

## Index

- abecarnil 310, 311, 312  
 Abnormal Involuntary Movement Scale (AIMS)  
 250–1, 259, 394  
 acetaldehyde dehydrogenase 376  
 acetazolamide 346  
 adenosine deaminase acting on RNA (ADAR) 128,  
 144–5  
 aging influence on drug metabolism 168–9  
 alcohol dehydrogenase 376  
 alcoholism 28, 308  
 alcohol dependence 374, 376, 377  
*OPRM1* alleles and 378  
*see also* substance dependence  
 allele refractory mutation system (ARMS) 423  
 allele-specific amplification 423  
 allele-specific hybridization 426  
 allele-specific ligation 426–8  
 $\alpha$ -adrenoceptors, clozapine response and 232–3  
 Alzheimer's disease (AD) 78, 361–9  
 amyloid precursor protein (APP) relationship  
 405–6  
 apolipoprotein E (ApoE) relationships 363–9,  
 391–3, 407  
 brain imaging studies 392–3, 395  
 cholinergic treatments 363–7, 402  
 noncholinergic treatments 367–9  
 Alzheimer's Disease Assessment Scale–Cognition  
 (ADAS-Cog) 361  
 $\gamma$ -aminobutyric acid *see* GABA  
 amitriptyline 194–5  
 AMPA receptors 138–9  
 amphetamines 201  
 amyloid precursor protein (APP), Alzheimer's  
 disease relationship 405–6  
 angiotensin 1-converting enzyme (ACE) 413  
 animal studies 339–40  
 benzodiazepine pharmacogenetics 343–4  
 tardive dyskinesia 246–7  
*see also* mouse models  
 ANOVA 83  
 anticonvulsant drugs (ACDs) 333–48  
 bipolar disorder treatment 328  
 genetic influences on pharmacology 335–47  
 barbiturates 344–6  
 benzodiazepines 342–4  
 carbamazepine 340–1  
 hydantoin 337–40  
 valproic acid 341–2  
*see also specific drugs*  
 antidepressant drugs 283–4  
 achiral antidepressants with chiral metabolites  
 194  
 chiral antidepressants 183–96  
 drug response  
 antidepressant-induced mania 290–4  
 genetic predictors of 284–94  
 heritability of 23–4  
 pharmacogenetic differences 62–3  
 serotonin transporter gene and 269–73,  
 285–90  
*see also specific drugs*  
 antipsychotic drugs  
 achiral drugs with chiral metabolites  
 199–200  
 chiral drugs 196–9  
 heritability of drug response 24  
*see also specific drugs*  
 anxiety disorders 285, 300–1  
 GABA-A receptor subunit role 307–8  
 generalized anxiety disorder 285, 305  
 apolipoprotein E (ApoE) 361–2  
 Alzheimer's disease relationships 363–9, 391–3,  
 407  
 brain imaging studies 392–3, 395  
 cholinergic treatments 363–7, 402  
 noncholinergic treatments 367–9  
 association studies 25–6, 74–5, 78–86, 406–8  
 case-control design 25–6, 83  
 limitations of 26–9, 74–5  
 tardive dyskinesia 247–8  
*see also* candidate gene approach  
 asthma, candidate gene approach 25–6  
 barbiturates 336, 344–6  
 GABA-A receptor interactions 336, 344–5  
*see also specific drugs*  
 benign familial neonatal convulsions 346  
 benzodiazepines (BDZs) 301, 302, 336, 342–4  
 GABA-A receptor interactions 306–10, 336,  
 343  
 mechanism of action 302–3  
*see also specific drugs*

**440** Index

- bipolar disorder (BP) 287, 289, 320  
 antidepressant-induced mania 291, 292–4  
 response to mood stabilizers 328–9  
*see also* lithium
- Bleuler, Eugen 44
- bovine spongiform encephalopathy 405
- brain development 105–7  
 epistatic interaction relevance 115–17  
 mouse models 107–11  
 serotonin role 106–7, 108–11
- brain imaging 391–6  
 Alzheimer's disease 392–3, 395  
 schizophrenia 393–4, 395  
 tardive dyskinesia 393–4, 395
- brain-derived neurotrophic factor (BDNF) 393
- Brief Psychiatric Rating Scale (BPRS) 221
- bupropion 194
- calcium channels 337
- candidate gene approach 9, 25–6  
 limitations of case-control association studies 26–9  
 lithium response 326–7  
 manic-depressive illness 38–9  
 sample size required 80–3  
 schizophrenia 38–9  
 study design 83–5  
 tardive dyskinesia 247–8, 249–58  
 dopaminergic receptors 248, 250–2  
 metabolic enzymes 248, 256–8  
 serotonergic genes 252–6
- carbamazepine 336, 340–1  
 adverse effects 340  
 bipolar disorder treatment 328–9
- case-control design 9–10, 25, 31, 74–5  
 association studies 25–6, 83  
 limitations of 26–9, 74–5
- catechol-O-methyltransferase (COMT) 275–6
- chi-square test 83
- chiral psychotropic drugs 181–203  
 antidepressants 183–94  
 achiral antidepressants with chiral metabolites 194–6  
 recent antidepressants 193–4  
 selective serotonin reuptake inhibitors 187–92  
 tricyclic antidepressants 183–7
- antipsychotics 196–200  
 achiral antipsychotics with chiral metabolites 199–200
- opioid substitutes 201–2  
 stimulants and illicit drugs 201  
 tranquilizers and hypnotic agents 200–1
- chiral switch 187–8
- chlorpromazine 157–8
- cholinergic muscarinic receptors, clozapine  
 response and 232
- cigarette smoking *see* smoking
- citalopram 187–9
- citicoline 367–9
- Clinical Global Impression scale (CGI) 221, 286
- clomipramine, obsessive-compulsive disorder  
 treatment 285–6
- clonazepam 336, 342
- clozapine 217–35, 248  
 drug response 220–4  
 criteria 220–2  
 genetic predictors of 412, 414  
 heritability of 24  
 time taken for response 222  
 genetic variation in receptors 222–34  
 $\alpha$ -adrenoceptors 232–3  
 cholinergic muscarinic receptors 232  
 dopamine receptors 224–7  
 epistatic interaction between genes 233–4  
 GABA receptors 233  
 histamine receptors 231  
 serotonin receptors 227–31  
 pharmacology 222–3
- cocaine dependence 373–4  
 cocaine-induced paranoia as a phenotype 380–1  
*see also* substance dependence
- CODE-system 47–8
- codeine 377  
*see also* opioid dependence
- complex traits 119, 421  
 drug responses as 96–7, 406, 420–1  
 heritability 97
- Creutzfeldt–Jacob disease 405
- CYP enzymes 63, 65, 159–60  
 intraindividual variability 166–70  
 aging influence 168–9  
 dietary influences 166–7  
 disease influence 169–70  
 drug–drug interactions 167  
 nutraceutical influences 167–8  
 nomenclature 159–60  
 phenotyping/genotyping 409–10  
 polymorphism 163  
 tardive dyskinesia and 248  
*see also* drug metabolism; *specific CYP enzymes*
- CYP1A2 257  
 drug metabolism 185  
 induction by smoking 173, 257  
 polygenic control 164  
 tardive dyskinesia and 257, 411
- CYP2A6 341  
 nicotine dependence and 381–2
- CYP2B 341
- CYP2C9, drug metabolism 189, 190, 194, 202, 338, 341
- CYP2C19, drug metabolism 187–9, 193–4, 198, 202, 337–8, 342
- CYP2D6 164, 256  
 drug metabolism 184–202  
 phenotyping/genotyping 409–10  
 polymorphism 160–2, 256, 377  
 substance dependence and 377, 381–2  
 tardive dyskinesia and 256  
 tricyclic antidepressant toxicity and 63, 66–7, 69
- CYP3A4, drug metabolism 187–9, 194, 199–202, 340
- CYP4B 341
- cytochrome P-450 *see* CYP enzymes

**441**      **Index**

- DCR Budapest–Nashville classification system 46–7
- de Sauvages, Boissier 42
- deletion polymorphisms 8
- demographic variables 10
- denaturing high performance liquid chromatography (DHPLC) 426, 428–9
- dependence *see* substance dependence
- depressive illness  
 delusional depression 270  
 heterogeneity 39–40, 63–4  
 major depression 40, 63, 285, 287–9  
*see also* antidepressant drugs
- development, brain 105–7  
 mouse models 107–11  
 regulatory genes 111–12  
 relevance of epistatic interactions 115–17  
 serotonergic neuron specification and differentiation 112–15
- dexfenfluramine 201
- dextroamphetamine, heritability of drug response 24
- diabetes 78
- diagnostic instruments for research 46–8  
 ADAS-Cog 363  
 AIMS 50–1, 259  
 BPRS 221  
 CGI 221, 286  
 CODE-system 47–8  
 GAS 219  
 DCR Budapest–Nashville 46–7  
 MMSE 364  
 PANSS 221, 251  
 Y-BOCS 286
- diazepam 307, 338, 342, 344
- dietary influence on drug metabolism 166–7
- disease influence on drug metabolism 169–70
- DNA databases 408–9
- donepezil 366
- dopamine  $\beta$ -hydroxylase (DBH), cocaine dependence and 380–1
- dopamine receptors 248  
 D<sub>1</sub> receptor, clozapine response and 224  
 D<sub>2</sub> receptor 28, 29, 252  
   aberrant alternative RNA splicing 135–7  
   clozapine response and 224–5  
   lithium response and 327–8  
   tardive dyskinesia and 252  
 D<sub>3</sub> receptor 250–2  
   aberrant alternative RNA splicing 135–7  
   clozapine response and 225–6  
   tardive dyskinesia and 250–2, 394  
 D<sub>4</sub> receptor 27, 29, 115–16  
   clozapine response and 226–7  
 D<sub>5</sub> receptor, clozapine response and 224  
 role in schizophrenia 250–1
- dopaminergic enzymes 248
- drug dependence *see* substance dependence
- drug development 401–15  
 genomics application 403–6  
 pharmacogenetic differences and 61–5  
 pharmacogenetics and drug toxicity 411–12
- phenotyping/genotyping drug metabolism 409–11
- polymorphism application 406–8
- predictors of drug response 412–14
- prospective enrichment of trials through genotyping 414–15
- drug efficacy 67–9, 220  
 poor signal:noise ratio 60–1, 64  
*see also* drug response; therapeutic drug monitoring
- drug metabolizing enzymes (DMEs) 158, 171, 409  
 genetic variability 160–4  
   relevance for study design 164–5  
*see also* CYP enzymes
- drug metabolism 157, 158  
 genetic variability 160–4, 170–1  
 CYP1A2 regulation 164  
 CYP2D6 polymorphism 160–2
- intraindividual variations 165–70  
 aging influence 168–9  
 dietary influences 166–7  
 disease influence 169–70  
 drug–drug interactions 167  
 nutraceutical influences 167–8
- phase I and phase II metabolism 158–9
- phenotyping/genotyping 409–11  
*see also specific drugs*
- drug response 57–8, 158  
 as a complex trait 96–7, 406, 420–1  
 genetic variability and 335  
 heritability of 22–4  
   antidepressants 23–4  
   antipsychotics 24  
 influences 221–2  
 medicine response profiling 383  
 methodological issues 24–6  
 pharmacogenetic differences 59–60  
   drug development and 61–5  
   existing drugs and 65  
 phenotype definition 76–8  
   responder/nonresponder phenotype 76–7  
   side effect phenotype 77–8, 219–20  
   tardive dyskinesia 248–9  
 predictors of 284–94, 412–14  
*see also* drug efficacy; drug metabolism; *specific drugs*; therapeutic drug monitoring
- drug toxicity 77–8, 219–20  
 carbamazepine 340  
 extrapyramidal side effects 219  
 pharmacogenetics and 411–12  
 surrogate markers 68–9  
 tricyclic antidepressants 68–9  
 CYP2D6 role 63, 66–7, 69  
 surrogate markers 68–9  
*see also* tardive dyskinesia
- drug–drug interactions 167
- dye-labeled oligonucleotide ligation (DOL) 430
- dystonia 246
- Ecstasy (MDMA) 203  
 efficacy *see* drug efficacy

**442** Index

- electrophoresis 428  
 epidemiological genetics 37  
 epilepsy 311, 333  
   benign familial neonatal convulsions 346  
   *see also* anticonvulsant drugs  
 epistasis 9, 11  
   clozapine response and 233–4  
   relevance to brain development 115–17  
 Esquirol, Jean-Etienne Dominique 42  
 ethanol metabolism 376  
   *see also* alcoholism  
 ethnic diversity 10, 29, 338  
   drug toxicity 411  
   genomic control method 31  
   nicotine metabolism 382  
 Eve (MDE) 203  
 exonic splicing enhancers (ESEs) 137  
 exonic splicing suppressors (ESSs) 137  
 5' exonuclease assay 429–30  
 extrapyramidal side effects (EPS) 219  
   *see also* tardive dyskinesia
- family studies 406–7  
   *see also* twin studies  
 felbamate 346  
 flumazenil 307, 311  
 flunitrazepam 307  
 fluorescence energy resonance transfer (FRET)  
   428, 429  
 fluorescence polarization 429  
 fluorodeoxyglucose (FDG) imaging, schizophrenia  
   394  
 fluoxetine 189–92  
 flurazepam 338  
 fluvoxamine, drug response  
   COMT polymorphism and 276  
   heritability 23  
   pindolol augmentation 270–2, 288–9  
   serotonin transporter gene linked  
     polymorphic region (5-HTTLPR) and  
     269–71, 287–9  
 functional magnetic resonance imaging (fMRI),  
   Alzheimer's disease 392
- GABA 133, 300  
 GABA receptors 302, 343  
   GABA-A receptor 133–4, 302–13  
     aberrant alternative splicing 134  
     barbiturate interactions 336, 344–5  
     benzodiazepine interactions 306–10, 336,  
     343  
     clozapine response and 233  
     drug development 311–12  
     mutation studies 308–9  
     neurosteroids and 312  
     possible interventions 309–11  
     role in anxiety 307–8  
     subunit functions 306–7  
 gabapentin 346  
 galantamine 366  
 gamma-aminobutyric acid *see* GABA  
 ganaxolone 312
- GATA3 transcription factor 114  
 gene expression 12, 96  
   pharmacodynamic factors 98–100  
   regulation 96, 98  
 gene–environment interactions 165–6  
   clozapine response and 232–4  
   relevance to brain development 115–17  
 gene–gene interactions 11, 86, 115  
   *see also* complex traits  
 generalized anxiety disorder 285, 305  
 genetic variation  
   drug responsiveness and 335  
   nature of 334  
   *see also* polymorphism  
 genomic control method 31, 83  
 genomics 433  
   application to drug development 403–6  
   *see also* pharmacogenomics  
 genotyping  
   allele detection 428–9  
     denaturing high performance liquid  
     chromatography (DHPLC) 428–9  
     electrophoresis 428  
     fluorescence polarization 429  
     fluorescence resonance energy transfer  
     429  
     labeling the amplified product 428  
     MALDI-TOF mass spectrometry 429  
     molecular conformation 428  
   allele discrimination 423–8  
     allele-specific amplification 423  
     allele-specific hybridization 426  
     allele-specific ligation 426–8  
     heteroduplex/homoduplex resolution 426  
     primer extension and minisequencing 426  
     restriction endonuclease digestion 423  
   drug metabolism 409–11  
   highly specialized probes 429–31  
     dye-labeled oligonucleotide ligation 430  
     molecular beacons 430  
     peptide nucleic acid hybridization probes  
     430–1  
     TaqMan (5' exonuclease assay) 429–30  
     template-directed dye incorporation 430  
   Invader assay 431  
   kinetic polymerase chain reaction 433  
   ligase chain reaction 431  
   light-up probes 431  
   padlock probes 431  
   prospective enrichment of drug trials 414–15  
   realtime polymerase chain reaction 432  
 Gli2 transcription factor 113  
 Global Assessment Scale (GAS) 221  
 glutamate receptors, RNA transcript editing  
   alterations 138–41  
 glutathione S-transferase 411  
 growth factors 114
- haloperidol 199, 247  
   brain imaging studies 394  
 haplotypes 28, 85  
 Heinrichs–Carpenter scale 221

**443**      **Index**

- heritability  
   complex traits 97  
   drug response 22–4  
     antidepressants 23–4  
     antipsychotics 24  
     lithium 321–5  
   manic-depressive illness 37, 38–9  
   mathematical models of inheritance 38  
   schizophrenia 37, 38–9  
   substance dependence 374  
 heteroduplex/homoduplex resolution 426  
 hexobarbital 345  
 histamine receptors, clozapine response and 231  
 5-HT *see* serotonin  
 5-HTTLPR *see* serotonin linked polymorphic region  
 Human Genome Project 30  
 human leukocyte antigen (HLA), tardive dyskinesia and 246  
 hydantoin 337–40  
*Hypericum perforatum* (St. John's wort) 167–8  
  
 identity by descent (IBD) 406–7  
 imidazenil 310  
 imipramine, heritability of drug response 23  
 infection influence on drug metabolism 169  
 inflammation influence on drug metabolism 169  
 inheritance *see* heritability  
 inositol polyphosphate 1-phosphatase 328  
 insertion polymorphisms 8  
 Invader assay 431  
  
 Kahlbaum, Karl 42–3  
 kainate receptors 138–9  
 kinetic polymerase chain reaction (PCR) 433  
 Kleist, Karl 44–5  
 Kraepelin, Emil 43–4  
  
 labeling 428  
 Lehman Quality of Life Interview 221  
 Leonhard, Karl 45  
 ligase chain reaction 431  
 light-up probes 431  
 linkage analysis 24–5, 406–7  
   lithium response 327  
   manic-depressive illness 38  
   schizophrenia 38  
 linkage disequilibrium (LD) 9, 74, 81, 83–5  
 lithium 157–8, 320, 410  
   drug response 320–8  
   as a phenotype 325–6  
   family and family-history studies 321–5  
   mode of inheritance 325  
   studies comparing responders and nonresponders 327–8  
   studies of responders as a homogenous subtype 326–7  
 liver disease influence on drug metabolism 169–70  
  
 major depression 40, 63, 285, 287–9  
 MALDI-TOF mass spectrometry 429  
  
 manganese superoxide dismutase (MnSOD), tardive dyskinesia and 257–8  
 mania, antidepressant-induced 290–4  
   epidemiology 290–1  
   pharmacogenetics 291–2  
 manic-depressive illness, heritability 37, 38–9  
   candidate gene approach 38–9  
   linkage analysis 38  
 Mantel-Haenszel test 83  
 mass spectrometry 426, 429  
 MDE (Eve) 203  
 MDMA (Ecstasy) 203  
 medicine response profiling 383  
 mephenytoin 337–8  
 mephobarbital 344, 345  
 methadone 201–2  
 N-methyl-D-aspartate (NMDA) receptor 131  
   aberrant alternative splicing of NR1 subunit 132–3  
   role in schizophrenia 131–3  
 metrifonate, Alzheimer's disease treatment 363–5  
 mianserin 183–5  
 microsatellites 9  
 midazolam 342, 343  
 milnacipran 193  
 Mini-Mental Status Examination (MMSE) 364  
 minisatellites *see* variable number tandem repeats (VNTRs)  
 minisequencing 426  
 mirtazapine 185–6  
 missense mutations 334  
 molecular beacons 430  
 molecular conformation 428  
 monoamine oxidase (MAO) 273–4  
   citalopram metabolism 187–9  
   MAO-A 104–5  
   Parkinson's disease and 274–5  
 monoamine oxidase inhibitors (MAOIs) 284  
 mood stabilizers, response to 328–9  
   *see also* lithium  
 mouse models  
   brain development 107–11  
   GABA-A receptor subunit role in anxiety 307–8  
   RNA transcript editing alterations 139–40  
   *see also* animal studies  
 multifactorial traits 9  
  
 naltrexone 377  
 neuropsychopharmacology 41  
 neurosteroids 312  
 neurotrophins 113–15, 116  
 nicotine metabolism 382  
   *see also* smoking  
 NNDA receptor 131  
 norfluoxetine 190–2  
 nortriptyline 194–6  
 nosological matrix 48–50  
 nosology *see* psychiatric nosology  
 nutraceutical influences on drug metabolism 167–8

**444** Index

- obsessive-compulsive disorder (OCD) 285  
 antidepressant response 272  
 comorbid tic disorder and 286–7  
 serotonin transporter gene and 285–7
- olanzapine 402
- oligonucleotide ligation assay (OLA) 426–8
- opioid dependence 373, 375, 377–80  
 CYP2D6 and 377  
 receptor/ligand interactions 377–80  
*see also* substance dependence
- opioid receptor *OPRM1* alleles 377–80  
 polymorphisms 378–80
- oxazepam 200
- P-450 *see* CYP enzymes
- padlock probes 431
- panic disorder 285
- Parkinson's disease (PD) 246  
 MAO-A polymorphism and 274–5  
 SSRI response 272–3
- paroxetine response, serotonin transporter gene  
 linked polymorphic region (5-HTTLPR)  
 and 269–71, 287
- peptide nucleic acid (PNA) hybridization probes  
 430–1
- Pet1 transcription factor 113–14
- pharmacodynamics 8, 96
- pharmacogenetics 6, 72–3, 218, 360–1  
 definition of terms 6–8  
 drug development and 61–5  
 historical perspective 5–6  
 pharmacogenetic traits 73–6  
 research *see* research design  
*see also* pharmacogenomics;  
 psychopharmacogenetics
- pharmacogenomics 6–7, 73, 421, 433  
*see also* genomics; pharmacogenetics
- pharmacokinetics 8
- phenobarbital 336, 340, 344, 345–6
- phenotype  
 alternative phenotypes 40–1, 290  
 definition and evaluation 10, 76–8  
 responder/nonresponder phenotype 76–7  
 side effect phenotype 77–8  
 tardive dyskinesia 248–9  
*see also* drug response
- phenytoin 336, 338–40
- phospholipase C 326
- pindolol, SSRI treatment augmentation 270–2,  
 288–9
- Pinel, Philippe 42
- polygenic traits 9
- polymerase chain reaction (PCR) 423  
 kinetic PCR 433  
 realtime PCR 432
- polymorphism 8–9, 79–80, 97  
 application to drug development 406–9  
 deletion polymorphisms 8  
 insertion polymorphisms 8  
 predictors of drug response 412–14  
 regulatory genes 98–100  
 simple tandem repeats (STRs) 9  
 variable number tandem repeats (VNTRs) 8–9  
*see also* single nucleotide polymorphisms *specific polymorphic molecules*
- population effects 10
- Positive and Negative Symptom Scale (PANSS)  
 221, 251
- positron emission tomography (PET), Alzheimer's  
 disease 392–3
- post-transcriptional RNA processing *see* RNA  
 processing
- primer extension 426
- progesterone 312
- proteomics 403, 405
- psychiatric nosology 41–6  
 Bleuler, Eugen 44  
 de Sauvages, Boissier 42  
 Esquirol, Jean-Etienne Dominique 42  
 Kahlbaum, Karl 42–3  
 Kleist, Karl 44–5  
 Kraepelin, Emil 43–4  
 Leonhard, Karl 45  
 nosological matrix 48–50  
 Pinel, Philippe 42  
 Schneider, Kurt 45–6  
 Wernicke, Carl 44
- psychopharmacogenetics 95–6  
 phenotype definition 76–8  
 responder/nonresponder phenotype 76–7  
 side effect phenotype 77–8  
 rationale for 4–5  
*see also* drug response; pharmacogenetics
- quantitative trait loci (QTL) 96, 98, 247, 249  
 QTL mapping 339
- realtime polymerase chain reaction 432
- reboxetine 194
- research design issues 9–12  
 demographic variables 10  
 gene expression 12  
 interaction among multiple loci 11, 86  
 phenotype definition and evaluation 10  
 population effects 10  
*see also* study design
- restriction endonuclease digestion 423
- retigabine 346
- risperidone 200, 402
- RNA processing 128–9  
 aberrant alternative splicing in psychiatric  
 disorders 131–8  
 dopamine D<sub>2</sub> and D<sub>3</sub> receptors 135–7  
 GABA-A receptor 133–4  
 mechanisms 137–8  
 NMDA receptor NR1 subunit 131–3  
 editing alterations implicated in psychiatric  
 disorders 138–45  
 glutamate receptors 138–41  
 mechanisms 143–5  
 serotonin 2C receptor 141–3
- S12024 367
- St. John's wort (*Hypericum perforatum*) 167–8

**445**      **Index**

- salbutamol 26
- schizophrenia  
 alternative phenotypes 40–1  
 brain imaging studies 393–4, 395  
 dopamine D<sub>3</sub> receptor role 250–1  
 heritability 37, 38–9  
 candidate gene approach 38–9  
 linkage analysis 38  
 RNA processing and  
 GABA-1 receptor 134  
 NMDA receptor 131–3  
*see also* tardive dyskinesia
- Schneider, Kurt 45–6
- scorpion primers 430
- selective serotonin reuptake inhibitors (SSRIs)  
 255–6, 284, 285, 402  
 anxiety treatment 302  
 chiral drugs 181–94, 196–9, 200–2  
 drug response  
 comorbid tic disorder and 286–7  
 obsessive-compulsive disorder 285–7  
 serotonin transporter gene linked  
 polymorphic region (5-HTTLPR) and  
 269–73, 285–9  
 Parkinson's disease treatment 272–3  
 pindolol augmentation 270–2, 288–9  
*see also* antidepressant drugs; *specific drugs*
- serotonin (5-HT) 284  
 role in brain development 105–7, 108–11  
 serotonergic neuron developmental specification  
 and differentiation 112–15
- serotonin receptors  
 5-HT<sub>1A</sub> receptor, clozapine response and 227  
 5-HT<sub>2A</sub> receptor 252  
 clozapine response and 228–9  
 tardive dyskinesia and 252–4  
 5-HT<sub>2C</sub> receptor 141, 254  
 clozapine response and 228–9  
 RNA transcript editing alterations 141–3  
 tardive dyskinesia and 254–5  
 5-HT<sub>3</sub> receptor, clozapine response and 229–30  
 5-HT<sub>5A</sub> receptor, clozapine response and 230  
 5-HT<sub>6</sub> receptor, clozapine response and 230  
 5-HT<sub>7</sub> receptor, clozapine response and 231  
 genomic variants 100–2
- serotonin reuptake inhibitors (SRIs)  
 obsessive-compulsive disorder treatment 272  
*see also* selective serotonin reuptake inhibitors  
 (SSRIs)
- serotonin transporter (5-HTT) 269, 285  
 antiobsessional response and 285–7  
 clozapine response and 231  
 genomic variants 102–4, 116–17  
 lithium response and 328  
 tardive dyskinesia and 255–6  
 variable number of tandem repeats 283  
 serotonin linked polymorphic region 5-HTTLPR  
 256, 269–73, 285  
 antidepressant response and 269–73, 285–90  
 role in antidepressant-induced mania 291–4
- side effects *see* drug toxicity
- signal:noise ratio, drug efficacy trials 60–1, 64
- silent mutations 334
- simple tandem repeats (STRs) 9
- single nucleotide polymorphisms (SNPs) 8, 79–80,  
 118, 278, 334, 408, 433–4  
 frequency of 79  
 genotyping technology 32, 422–33  
 allele detection 428–9  
 allele discrimination 423–8  
 highly specialized probes 429–31  
 non-PCR based strategies 431–3  
 identification of 12, 30, 383–4  
 interactions among multiple loci 11  
 properties of 422  
 role in pharmacogenomic research 422  
 sample size required for candidate gene studies  
 80–3
- SLC6A4 gene 285, 289  
*see also* serotonin transporter (5-HTT)
- smoking  
 CYP1A2 induction 173, 257  
 nicotine dependence 373–5  
 CYP enzymes and 381–2  
*see also* substance dependence
- SNPs *see* single nucleotide polymorphisms
- sodium channels 336
- spliceosome 129
- splicing *see* RNA processing
- statistical approaches  
 gene interactions 86  
 methodological developments 31  
 pharmacogenetic traits 73–6  
 sample size required for candidate gene studies  
 80–3  
 study design 83–5
- stereoselective drugs *see* chiral psychotropic  
 drugs
- study design 11, 83–5  
 case-control design 9–10, 25, 31, 74–5  
 association studies 25–9, 83  
 limitations of 26–9, 74–5  
 developments in statistical methodologies 31  
 linkage analysis 24–5  
*see also* research design issues
- substance dependence  
 genetics of 373–5  
 heritability 374  
 pharmacodynamic effects 375–6  
 pharmacogenetics 376–83  
 cocaine dependence 380–1  
 opioid dependence 377–80  
 tobacco dependence 381–2  
 pharmacokinetic effects 376
- substance P 413–14
- sulpiride 199
- sunrise probes 430
- t-test 83
- tacrine  
 Alzheimer's disease treatment 363, 365–6  
 toxicity 411
- Taq A1 allele 28, 29
- TaqMan (5' exonuclease assay) 429–30

**446** Index

- tardive dyskinesia (TD) 245–61, 411  
 additive small gene effects 258  
 brain imaging studies 393–4, 395  
 candidate gene studies 247–8, 249–58  
 dopaminergic enzymes and receptors 248, 250–2, 394  
 metabolic enzymes 248, 256–8  
 serotonergic genes 252–6  
 evidence for genetic basis 245–6  
 animal data 246–7  
 phenotype definition 248–9  
 template-directed dye incorporation (TDI) 430  
 terfenadine 411  
 therapeutic drug monitoring (TDM) 67–9, 171  
 tricyclic antidepressants 66–7  
 thiopurine toxicity 411  
 thioridazine 196–8  
 tic disorder comorbidity with obsessive-compulsive disorder 286–7  
 tobacco dependence *see* smoking  
 total sleep deprivation (TSD) 273, 287  
 Tourette syndrome comorbidity with obsessive-compulsive disorder 286–7  
 toxicity *see* drug toxicity  
 transcription factors 112  
*see also specific factors*  
 transcriptional profiling 405  
 transmission disequilibrium test (TDT) 75  
 triazolopyridazine 311  
 tricyclic antidepressants (TCAs) 283–4  
 chiral drugs 183–7  
 pharmacogenetic differences in response 62–3  
 therapeutic drug monitoring 66–7  
 toxicity 68–9  
 CYP2D6 role 63, 66–7, 69  
 surrogate markers 68–9  
*see also* antidepressant drugs; *specific drugs*  
 trimipramine 186–7  
 tropicamide 366–7  
 twin studies  
 heritability of drug response 22–3, 24  
 manic-depressive illness 37  
 schizophrenia 37  
 substance dependence 374  
 tyrosine hydroxylase 326, 327  
 valproic acid 336–7, 340, 341–2  
 bipolar disorder treatment 328  
 variable number tandem repeats (VNTRs) 8–9  
 serotonin transporter gene 285  
 venlafaxine 193–4  
 viloxazine 194  
 warfarin 411  
 Wernicke, Carl 44  
 WHOQOL-100 221  
 xanomeline 367  
 Yale–Brown Obsessive-Compulsive Scale (Y-BOCS) 286  
 zolpidem 310, 311–12, 343  
 zopiclone 201, 310