   glutamate theory of schizophrenia
      mRNA binding, 291–292
      schizophrenia pharmacotherapy
      drug development for, 392

Kappa opioid receptors
   psychostimulant abuse and, 578–579
   structure and function, 751–752

Ketamine
   glutamate theory of schizophrenia
      history of, 289–290
      overview, 636
      pharmacological effects, 636–637

Ketoconazole
   psychostimulant abuse, 577–578

Knockin mice
   benzodiazepine functional diversity, 112–114

Knockout mice
   anxiety neurobiology
      neuronal messenger alterations, 24–26
      neurotransmitter receptor/CMAP deficits, 26–30
   benzodiazepine functional diversity studies, 112–114
   calcitonin gene-related peptide studies, 760–761
   transient receptor potential V1 (TRPV1) receptor models, 736

LAAM (<i>l</i>-a-Acetyl methadon)
   addiction pharmacotherapy and, 454–457
   treatment statistics, 695–696

Lamotrigine
   anxiety disorder therapy, 75
   schizophrenia pharmacotherapy
      NMDA targeted drug development, 392–393

Lateral hypothalamus (LH)
   alcohol abuse studies
      dopamine neuronal systems and substrates, 481–485
      D<sub>2</sub> dopaminergic regulation, hypothesized mechanisms, 481–485

Leptin
   cannabinoid receptors and, 671–672

Lesion models
   in schizophrenia, 265

Ligand-gated ion channels
   neuroactive steroids, 137–141

Light-dark box
   mouse models of anxiety
      neurosteroid effects, 146–147

LIS1 gene
   DISC1 schizophrenia candidate gene molecular interactions, 351–352

Lithium
   anxiety disorder therapy, 75
   Locomotor sensitization
      psychostimulant abuse
         chronic exposure and sensitization effects, 581–585
Lofexidine
opiate addiction and, 699
Long-term therapy
selective serotonin reuptake inhibitors, 68–69
LY206130
nicotine dependence and withdrawal withdrawal substrate specificity, 542–543
LY274600
nicotine dependence and withdrawal withdrawal substrate specificity, 542–543
LY354740 Glu analog
nicotine dependence and withdrawal withdrawal substrate specificity, 542–543
Lysergic acid diethylamide (LSD), 637–640
addiction, 639–640
mechanism of action, 638–639
pharmacology, 638
M100907 compound
schizophrenia therapy
serotonin receptor 5-HT2A, 419–421
Magnetic resonance imaging (MRI)
obsessive-compulsive disorders
brain imaging studies, 217–218, 220
schizophrenia analysis, 256
Magnetic resonance spectroscopy (MRS)
glutamate theory of schizophrenia, 293
schizophrenia analysis, 256–257
MAPK/ERK signaling
anxiety neurobiology and, 36–37
Marijuana
endocannabinoid system, 662–665
cannabinoid receptors and signaling, 662–663
prenatal developmental effects, 664–665
reward, tolerance and dependence mechanisms, 675–676
synthesis and metabolism, 663–664
future research on, 676
pharmacology
appetite regulation, 670–672
cognitive function, 669–670
emesis, 673–674
endocannabinoid system physiology, 665–666
neurotoxicity, 672–673
overview, 659–662
pain management, 666–669
Mast cells
calcitonin gene-related peptide sites and migraine therapy targeting, 762
MATRICS program
schizophrenia-related cognitive dysfunction, 254–255
Mazindol
psychostimulant abuse therapy, 587
mCCP serotonin receptor agonist obsessive-compulsive disorders, 234
Mecamylamine
nicotine dependence and withdrawal therapy, 549
Medial prefrontal cortex (MPFC)
anxiety neurobiology
brain imaging studies, 15
Melanocyte-inhibiting factor (MIF) peptides
pain management and
Memantine
schizophrenia pharmacotherapy, 392
Memory deficits
cannabinoid receptors and, 669–670
3,4-methylenedioxymethylamphetamine and, 630–631
schizophrenia
animal models, 263
schizophrenia and, 254–255
Mesoaccumbens system
alcohol abuse studies
dopaminergic receptor systems and substrates, 472–473
GABA_A benzodiazepine receptor complex
site-specific microinjection techniques, 494–496
Mesolimbic pathway
alcohol abuse studies
dopaminergic receptor systems and substrates, 472–473
psychostimulant abuse
dopamine system, 574–575
Mesopallidal system
alcohol abuse studies, 476–480
Metabolic syndrome
antipsychotics and, 254
Metabolism kinetics
endocannabinoid system, 663–664
3,4-methylenedioxymethylamphetamine neurotoxicity and, 621–622
nicotine dependence and withdrawal, 544–545
Metabolites
3,4-methylenedioxymethamphetamine neurotoxicity and mechanisms of, 621–622

Metabotropic glutamate receptors
atypical antipsychotics, 427–429
 glutamate theory of schizophrenia, 293–294
 history of, 290–291
 pathological evidence, 292
 psychostimulant abuse, 576
 schizophrenia pharmacotherapy
 group II receptor targeting, 391–392

Methadone
heroin addiction pharmacotherapy
 history of, 453–457
 in "office-based practice," 700
 opiate addiction therapy
 buprenorphine comparisons with, 697–698
 psychostimulant abuse therapy, 585–586
 treatment statistics, 694–696

Methamphetamine. See also 3,4-Methylenedioxymethamphetamine (MDMA)
3,4-methylenedioxymethamphetamine and
 behavioral effects, 630–631
 monoamine neuropharmacology, 571–575

α-Methylparatyrosine (AMPT)
schizophrenia dopamine hypothesis, 372–373
 schizophrenia therapy
 D2 receptor occupancy and effect, 376–378

Methylation techniques
3,4-methylenedioxymethamphetamine neurotoxicity and, 622
3,4-Methylenedioxymphetamine (MDA)
3,4-methylenedioxymethamphetamine neurotoxicity and, 621–622
3,4-Methylenedioxymethamphetamine (MDMA)
 behavioral effects, 618–619
 body temperature effects, 617–618
 brain biochemistry and function, 631–632
 monoamine release, 616
 neuroendocrine and immune responses, 618
 neurotoxicity, 619–628
 animal models, 620–621
 cytokines and microglia, 627–628
 hyperthermia, 624–625
 long-term neurochemical change, 619–620
 metabolite mechanisms, 621–622
 monoaminergic transporter, 625–627
 oxidative stress, 623–624
 neurotoxic lesions
 behavioral effects, 629–631
 thermoregulation effects, 629
 neurotransmitter receptors and transporters, 617
 overview, 614
 reinforcing properties, 614–616
 tryptophan hydroxylase, 616–617

Methylphenidate
chronic exposure and sensitization effects, 580–585
 monoamine neuropharmacology, 571–575
 psychostimulant abuse therapy, 587

Microglia
3,4-methylenedioxymethamphetamine effects on, 627–628

Microinjection studies
alcohol abuse
 GABA_A benzodiazepine receptor complex modulation, 505–507

Migraine headaches
history and definition, 758–759
 therapy
 calcitonin gene-related peptide and, 759–763
 injection techniques, 763
 neurovascular model, 759–760
 receptor antagonist therapeutic efficacy, 763–764
 synthesis and actions, 760–761
 trigeminovascular sites, 761–763
 future trends in, 768–769
 history of, 758–759
 migraine diagnostic criteria, 758–759
 overview, 758
 pharmacology, 764–768
 acute therapy, 764–765
 preventive therapy, 766–768

Mild mental stress models
 neurosteroid effects, 151–152

Mineralocorticoid receptors
 psychostimulant abuse, 577–578

Mirrored chamber
 mouse anxiety models
 neurosteroid effects, 147–148

Mirtazapine
 anxiety disorder therapy, 70
Missense mutations
PRODH gene
schizophrenia molecular genetics, 329–330
Mitogen-activated protein kinase
transient receptor potential V1 (TRPV1) receptor expression, 729
Mitotic inhibitor methylazoxymethanol (MAM)
in schizophrenia, 265
Moclobemide
anxiety disorder therapy, 70
Modafinil
psychostimulant abuse therapy, 588
schizophrenia therapy, 389
Modified forced-swim test
animal anxiety models
neurosteroid effects, 150–151
Modulation therapy
addictive disorders, 458–459
Molecular genetics
corticotropin-releasing factor receptor antagonists
ligand binding mechanisms, 191–195
GABA_A benzodiazepine receptor complex
alcohol abuse studies, 487–501
alcohol/modulator commonalities, 487–488
CA1/CA3 hippocampus, 511–516
efficacy of βCCT/3PBD modulation, 
GABA_A1,2,3,5 receptors, 499–501
future research issues, 517–518
GABA-DA interaction hypothesis, 496–498
ligand selectivity with GABA_A1 subunits, 498–499
microinjection studies, 505–506
naltrexone antagonist, 507–511
novel CNS GABAergic substrates, 498
oral administration, βCCT/3PBD anxiety reduction, 510–511
vs. naltrexone, 507–511
probe applications, 488–493
site-specific microinjection, 493–496
subunit selectivity vs. intrinsic efficacy, 516–517
systemic administration, 492–493, 503–504
ventral pallidum, 501–502
schizophrenia, 323–325
candidate genes, 325–328
chromosomal abnormalities, 328–331
functional candidate genes, 331–332
future research issues, 333
gene linkage studies, 323–324
neurochemistry and, 261–262
positional candidate genes, 325
susceptibility genes, 351–355
DISC1 gene, 351–352
DTNBP1 gene, 352–353
function, 332–333
NRG1 gene, 353–355
Molecular path model
benzodiazepine activity, 115
Molecular targeting
schizophrenia-related cognitive dysfunction therapy, 254–255
Monoamine neurotransmitters
anxiety disorder anxiolytics, 63–72
antidepressants, 64–70
antipsychotics, 71–72
beta blockers, 71
cannabinoid analgesics and, 668–669
dopamine hypothesis of schizophrenia, 371–373
3,4-methylenedioxymethamphetamine effects, 616
psychostimulant abuse and, 569–575
Monoamine oxidase inhibitors (MAOIs)
anxiety disorder therapy, 70
obsessive-compulsive disorders
metabolism studies, 223
schizophrenia therapy, 394
Monoaminergic transporter
3,4-methylenedioxymethamphetamine neurotoxicity and, 625–627
Monotherapies
obsessive-compulsive disorders
controlled trials, 225
MOR-1 opioid receptor
pain management and, 716–717
structure and function, 748–751
Morphine compounds
mu opioid receptors and, 748–751
obsessive-compulsive disorder therapy, 234
peripheral-central interactions, 719–721
spinal-supraspinal interactions, 718–720
Mouse studies
anxiety neurobiology
anxiety-like behavior, genetically altered mice, 19–24
neuroticism (N trait), 6–9
oligogenic anxiety-like conditions, 32–33
QTL studies, 19
benzodiazepine functional diversity, 112–114
MPEP antagonist
psychostimulant abuse and, 576
Multipoint linkage analysis
anxiety neurobiology, 4
Mu opioid receptors
obsessive-compulsive disorders, 234
psychostimulant abuse and, 578–579
structure and function, 748–751
Muscarinic receptor agonists
atypical antipsychotics and cholinergic agents, 429–430
schizophrenia therapy, 393–394
Muscimol
alcohol abuse studies
GABA_A benzodiazepine receptor complex manipulation, 494–496
Naloxone
nicotine dependence and withdrawal, 540
opiate addiction therapy regulatory studies, 696–697
Naltrexone
alcohol abuse studies
oral administration of βCCT/3PBC vs., 507–511
nicotine dependence and withdrawal, 540
pharmacotherapy, 550–551
opiate addiction therapy, 698–699
psychostimulant abuse therapy, 585–586
NAN-190 antagonists
nicotine dependence and withdrawal withdrawal substrate specificity, 542–543
N-back task analysis
schizophrenia cognitive dysfunction and, 259
NDMC metabolite
cholinergic mechanisms and, 429–430
N-domain fragments
corticotropin-releasing factor receptor antagonists
ligand binding mechanisms, 192–195
Negative affect
in schizophrenia, 255–256
neural network studies, 258–259
NEO-five factor inventory (NEO-FFI)
anxiety neurobiology
 genetic susceptibility studies, 18–19
NEO personality inventory
anxiety neurobiology, 5–6
 human personality traits, 9–12
Neospinthalamic pain pathways
classification of, 711–714
Nerve-growth factor (NGF)
 transient receptor potential V1 (TRPV1) receptor expression, 729
Neural networks
 glutamate theory of schizophrenia
 history of, 290–291
 schizophrenia
cognitive dysfunction and, 259
 future research issues, 266
 negative affect and, 255–256, 258–259
 psychosis and, 257–258
Neuregulin I (NRG1)
schizophrenia candidate gene, 326–327
ErbB3 receptor, 328
functional implications, 332–333
molecular interactions, 352–353
susceptibility identification, 350
Neuroactive steroids
anxiety disorders
 alcohol effects, 157–159
 animal models, 142–152
 behavioral effects, 142
 brain and peripheral sources, 135–137
 chemistry and pharmacology, 135–142
 enantiomeric selectivity, 141–142
 GABA_A receptors and ligand-gated ion channels, 137–141
HPA axis function, 154–156
overview, 134–135
stress-induced behaviors
drug abuse relapse, 159–160
HPA axis, 153–154
overview, 152–153
Neuroanatomical controls
alcohol abuse studies in alcohol-preferring rats, 469–470
Neurobiology
obsessive-compulsive disorders, 216–224
brain imaging studies, 217–222
functional imaging studies, 219–220
magnetic resonance spectroscopy, 220
Neurochemistry
3,4-Methylenedioxymethamphetamine (MDMA) neurotoxicity
long-term changes in, 619–620
schizophrenia, 260–262
hypotheses, 371–376
dopamine hypothesis, 371–373
glutamate receptor hypothesis, 373–374
integrated dopamine/glutamate hypotheses, 374–376
Neurodevelopmental animal model
schizophrenia, 265
Neuroendocrine systems
3,4-methylenedioxymethamphetamine effects on, 618
psychostimulant abuse chronic exposure and sensitization effects, 580–585
Neurogenesis
atypical antipsychotics and, 430
schizophrenia disruption of, 265
Neurogenic inflammation
vanilloid receptors and, 728–729
Neuroimaging studies
3,4-methylenedioxymethamphetamine neurotoxicity
brain biochemical and functional changes, 631–632
obsessive-compulsive disorders, 219–220
psychostimulant abuse chronic exposure and sensitization effects, 582–585
monoamine neuropharmacology, 573–575
Neurokinin 3 receptors
antipsychotic mechanisms with, 430
Neurokinin antagonists
schizophrenia therapy, 391
Neuronal cell adhesion molecules (NCAM) anxiety neurobiology, 30
Neuronal pathways
anxiety neurobiology and, 15–18
knockout mice studies, 24–26
mouse studies, 19–20
pain management
anatomical drug interactions, 718–720
descending modulatory pathways, 712–714
neospinothalamic/paleospinothalamic pathways, 711–712
overview, 709–710
Neuronal systems and substrates
calcitonin gene-related peptide sites and migraine therapy targeting, 762
dopaminergic receptors
alcohol abuse studies, 471–486
bed nucleus of stria terminalis, 473–475
dopaminergic regulation, early research, 472–473
evralateral dopamine, 485–486
future research issues, 517–518
GABAergic interactions with, 486
lateral hypothalamus, 481–485
\(D_2\) dopaminergic regulation, hypothesized mechanisms, 481–485
ventral pallidum, 476–480
dopaminergic regulation hypothesized mechanisms, 478–480
nicotine dependence and withdrawal nicotine reinforcement substrates, 537–540
withdrawal neurosubstrates, 541–543
Neuropeptide FF
pain management and, 716–717
Neuropeptides
anxiety neurobiology, 16–17
psychostimulant abuse and, 578–579
Neuropeptide Y (NPY)
alcohol abuse studies in alcohol-preferring rats, 471
anxiety neurobiology and, 17
knockout mice studies, 25–26
Neuropharmacology
obsessive-compulsive disorders, 225–235
antipsychotic agents, 229–234
augmenting agents, 225, 229–234
brain imaging studies, 220–222
current trials, 234
monotherapy trials, 225
serotonin uptake inhibitor efficacy, 226–228
schizophrenia dopamine hypothesis, 287
Neuroprotective agents
3,4-methylenedioxymethamphetamine neurotoxicity and, 625
Neuroreceptor imaging
schizophrenia, 259–260
Neurosteroids
  schizophrenia therapy, 394
Neurosurgery
  obsessive-compulsive disorders, 235–237
Neurotensin agonist/antagonist
  psychostimulant abuse and, 579
  schizophrenia therapy, 390
Neuroticism (N trait)
  anxiety neurobiology, 5–6
  mouse behavior, 6–9
Neurotoxicity
  cannabinoid receptors and, 672–673
  3,4-Methylenedioxymethamphetamine (MDMA), 619–628
  animal models, 620–621
  cytokines and microglia, 627–628
  hyperthermia, 624–625
  long-term neurochemical change, 619–620
  metabolite mechanisms, 621–622
  monoaminergic transporter, 625–627
  oxidative stress, 623–624
Neurotransmitters. See also specific Neurotransmitters
  addictive disorders
    modulator therapy and, 458–459
  anxiety neurobiology
    knockout mice studies, 24–26
    anxiety neurobiology and, 15–18
  endocannabinoid system, 663
  3,4-methylenedioxymethamphetamine effects on
    receptor/transporter effects, 617
  obsessive-compulsive disorders
    metabolism studies, 223
  pain neuropharmacology, 714–717
    drug action localization, 718
    psychostimulant abuse
      chronic exposure and sensitization effects, 580–581, 583–585
Neurovascular model
  migraine therapy, calcitonin gene-related peptide, 759–760
NF-κB transcription factor family
  anxiety neurobiology and, 31
Nicotine
  basic properties, 535–536
  patches
    obsessive-compulsive disorder therapy, 234
  pharmacology, 536–545
  absorption pharmacokinetics, 543–544
dependence and withdrawal therapy
  bupropion, 549–550
  cannabinoid antagonists, 550
  nicotinic antagonists, 548–549
  nicotinic partial agonists, 548
  nonnicotinic agents, 549–551
  opioid antagonists, 550–551
  overview, 545–546
  public health policy and, 551–552
  replacement medications, 546–548
  tricyclic antidepressants, 550
  distribution pharmacokinetics, 544
  metabolism and elimination pharmacokinetics, 544–545
  nicotine reinforcement neurosubstrates, 537–540
  nicotinic acetylcholine receptors, 537
  functional adaptations, 540–541
  withdrawal neurosubstrates, 541–543
Nicotine gum
  nicotine dependence and withdrawal therapy, 547–548
Nicotine-N-oxide
  nicotine dependence and withdrawal metabolism and elimination pharmacokinetics, 544–545
Nicotinic acetylcholine receptors (nAChRs)
  nicotine dependence and withdrawal classification and function, 537
  functional adaptations mechanisms, 540–541
  nicotine reinforcement substrates, 538–540
  nicotinic partial agonist therapy, 548
  nicotinic partial antagonist therapy, 548–549
  overview, 536–537
  withdrawal substrates, 542–543
NRG1 molecular interaction, 354–355
schizophrenia pharmacotherapy
  cholinergic agents, 393–394
Nicotinic agonists
  anxiety neurobiology and
    receptor deficits and, 29–30
Nicotinic antagonists
  nicotine dependence and withdrawal therapy, 548
Nicotinic partial agonists
  nicotine dependence and withdrawal therapy, 548
Nitric oxide synthase (NOS) inhibitor
3,4-methylenedioxymethamphetamine neurotoxicity, 623–624
Nitrogen ohne radikal (NOR) metabolites benzodiazepine receptor ligand metabolism, 102
Nociception defined, 710 drug action localization, 718 pain pathways and, 711–712 transient receptor potential V2 (TRPV2), 736–737
Nonopiate analgesics migraine management, 765
Nonpeptide ligands corticotropin-releasing factor receptor antagonists, 195–196
Nonpharmacological therapy obsessive-compulsive disorders and, 235–237
Nonsteroidal anti-inflammatory drugs migraine management, 765, 768 Noradrenergic systems psychostimulant abuse chronic exposure and sensitization effects, 584 schizophrenia pharmacotherapy, 393
Norepinephrine (NE) alcohol abuse studies dopaminergic receptor systems and substrates, 472–473 anxiety neurobiology, 15–17 3,4-methylenedioxymethamphetamine effects on, 616 receptor/transporter effects, 617 psychostimulant transporter effects, 617 chronic exposure and sensitization effects, 584 neuropharmacology, 570–575 schizophrenia pharmacotherapy noradrenergic agent development, 393
Norepinephrine transporter (NET) anxiety neurobiology and knockout mice studies, 24–26
Nucleus accumbens (NAcc) alcohol abuse studies in alcohol-prefering rats, 470–471 dopaminergic receptor systems and substrates, 471–472 GABA_A benzodiazepine receptor complex manipulation site-specific microinjection studies, 493–496 3,4-methylenedioxymethamphetamine (MDMA) reinforcing properties, 614–616 NUDEL gene DISC1 schizophrenia candidate gene molecular interactions, 351–352 Nur transcription factors schizophrenia therapy dopamine neurotransmission and, 422
immunomodulatory treatments, 235
neurobiology, 216–224
brain imaging studies, 217–222
functional imaging studies, 219–220
magnetic resonance spectroscopy, 220
neuropharmacology
brain imaging studies, 220–222
neurosurgery, 235–237
nonpharmacological experimental treatments, 235–237
pharmacotherapy, 77–78
serotonin/noradrenaline reuptake inhibitors, 69
summary of therapeutic advances, 237
symptom induction, 234
transcranial magnetic stimulation, 236
tricyclic antidepressants, 69–70
Ocapridone
schizophrenia therapy, 389
8-OH-DPAT
nicotine dependence and withdrawal withdrawal substrate specificity, 542–543
serotonin receptors 5-HT2A/5-HT2C interactions, 422–424
Olanzapine
D2 receptor blockade, 414–415
neurogenesis and, 430
schizophrenia therapy brain-derived neurotrophic factor and, 421–422
clinical profile, 383–387
D2 receptor occupancy and effect, 376–378
safety and tolerability, 388–389
serotonin receptor 5-HT2A, 420–421
Oligogenic anxiety-like conditions anxiety neurobiology mouse studies, 32–33
Open-field activity mouse anxiety models neurosteroid effects, 148–149
Opiates addiction and buprenorphine studies, 696–698
drug discovery survey, 699–700
epidemiology, 691–694
future research issues, 698–699
treatment statistics, 694–696
pain management anatomical interactions, 718–720
Opioid agonists/antagonists migraine management, 765
nicotine dependence and withdrawal therapy, 550–551
Opioid receptor system addictive disorders reward therapy and, 458–459
alcohol abuse studies oral administration of βCCT/3PBC vs. agonists, 507–511
delta receptors, 751
dimerization, 752
endogenous opioids, 746–748
future research on, 752
kappa receptors, 751–752
mu receptors, 748–751
nicotine dependence and withdrawal, 540
withdrawal substrate specificity, 543
orphanin FQ/nociceptin and receptor, 752
overview, 745–746
pain management and, 716–717
targeting mechanisms, 718
psychostimulant abuse and, 578–579
chronic exposure and sensitization effects, 584
short-acting addiction pharmacotherapy and, 453–457
Orbitofrontal-dorsomedial thalamic loop obsessive-compulsive disorders neuropharmacology, 221–222
Orphanin FQ/nociceptin (OFQ/N) receptor anxiety neurobiology and knockout mice studies, 25–26
structure and function, 748, 752
Oxidative stress 3,4-methylenedioxymethamphetamine neurotoxicity and, 623–624
Oxycodone abuse of incidence and prevalence, 692–694
Pain perception and management calcitonin gene-related peptide for, 768–769
marijuana and, 666–668
neuronal pathways descending modulatory pathways, 712–714
neospinothalamic/paleospinothalamic pathways, 711–712
overview, 709–710
neuropharmacology, 714–717
anatomically-based interactions, 718–721
drug targeting mechanisms, 718
transient receptor potential V1 (TRPV1) receptors
antagonists, 733
capsaicin, protons, and heat, 730–732
chemical activators, 732–733
cloning of, 728–729
desensitization, 735–736
expression, 729
knockout mouse models, 736
nociception channels, 736–737
sensitization, 733–735
Paleospinothalamic pain pathways
classification of, 711–712
Paliperodone
schizophrenia therapy, 389
Panic disorders
antiepileptic therapy, 74–75
anxiety disorder therapy, 78
brain regions related to, 13–15
diagnostic criteria, 10–12
neuroactive steroids, 155
Peptide ligands
corticotropin-releasing factor receptor antagonists
basic properties, 180–181
CRF₁/CRF₂ binding mechanisms, 190–195
CRF₁/CRF₂ pharmacology, 185–195
CRF₁/CRF₂ receptor pharmacology, 185–195
structure and function, 179–185
subtypes and distribution, 181–185
Periaqueductal gray (PAG) stimulation
cannabinoid analgesics and, 667–668
Peripheral benzodiazepine receptors (PBRs)
stress-induced behavior
neuroactive steroids, 155–156
Personality traits
continuous expression
anxiety neurobiology, 9–12
Pharmacophore models
benzodiazepine activity, 116
Pharmacotherapy
addictive disorders
history of, 451–457
reward modulation/countermodulation and, 458–459
risk factors for addiction development, 457–458
anxiety disorders
anxiolytic drugs, 62–75
amino acid neurotransmission, 72–75
anticonvulsants, 74–75
antidepressants, 64–70
antihistamines, 75
antipsychotics, 71–72
benzodiazepines, 73–74
beta-blockers, 71
lithium, 75
monoamine neurotransmission, 63–72
serotonin receptor agonists, 70–71
depressive disorders, 80
future research issues, 81
generalized anxiety disorder, 77
obsessive-compulsive disorder, 77–78
overview, 60
panic disorder/agoraphobia, 78
phobias, 78, 80
posttraumatic stress disorder, 79
social anxiety disorder, 79–80
treatments chart, 76
obsessive-compulsive disorders
overview, 216
schizophrenia
antipsychotic drug profiles
first-generation (conventional) agents, 383
safety and tolerability, 387–388
second-generation (atypical) agents, 383–387
antipsychotic mechanisms of action, 376–382
D₁ receptors, 380–381
D₂/D₃ and D₄ antagonism and regional specificity, 380
D₂ occupancy thresholds and rapid dissociation, 378–380
D₂ receptor occupancy, 376–378
dopamine release, 381
NMDA receptor function, 381
synthesis reactions, 381–382
current developments and future directions, 388–394
cannabinoid hypothesis, 394
cholinergic agents, 393–394
D₁ agonists and antagonists, 390
D₃ antagonists, 390
D₄ antagonists, 390
dopamine system targeting, 389
glutamate system targeting, 391–393
neurokinin antagonists, 391
neurosteroids, 394
neurotensin agonist/antagonist, 390
noradrenergic agents, 393
future research issues, 394–395
high 5-HT2A vs. D2 affinity, 378
neurochemical hypotheses, 371–376
overview, 370–371
Phencyclidine. See also Ketamine
 glutamatergic theory of schizophrenia
 history of, 289–290
 neurochemistry of, 374
 ketamine derivative, 636–637
 schizophrenia neurochemistry and, 260–262
Phenothiazines
 schizophrenia therapy
 clinical profiles, 383
Phenotype analysis
 obsessive-compulsive disorders, 237
 schizophrenia, 262–263
 genetic epidemiology, 322–323
Phenylalkylamines, 637–640
 addiction, 639–640
 mechanism of action, 638–639
 pharmacology, 638
 α-Phenyl-N-tert-butyl nitronate (PBN)
 3,4-methylenedioxymethamphetamine
 neurotoxicity
 oxidative stress, 623–624
Phobias
 brain regions related to, 13–15
 pharmacotherapy, 79–80
Phosphoinositol 3-kinase-AKT signaling
 pathway
 dystrobrevin binding protein 1 (DTNBP1)
 molecular interactions, 353
Phosphoinositol-4,5-bisphosphate (PIP2)
 transient receptor potential V1 (TRPV1)
 receptor sensitization, 734–735
Phospholipase C
 transient receptor potential V1 (TRPV1)
 receptor sensitization, 734–735
Phosphorus MRS
 schizophrenia analysis, 257
Picrotoxin
 alcohol abuse studies
 GABA A benzodiazepine receptor complex, 487–488
GABAergic modification of dopamine agonists, 496–497
p-MPPI receptor antagonist
 nicotine dependence and withdrawal
 withdrawal substrate specificity, 542–543
Positional candidate genes
 schizophrenia genetics, 325
Positional cloning
 schizophrenia genetics, 324
Positron emission tomography (PET)
 obsessive-compulsive disorders, 219–220
 schizophrenia
 dopamine hypothesis, 286
 schizophrenia analysis, 257
Postmortem studies
 schizophrenia, 260–262
 dopamine hypothesis and, 285
 future research issues, 355–356
 overview, 343–344
 susceptibility gene identification, 344–351
 susceptibility gene interactions, 351–355
Postpartum depression
 neuroactive steroids, 156–157
Posttraumatic stress disorder (PTSD)
 anticonvulsant therapy, 74–75
 brain regions related to, 13–15
 diagnostic criteria, 10–12
 mirtazapine therapy, 70
 neuroactive steroids, 154–155
 pharmacotherapy, 79
PPP3CC gene
 schizophrenia molecular genetics, 328
P rat line. See Alcohol-preferring rats
Predictive validity
 animal anxiety-like behavior and, 12
 "Preemptive analgesia"
 pain management and, 717
Prefrontal cortex (PFC)
 integrated glutamate/dopamine hypotheses of schizophrenia, 374–376
Pregnancy
 marijuana effects in, 664–665
 3,4-methylenedioxymethamphetamine and, 630–631
Pregnenolone sulfate (PREGS)
 in brain, 137
Prenatal development
 marijuana effects on, 664–665
Prescription drugs. See also Opiates
abuse of
incidence and prevalence, 692–694
Preventive therapy
migraine management, 766–768
PRODH gene
schizophrenia molecular genetics, 329–330
Prodromal period
schizophrenia therapy
second-generation antipsychotics, 386–387
Progesterone levels
depression
neuroactive steroids, 156–157
Pro-opiomelanocortin peptide group
nicotine dependence and withdrawal, 540
3-Propoxy-β-carboline hydrochloride (3BPC)
alcohol abuse studies
anxiety reduction with, 510–511
GABA_A,2,3,5 receptor subunit modulation, 499–501
GABA_A receptor subunit selectivity, 498–499
microinjection techniques, 505–507
oral administration, 507–511
systemic administration, 503–504
Protein kinase A
transient receptor potential V1 (TRPV1) receptor sensitization, 733–735
Protein kinase C
transient receptor potential V1 (TRPV1) receptor sensitization, 733–735
Protein kinase C_γ
anxiety neurobiology and, 31
Protons
transient receptor potential V1 (TRPV1) receptor expression, 730–732
Psilocybin
schizophrenia therapy
serotonin receptor 5-HT_2A_, 420–421
Psychoeducation
anxiety management with, 60–61
Psychological traits
anxiety neurobiology
continuous expression of normal personality, 9–10
genetic basis of, 4–6
mouse behavior extrapolation studies, 6–9
Psychosis
in schizophrenia, 253–254
animal models, 264–265
neural network studies, 257–258
second-generation antipsychotics and, 386–387
Psychostimulants
abuse-related neuropharmacology, 569–579
γ-aminobutyric acid, 576–577
glutamate, 575–576
hypothalamic-pituitary-adrenal axis, 577–578
monoamines, 570–575
neuropeptides, 578–579
addiction therapy development, 585–586
chronic exposure-related neurobiology, 579–589
neurotransmitter/neuroendocrine systems, 580–584
signal transduction mechanisms and gene expression, 584–585
future research issues, 588–589
therapeutic applications of, 567–569
Public health policy
nicotine dependency and withdrawal therapy, 551–552
Pyrazolopyrimidine
corticotropin-releasing factor receptor antagonists
anxiety/depression therapeutic potential, 197–198
Pyrazoloquinoline
alcohol abuse studies
GABA_A benzodiazepine receptor complex, 490–493
Quantitative behavioral genetics
anxiety neurobiology, 6
Quantitative trait locus (QTL) analysis
anxiety neurobiology, 4
emotionality studies in mice, 8–9
mice studies, 19
oligogenic anxiety-like conditions, 32–33
Quetiapine
schizophrenia therapy
clinical profile, 383–387
safety and tolerability, 389
Quinlorane
alcohol abuse studies
dopaminergic receptor systems and substrates, 472–473
Quinpirole
alcohol abuse studies
dopaminergic receptor systems and substrates, 472–473

Raclopride
alcohol abuse studies
dopaminergic receptor systems and substrates, 472–473
chronic exposure and sensitization effects, 582–585

¹¹C-Raclopride
striatal D₂ receptor blockade, 414–415

Radiolabeled peptides
corticotropin-releasing factor receptor antagonists
peptide ligand pharmacology, 187–195

Rapid dissociation
schizophrenia pharmacotherapy
D₂ receptor occupancy thresholds, 379–380

Receptor activity modifying protein 1 (RAMP1)
calcitonin gene-related peptide sites and migraine therapy targeting, 762

Receptor density assessment
schizophrenia
dopamine hypothesis and, 285
schizophrenia neuroreceptor imaging, 259–260

Receptor ligand pharmacology
benzodiazepines, 97–102
endogenous site, 98–99
metabolism functions, 101–102
single-cell GABA response modulation, 99–100
therapeutic action, 97–98
tolerance and dependence characteristics, 100–101

Regional cerebral blood flow (rCBF)
schizophrenia, 257–259

Regional specificity
schizophrenia therapy
D₂/D₃ and D₄ receptor antagonism and, 380

"Region-specific" neuroanatomical controls
alcohol abuse studies in alcohol-preferring rats, 469

Reinforcing mechanisms
alcohol abuse studies in alcohol-preferring rats, 469
3,4-methylenedioxymethamphetamine (MDMA), 614–616

Resiniferatoxin (RTX)
cloning of, 727–729
transient receptor potential V₁ (TRPV₁) receptor expression, 733

Respiratory system
γ-hydroxybutyric acid (GHB) effects, 634

Reuptake inhibitors
psychostimulant abuse
monoamine neuropharmacology, 571–575

Reversible inhibitor of monoamine oxidase A (RIMA)
anxiety disorder therapy, 70

Reward effects
addictive disorders, 458–459
endocannabinoids and, 675–676
3,4-methylenedioxymethamphetamine (MDMA), 614–616
psychostimulant abuse
chronic exposure and sensitization effects, 581–585

Rhodopsin
corticotropin-releasing factor receptor antagonists
ligand binding mechanisms, 191–195

Riluzole
obsessive-compulsive disorder therapy, 234

Rimonabant
appetite regulation, 670–672
cannabinoid receptors and, 661–662
cognition and, 669–670
endocannabinoid physiology and, 665–675
nicotine dependence and withdrawal therapy, 550
opiate dependence therapy and, 699
pain management and, 667–668
reward, tolerance, and dependence, 675–676

Risperidone
neurogenesis and, 430
schizophrenia therapy
clinical profile, 383–387
safety and tolerability, 389
serotonin receptor 5-HT₂A, 418–421
Ritanserin
3,4-methylenedioxymethamphetamine effects on, 616
RO19-4603 inverse agonist
alcohol abuse studies
GABA_A benzodiazepine receptor complex, 488–493
site-specific microinjection techniques, 494–496
systemic administration studies, 492–493
Rohypnol. See Flunitrazepam
ROI15-4513 inverse agonist
alcohol abuse studies
GABA_A benzodiazepine receptor complex
alcohol-modulator commonalities, 487–488
RU34000 imidazopyrimidine inverse agonist
alcohol abuse studies
GABA_A benzodiazepine receptor complex, 490–493
site-specific microinjection techniques, 496
RY 023 inverse agonist
alcohol abuse studies
GABA_A5 receptor specificity, 512–516
Safety
schizophrenia therapy
second-generation antipsychotics, 387–388
Samson test procedure
alcohol abuse studies in alcohol-preferring rats, 468–470
SB-271046
serotonin receptor 5-HT_6 and, 425–426
SB-399885
serotonin receptor 5-HT_6 and, 426
SCH 23390 compound
alcohol abuse studies
bed nucleus of stria terminalis system, 475
lateral hypothalamus, effects on, 481–485
ventral pallidum receptor blockade, 477–480
Schizophrenia
animal models, 263–265
biological mechanisms, 256–263
brain imaging studies, 256–260
characteristics of, 252
clinical phenomenology and treatment, 252–256
cognitive dysfunction, 254–255
dopamine hypothesis
cortical vs. striatal dopamine, 287–289
gene evidence, 286–287
history, 284–285
imaging evidence, 285–286
pathological evidence, 285
pharmacological evidence, 287
pharmacotherapy, 371–373
evolution of theories on, 283–284
future research issues, 265–266
gene epidemiology, 321–323
phenotype definition, 322–323
genetics and phenotypes, 262–263
glutamate theory of
genetic evidence for, 293–294
history, 289–291
imaging evidence for, 292–293
pathological evidence for, 291–292
pharmacological evidence for, 294–295
pharmacotherapy, 373–374
integrated glutamate/dopamine hypotheses, 295–297
pharmacotherapy, 374–376
molecular genetics, 323–325
candidate genes, 325–328
chromosomal abnormalities, 328–331
functional candidate genes, 331–332
future research issues, 333
susceptibility gene function, 332–333
negative affect, 255–256
neural network studies and, 255–259
neurochemistry, 260–262
neurogenesis in, 430
neuroreceptor imaging, 259–260
pharmacotherapy
antipsychotic drug profiles
first-generation (conventional) agents, 383
safety and tolerability, 387–388
second-generation (atypical) agents, 383–387
antipsychotic mechanisms of action, 376–382
D_1 receptors, 380–381
D_2/D_3 and D_4 antagonism and regional specificity, 380
D₂ occupancy thresholds and rapid dissociation, 378–380
D₂ receptor occupancy, 376–378
dopamine release, 381
NMDA receptor function, 381
synthesis reactions, 381–382
current developments and future directions, 388–394
cannabinoid hypothesis, 394
cholinergic agents, 393–394
D₁ agonists and antagonists, 390
D₃ antagonists, 390
D₄ antagonists, 390
dopamine system targeting, 389
glutamate system targeting, 391–393
neurokinin antagonists, 391
neurosteroids, 394
neurotensin agonist/antagonist, 390
noradrenergic agents, 393
future research issues, 394–395
high 5-HT₂A vs. D₂ affinity, 378
neurochemical hypotheses, 371–376
overview, 370–371
postmortem studies, 260–262
dopamine hypothesis and, 285
future research issues, 355–356
overview, 343–344
susceptibility gene identification, 344–351
susceptibility gene interactions, 351–355
prevalence, 252–253
psychosis and, 253–254
symptom classification, 253
Second-generation antipsychotics (SGAs)
Schizophrenia therapy
clinical profile, 383–387
D₂/D₃ and D₄ receptor antagonism and regional specificity, 380
D₂ receptor occupancy thresholds and rapid dissociation, 378–380
history of, 370–371
NMDA receptor antagonists, 381
safety and tolerability, 387–388
Selective serotonin reuptake inhibitors (SSRIs)
anxiety disorder therapy, 66–69
obsessive-compulsive disorders
controlled trials, 225
panic disorder therapy, 78
posttraumatic stress disorder therapy, 79
social anxiety disorder therapy, 79–80
Selegeline
schizophrenia therapy, 394
Sensitivity
psychostimulant abuse and reduction of neurobiology of, 579–585
transient receptor potential V₁ (TRPV₁) receptor expression, 733–735
Sensory neurons
pain pathways, 711–712
Separation-induced ultrasonic vocalizations
animal anxiety models
neurosteroid effects, 150
Sequence homology
corticotropin-releasing factor receptor antagonists
ligand binding mechanisms, 191–195
Serotonin (5-HT)
antipsychotic drugs and release of, 426
anxiety disorder anxiolytics
monoamine neurotransmission, 63–72
anxiety neurobiology, 4
fall genetic susceptibility studies, 18–19
neurotransmission mechanisms, 15–17
3,4-methylenedioxymethamphetamine effects on, 616
long-term neurochemical effects, 619–620
oxidative stress, 623–624
receptor/transporter effects, 617
nicotine dependence and withdrawal withdrawal substrates, 542–543
obsessive-compulsive disorders
geneic studies, 222–224
psychostimulant abuse
neuropharmacology, 570–575
Serotonin and noradrenaline reuptake inhibitors (SNRIs)
anxiety disorder therapy, 69
Serotonin hypothsis
obsessive-compulsive disorders
neuropharmacology, 221–222
Serotonin receptor 5-HT/D₂ hypothesis
atypical antipsychotics, 417–418
serotonin receptor 5-HT₂A, 419–421
Serotonin receptors
atypical antipsychotics
adrenergic mechanisms, 426–427
serotonin receptor 5-HT₁A-S-HT₂A interactions, 421–425
serotonin receptor 5-HT₂A, 418–421
cortical dopamine efflux and cognitive function, 421–422
extrapyramidal function, 422
serotonin receptor 5-HT\textsubscript{2A}-5-HT\textsubscript{2C}
receptor interactions, 422–424
serotonin receptor 5-HT/D\textsubscript{2} hypothesis,
417–418
schizophrenia neurochemistry and,
261–262
schizophrenia pharmacotherapy
serotonin receptor 5-HT\textsubscript{2A} 
D\textsubscript{2} antagonism and, 381
serotonin 5-HT\textsubscript{1A} 
nicotine dependence and withdrawal,
542–543
serotonin 5-HT\textsubscript{2C} receptors
psychostimulant abuse, 574–575
serotonin receptor 5-HT\textsubscript{1A}
anxiety disorder therapy, 70–71
anxiety neurobiology and
knockout mice deficit studies, 27–30
serotonin receptor 5-HT\textsubscript{1B}
anxiety neurobiology and
knockout mice deficit studies, 28–30
serotonin receptor 5-HT\textsubscript{6} 
cortical dopamine efflux and cognitive
function, 421–422
extrapyramidal function, 422
LSD downregulation of, 638–640
schizophrenia pharmacotherapy
D\textsubscript{2} antagonism and, 381
serotonin receptor 5-HT\textsubscript{6} interactions
atypical antipsychotics, 425–426
triptan therapy for migraines, 764–765
Serotonin reuptake inhibitors (SRIs)
obsessive-compulsive disorders 
brain neuropharmacology, 221–222
neuropharmacology, 226–228
Serotonin transporter (5-HTT)
anxiety neurobiology 
environmental effects and, 34–35
anxiety neurobiology and
knockout mice studies, 24–26
3,4-methylenedioxymethamphetamine
neurotoxicity and, 625–627
obsessive-compulsive disorders 
abnormalities, 219–220
genetic studies, 222–224
Serotonin transporter (SERT) antagonists
obsessive-compulsive disorders, 223
Sertindole 
schizophrenia therapy
clinical profile, 383–387
Signal transduction mechanisms
psychostimulant abuse 
chronic exposure and sensitization
effects, 584–585
Single-nucleotide polymorphisms (SNPs)
addictive disorders vulnerability, 457–458
catechol-O-methyl transferase
as schizophrenia susceptibility gene,
347–348
schizophrenia genetics
DISC1 molecular interactions, 352
GRM3 gene, 349
positional candidate genes, 325
Single-photon-emission computerized
tomography (SPECT)
schizophrenia analysis, 257
Site-specific microinjection studies
alcohol abuse
GABA\textsubscript{A} benzodiazepine receptor
complex manipulation, 493–496
Smoking. See Nicotine
Social anxiety disorder
pharmacotherapy, 79–80
Social interaction paradigm
3,4-methylenedioxymethamphetamine
effects on, 630–631
Social isolation
animal anxiety model
neurosteroid effects, 151–152
schizophrenia
animal models, 264
Soluble N-ethylmaleimide-sensitive factor
attachment protein receptors
(SNAREs)
dystrobrevin binding protein 1 (DTNBP1)
molecular interactions, 353
"Speedball" psychostimulant combination
neuropeptide pharmacology and, 578–579
Splice variants
corticostatin-release factor receptor
antagonists
receptor subunits, 182–185
SR48692
psychostimulant abuse
neuropeptide pharmacology and, 579
SR144528 antagonist
cannabinoid receptors and, 661–662
Stimulant medications
psychostimulant therapy, 587–588
Stress
addictive disorders and response to, 459
cannabinoid analgesics and, 667–668
neuroactive steroid interactions
drug abuse relapse, 159–160
HPA axis, 153–154
overview, 152–153
psychostimulant abuse
chronic exposure and sensitization effects, 580–585
neuropharmacology and, 577–578
Striatal dopamine receptors
atypical antipsychotic drugs
clozapine D₂ receptor blockade, 414–415
schizophrenia dopamine hypothesis and, 287–288
Structural studies
obsessive-compulsive disorders, 217–218
Structure-activity relationships (SARs)
benzodiazepines, 114–116
Substance P
anxiety neurobiology and, 17
Substantia nigra
clozapine D₂ receptor blockade, 414–415
Sucrose-fading technique
alcohol abuse studies in alcohol-preferring rats, 467–470
Sulfate fraction
neuroactive steroids in brain, 137
Sulpiride
alcohol abuse studies
dopaminergic receptor systems and substrates, 472–473
ventral pallidum receptor blockade, 477–480
Sumatriptan
migraine management with, 764–765
obsessive-compulsive disorders, 234
Susceptibility genes
schizophrenia
future research issues, 355–356
gene linkage studies, 324
molecular genetics
functional implications, 332–333
molecular interactions, 351–355
postmortem studies
overview, 343–344
susceptibility gene identification, 344–351
susceptibility gene interactions, 351–355
Sweetened cocktail solution procedure
alcohol abuse studies in alcohol-preferring rats, 468–470
Synapsin I proteins
dystrobravin binding protein 1 (DTNBP1) molecular interactions, 353
Synaptosomal-associated protein 25 (SNAP25)
dystrobravin binding protein 1 (DTNBP1) molecular interactions, 353
Synthesis
antipsychotics
schizophrenia pharmacotherapy, 381–382
endocannabinoid system, 663–664
Systemic administration studies
alcohol abuse studies
GABA_A benzodiazepine receptor complex, 492–493
Systems biology theory
schizophrenia and, 255–256
"Systems neuroscience"
schizophrenia dopamine hypothesis and, 288
T-butyl agents
alcohol abuse studies
GABA_A benzodiazepine receptor complex
site-specific microinjection techniques, 494–496
Δ⁹-Tetrahydrocannabinol
analgesic properties, 666–669
appetite regulation, 670–672
cannabinoid receptor binding, 663
cognition and, 669–670
emesis modulation, 674–675
endocannabinoid physiology and, 665–675
isolation off, 660–661
neurotoxicity effects, 672–673
prenatal development and, 664–665
reward, tolerance, and dependence, 675–676
Thermoregulation
3,4-methylenedioxymethamphetamine effects on, 629
Thioxanthine
schizophrenia therapy
clinical profile, 383
THIP agonist
alcohol abuse studies
GABA_A benzodiazepine receptor complex, 488–493
Tiagabine
psychostimulant abuse therapy, 588

Tissue injury
transient receptor potential V1 (TRPV1)
receptor expression, 729–732

Tolcapone
schizophrenia therapy, 389

Tolerability
schizophrenia therapy
second-generation antipsychotics,
387–388

Tolerance mechanisms
benzodiazepines, 100
endocannabinoids, 675–676
psychostimulant abuse
neurobiology of, 579–585

Topiramate
migraine management, 766
psychostimulant abuse therapy, 688

Topological analysis
corticotropin-releasing factor receptor
antagonists
receptor subunits, 183–185

Tourette’s disorder
obsessive-compulsive disorder
comorbidity, 216

Tramadol
obsessive-compulsive disorder therapy, 234

Transcranial magnetic stimulation (TMS)
obsessive-compulsive disorders, 236

Transcriptional regulators
anxiety neurobiology and
mouse studies, 19, 22

Transdermal nicotine patch
mecamylamine in conjunction with, 549
nicotine dependence and withdrawal
therapy, 546–547

obsessive-compulsive disorder therapy, 234

Transient receptor potential V1 (TRPV1)
receptors
analgesic properties, 668–669
antagonists, 733
capsaicin, protons, and heat, 730–732
chemical activators, 732–733
cloning of, 728–729
desensitization, 735–736
endocannabinoid ligands, 664
expression, 729
knockout mouse models, 736
nociception channels, 736–737
sensitization, 733–735

Transient receptor potential V2 (TRPV2)
nociception and, 736–737

Transient receptor potential V3 (TRPV3)
nociception and, 737

Transient receptor potential V4 (TRPV4)
nociception and, 737

TRAR4 gene
schizophrenia molecular genetics, 328

Treatment Episode Data Set (TEDS)
opiate treatment statistics, 694–696

Tricyclic antidepressants (TCAs)
anxiety disorder therapy, 69–70
nicotine dependence and withdrawal
therapy, 550
panic disorder therapy, 78
psychostimulant abuse therapy,
586–587

Trigeminal ganglion
migraine therapy targeting of, 760

Trigeminovascular system
calcitonin gene-related peptide sites and
migraine therapy targeting, 761–762

Triptans
migraine management with, 764–765

Tryptophan hydroxylase
3,4-methylenedioxymethamphetamine
effects on, 616–617

Two-bottle water choice procedure
alcohol abuse studies in alcohol-preferring
rats, 468–470

Tyrosine-hydroxylase
schizophrenia dopamine hypothesis and,
288–289

Tyrosine kinase B (trkB)
anxiety neurobiology
receptor deficits and, 29–30

Urocortins
corticotropin-releasing factor receptor
antagonists
ligand structure, 180–181

Val66Met substitution polymorphism
anxiety neurobiology
genetic susceptibility studies, 18–19

schizophrenia
serotonin receptor 5-HT2A receptor
and, 421–422

Valproate
anxiety disorder therapy, 75
migraine management, 765–766
Vanilloid receptors
cloning, 727–729
transient receptor potential V1 expression, 729
antagonists, 733
capsaicin, protons, and heat, 730–732
chemical activators, 732–733
desensitization, 735–736
knockout mouse models, 736
nociception channels, 736–737
sensitization, 731–735
Varenicline
nicotine dependence and withdrawal therapy, 548
Variable numbers of tandem repeats (VNTR)
obessive-compulsive disorders dopamine genetics, 223
Velocardiofacial syndrome gene schizophrenia
chromosome mapping, 346
COMT catabolism and, 329
Venlafaxine
anxiety disorder therapy, 69
obessive-compulsive disorder therapy, 234
Ventral hippocampal lesions in schizophrenia animal models, 265
Ventral pallidum
alcohol abuse studies, 476–480
dopaminergic regulation hypotheses, 478–480
GABA_A subunit probe selectivity, 501–503
GABAergic modification of dopamine agonists, 497–498
Ventral tegmental area (VTA)
alcohol abuse studies
 dopaminergic receptor systems and substrates, 472–473
alcohol abuse studies in alcohol-preferring rats
control substrates in, 470
atypical antipsychotic drug mechanisms in clozapine D_2 receptors, 414–415
cannabinoid receptors in, 675–676
integrated glutamate/dopamine hypotheses of schizophrenia, 375–376
nicotine dependence and withdrawal nicotine reinforcement substrates, 538–540
withdrawal substrates, 542–543
psychostimulant abuse monoamine neuropharmacology, 571–575
neuropeptide pharmacology, 578–579
Vesicular glutamate transporter glutamate theory of schizophrenia pathological evidence, 292
Vesicular monoamine transporter (VMAT) protein dopamine hypothesis of schizophrenia, 284–285
Visual system
γ-hydroxybutyric acid (GHB) effects, 634
Vitamin D receptor (VDR) anxiety neurobiology and, 32
Vogel conflict test
mouse models of anxiety neurosteroid effects, 145–146
Vogel punished drinking test emotionality studies in mice, 8–9
WAY-100635 compound
5-HT_{2A}–5-HT_{2C} receptor interactions, 422–424
nicotine dependence and withdrawal withdrawal substrate specificity, 542–543
WIN 55,212-2 analgesic properties, 666–668
convulsant effects of, 673
pain management and, 667–668
Wisconsin card sort task (WCST) schizophrenia dopamine hypothesis genetic evidence, 286–287
Withdrawal syndrome benzodiazepines, 74
nicotine dependence and withdrawal withdrawal neurosubstrates, 541–543
opioid addiction and, 699
ZDHHC8 candidate gene schizophrenia molecular genetics, 330
Ziprasidone schizophrenia therapy safety and tolerability, 389
Zolpidem alcohol abuse studies
GABA_A receptor subunit selectivity, 499