

INDEX

Note: Page numbers followed by the letter b refer to boxes, those followed by f refer to figures, and those followed by t refer to tables.

- Abuse
 child, bipolar parents and, 217–18
 drug. *See* Substance abuse
- Acamprosate, for alcohol abuse, 944
- Acclimatization, seasonal affective disorder and, 682–83, 694n74
- Accomplishment, 402. *See also* Creativity
- N-Acetylaspartate
 lithium and, 579–80, 580f
 magnetic resonance spectroscopy, 639–41
- Acetylcholine. *See also* Cholinergic entries
 carbamazepine and, 503
 cholinergic-aminergic balance hypothesis, 498, 501, 641
 lithium and, 502
- Acne, from lithium, 807
- Acquired immune deficiency syndrome (AIDS) dementia, 111–12
- Activity. *See also* Hyperactivity
 in bipolar depression, 66–68, 70–71, 72, 73t
 cerebral. *See* Cerebral activity
 in hypomania, 39
 in mania, 33–37, 34f, 39–40, 60, 61t–62t
 motor, spontaneous, 286–88, 286b
- Adaptive flexibility, creativity and, 397
- Addiction. *See* Substance abuse
- S-Adenosylmethionine (SAMe), antidepressant effects, 791–92, 796nn69–70
- Adenyl cyclase. *See also* G_s/cAMP-generating signaling pathway
 carbamazepine and, 544
 G protein regulation, 538, 540–41, 540f, 541t
 lithium and, 543–44, 604n60
 pathway, 537f
- ADHD. *See* Attention-deficit/hyperactivity disorder (ADHD)
- Adherence. *See* Medications, adherence
- Adolescent, antidepressant use in, adverse psychiatric events, 930–32, 960, 973–75
- Adolescent-onset bipolar disorder, 196–204. *See also* Childhood-onset bipolar disorder
 assessment and diagnosis, 197, 376–78, 377t
 comorbidity, 202–3, 202t, 203t
 course and outcome, 178, 199–204
 depressive features, 198–99, 200b
 early, 124
 versus early-onset alcoholism, 938
 epidemiologic findings, 176–78, 177t, 186n7, 204–5
 implications, 205–6
 manic features, 197–98
 neurodevelopmental aspects, 203–4
 pre- and postmorbid adjustment and functioning, 200–201, 201b
 psychotherapy, 903
 puberty issue, 203–4
 symptoms and clinical presentation, 197–99
- Adoption studies
 of creativity, 396, 396t
 of manic-depressive illness, 421–22, 422t
 of suicide risk, 256–57, 258t
- Adrenergic challenge strategies, 479–80
- Adrenergic receptor(s)
 α_2 -, 478
 on blood cells, 478, 601n4
 β -, 478–79
- Advance directives, 883, 885, 887b, 964
- Affected sibling pair method, 426
- Affective Disorder Rating Scale (ADRS), 369
- Affective disorders. *See* Mood disorders
- Affective processing
 cerebral activity in, 627–52, 653, 653b. *See also* Cerebral activity
 characteristics, 609, 610t
 neuroimaging studies. *See* Neuroimaging studies
- Affective processing tasks, 304–5
- African Americans, epidemiologic findings, 182
- Age. *See also* Child; Elderly
 cerebral metabolic rate for glucose and, 627
 diagnostic issues related to, 158–59
 at first treatment, 121
 neuroimaging studies and, 611–12
 putamen volume and, 625
 subcortical hyperintensities and, 619, 621
- Age at onset
 cycle length and, 131, 152nn30–31
 distribution, 124, 124f
 early. *See also* Adolescent-onset bipolar disorder; Childhood-onset bipolar disorder
 in alcoholism, versus adolescent-onset bipolar disorder, 938
 genetics, 434
 versus late, 124
 in psychotic mania, 205
 in recurrent depression, 431
 suicide attempts and, 268–69
 in epidemiologic studies, 161–62
 false unipolar depression and, 133
 genetic subtypes and, 125, 434
 intermediate, 124
 late, 124
 literature on, 120–25, 122t–123t, 150–51nn4–16
 mixed states, 80
 neuroimaging studies and, 612
 outcomes and, 125, 151nn13–16
 psychotic symptoms and, 53, 125
 reduction in, proposed explanations, 121, 150nn6–7, 205, 206
 subcortical hyperintensities and, 619
 suicide and, 268–69, 268t
 very late, 124–25, 150n10
- Aggression
 in children and adolescents, 913, 914t, 929
 impulsive, suicide risk and, 258
- Agitation
 in depression, 14–15, 82, 97, 114n9
 suicide and, 265–66, 957–58, 959–60
- Agomelatine, 695n81
- Agranulocytosis
 from carbamazepine, 810
 from clozapine, 813, 845n34
- AIDS dementia, 111–12
- ALo82Do6, 529
- Alcohol abuse/dependence
 early-onset, versus adolescent-onset bipolar disorder, 938
 hypothetical relationships, 229–33, 229t
 methodological issues, 225
 in mixed states, 80
 modification of course, 232–33
 phase of illness and, 229–30, 229t
 as precipitant, 231
 questions on, 748
 rates, 226–27, 226t
 as self-medication, 230–31
 suicide and, 266–67
 treatment, 937–46, 940t–942t
- Alcoholics Anonymous (AA), 945
- Algorithms, medication, 889, 899
- Allele, 413
- Allergy
 seasonal affective disorder and, 681–82, 694n68
 suicide and, 254
- Altman Self-Rating Mania Scale (ASRM), 358
- Amantadine, for antipsychotic-related weight gain, 814
- Ambivalence, as psychotherapeutic issue, 876–77

- American Academy of Child and Adolescent Psychiatry, 977
- American Foundation for Suicide Prevention, 977
- American Psychiatric Association, 977
- American Psychological Association, 977
- Aminergic-cholinergic balance hypothesis, 498, 501, 641
- Amino acid, 423
- Amish study, 162–63
- Amisulpiride, for acute mania, 741
- Amnesia. *See* Memory deficits
- AMPA receptor potentiators (ARPs), 513, 514, 514f, 515f, 592t
- AMPA receptor trafficking, 512–13
- Amphetamine abuse, as precipitant, 231
- AMPT (α -methylparatyrosine), catecholamine depletion with, 480, 484
- Amygdala
 - activation studies, 628, 691n28
 - activity in depression, 635
 - kindling model, 470–72
 - volumetric studies, 624, 625
- Analytic epidemiology, 155
- Anemia, aplastic, from carbamazepine, 810
- Anger
 - in mixed states, 80
 - as psychotherapeutic issue, 875–76
- Angst' typology of bipolar disorder, 11–12, 126
- Animal models, 466–73
 - bipolar disorder, 468–73
 - depression, 467–68
 - protein kinase C signaling, 545, 547–48
- Anorexia nervosa, 240, 949
- Antalarmin, 528
- Anterior cingulate cortex
 - activation studies, 628
 - activity in depression, 633–34
 - atrophy, 559–61, 565t–566t
 - in sleep deprivation therapy, 676
 - volumetric studies, 622
- Anterior paralimbic structures, activation studies, 628–29, 629f, 636
- Antibiotics, Stevens-Johnson syndrome and toxic epidermal necrolysis risk with, 810t
- Anticonvulsants. *See also specific drugs*
 - for acute hypomania, 728
 - for acute mania, 726–27, 733–36
 - in children and adolescents, 912, 923, 924t–926t, 927, 934n3
 - plus electroconvulsive therapy, 743
 - for bipolar depression, 754, 762–65
 - in children and adolescents, 912, 923, 924t–926t, 927, 934n3, 935n18
 - for maintenance treatment, 809–11
 - plus antipsychotics, 841
 - in breast-feeding women, 818
 - differential response, clinical characteristics associated with, 828t
 - in pregnancy, 816t
 - in rapid cycling, 826t–827t
 - pharmacology, 716–17
 - Stevens-Johnson syndrome and toxic epidermal necrolysis risk with, 810t
 - for suicidal patient, 960, 967
- Antidementia agents, for cognitive impairment, 847n76
- Antidepressants. *See also* Monoamine oxidase inhibitors (MAOIs); Norepinephrine reuptake inhibitors; Serotonin/norepinephrine reuptake inhibitors; Serotonin reuptake inhibitors; Tricyclic antidepressants; *specific drugs*
 - adherence to, 854
 - age at onset and, 121, 205, 206
 - for bipolar depression, 754–56, 756b, 765–81
 - long-term efficacy, 770–71, 794nn38–41
 - plus thyroid hormones, 786
 - for bipolar-II depression, 769b
 - cell survival pathway regulation with, 581–87, 584f, 585f
 - in children and adolescents, adverse psychiatric events, 930–32, 960, 973–75
 - cycle acceleration with, 140, 750, 778–81, 779t, 780f
 - in children and adolescents, 930–31
 - discontinuation
 - lithium efficacy and, 827
 - relapse of depression after, 755, 793nn9–10
 - glutamatergic system as target, 513–14, 514f, 515f
 - hippocampal neurogenesis and, 586–87, 588f, 589f
 - lithium augmentation, 761–62, 762t, 793nn16–19
 - for maintenance treatment
 - in bipolar-II disorder, 799
 - combinations with, 839, 840t, 841
 - efficacy, 770–71, 794nn38–41
 - in pregnancy, 816t
 - in rapid cycling, 827
 - in recurrent unipolar depression, 799–800
 - mania induction with
 - in DSM-IV, 93
 - substance abuse and, 233, 245n3
 - melatonin secretion and, 673
 - neurotrophic actions, 582f, 584–89, 586b, 587f
 - pharmacogenetics, 453, 454t
 - pharmacology, 717–19
 - rapid onset, for suicidal patient, 967
 - recovery pattern, 882, 882f
 - recurrence and, 126
 - REM sleep and, 667
 - resistance to, bipolar disorder and, 771
 - suicide and, 254, 931–32, 960, 973–75, 976n3
 - for suicide prevention, 971–73, 972t, 973f
 - switches with, 750, 771–78, 773t–776t, 794–95nn42–54, 974
 - in children and adolescents, 930–31
 - tapering and switching, 756
 - tryptophan depletion problem, 586–87, 589f
- Antiepileptics. *See* Anticonvulsants
- Antimanic drug(s). *See also* Carbamazepine; Lamotrigine; Lithium; Oxcarbazepine; Valproate
 - naloxone as, 532, 603n46
 - protein kinase C inhibitors as, 553–55, 554f
 - tamoxifen as, 554, 555
- Antipsychotics. *See also specific drugs*
 - for acute mania, combinations with, 723
 - adherence to, 853–54, 855, 856t, 863
 - for aggression, 929
- atypical
 - for acute hypomania, 728
 - for acute mania, 723, 727, 737–41, 738t
 - in children and adolescents, 912, 913, 927–28, 932
 - for anxiety disorders, 947
 - for bipolar depression, 756–57, 781–82
 - central obesity from, 243
 - drug interactions, 814
 - extrapyramidal side effects, 812–13, 845nn31–33, 848n90
 - for maintenance treatment, 811–15
 - in breast-feeding women, 818
 - efficacy, 836–38
 - in pregnancy, 817
 - pretreatment evaluation and ongoing monitoring, 805t–806t
 - side effects, 812–14
 - manic/hypomanic symptoms from, 757, 793n12
 - metabolic syndrome from, 813, 845–46n35
 - pharmacology, 719
 - prolactin and, 932
 - side effects, 757
 - for suicidal patient, 960, 967, 975
 - teratogenicity, 817
 - weight gain from, 243, 813–14, 845–46nn35–38, 932
- for bipolar depression, 756–57, 781–82
- for maintenance treatment, combinations with, 841
- in mixed states, 782
- typical
 - for acute mania, 723, 727, 736–37, 746nn25–28
 - for bipolar depression, 781
 - for maintenance treatment, 811–12
 - in pregnancy, 817
 - pharmacology, 719
 - side effects, 720n18, 845n29
 - teratogenicity, 817
- Antithyroidglobulin, during lithium treatment, 808
- Anxiety, in delirious mania, 35–36
- Anxiety disorders, 233–39, 234t–236t, 238t, 909
 - in adolescent-onset bipolar disorder, 203
 - in childhood-onset bipolar disorder, 191, 192t
 - suicide and, 265–66
 - treatment, 946–48
- Anxiety Disorders Association of America, 977
- AP-7, 513
- Aplastic anemia, from carbamazepine, 810
- Appetite-suppressing agents, for antipsychotic-related weight gain, 814
- Arachidonic acid, suicide and, 254
- Arecholine, 667
- Areataeus of Cappadocia, 4, 32, 35, 40, 65–66, 82–83, 226
- Aripiprazole
 - for acute mania, 727, 730f, 730t, 738t, 741
 - in children and adolescents, 918t, 927–28
 - versus haloperidol, 737, 741
 - efficacy, strength of evidence, 838t
 - for maintenance treatment, 813
 - efficacy, 832t, 838, 848nn85–86

- pretreatment evaluation and ongoing monitoring, 806t
side effects, 807t
- Aristotle, 3–4, 379
- ARPs (AMPA receptor potentiators), 513, 514, 514f, 515f, 592t
- Artists. *See also* Creativity
biographical studies, 383–89, 384t–389t, 390f
living, studies, 389–93, 391t, 392f–394f, 394, 395t
- Asian samples, epidemiologic findings, 182–83
- Assessment, 355–78
analysis and comparison of scales, 365–68, 366f–368f
of bipolar risk, 369–71, 370t
of bipolar symptoms in children and adolescents, 195–96, 197, 376–78, 377t, 910
combined, of manic and depressive states, 368–69
conceptual challenges, 356
of course and outcome, 373–74, 373f. *See also* Course and outcome
of delusions, 53
of depressive states, 361–65, 366, 367f, 368, 368f, 376–78
diagnostic, 89–114. *See also* Diagnosis
of manic states, 358–61, 360t, 366, 366f, 367f, 376, 377t
methodological issues, 356–58
neuropsychological, 273–306. *See also* Neuropsychological evaluation
overview, 355–56
of personality, 323–34. *See also* Personality
of psychosocial adjustment, 374–76
screening
adults, 371–72, 372t
children and adolescents, 372–73
of suicide risk, 953–58
validity issue, 356
- Association for Methodology and Documentation in Psychiatry, 89
- Association studies, 436–46, 437t–442t, 459–60
family-based, 436, 436f
future directions, 455–56
linkage disequilibrium, 445
method, 436, 436f, 443
population isolates, 445–46
promising candidate genes, 443–45
- Associational patterns, lithium level and, 405f
- Assortative mating, 349
- Atmospheric temperature, seasonal affective disorder and, 688
- Atopy, suicide and, 254
- Atrophic changes in manic-depressive illness, 559–68, 564b, 565t–566t. *See also* Hippocampus, atrophy
- Attention and attention deficits, 289–91, 290f, 291f
generalized, 303
memory and, 296–98
neuropsychological evaluation, 273
suicide and, 303
- Attention-deficit/hyperactivity disorder (ADHD), 239, 909
adolescent-onset, 202, 203
adult, 107, 239
versus bipolar disorder, 106–7
- childhood-onset, 191–93, 192t, 193f
history of, in adult-onset bipolar disorder, 909
with oppositional defiant disorder, 913
- Augmentation
with lithium, 761–62, 762t, 793nn16–19
with monoamine oxidase inhibitors, 485–86
- Average Mood Symptom Score (AMSS), 374, 375f
- Axon regeneration, retinal ganglion cell, with lithium, 576, 577f
- Babcock, W.L., 383
- Baillarger, Jules, 5, 7
- Barcelona program, 900, 900b
- Basal ganglia
activity in depression, 635
hyperintensities, 618f, 619, 621
volumetric studies, 625
- Bcl-2
neuroprotective effects, 572
overexpression with lithium and valproate, 572–74, 573f, 581, 583f
upregulators, 594t
- BDNF. *See* Brain-derived neurotrophic factor (BDNF)
- Beat phenomenon, 661, 661f, 669
- Bech-Rafaelsen Mania Scale, 360–61
- Bech-Rafaelsen Melancholia Rating Scale, 364–65
- Beck Depression Inventory (BDI), 361–62
- Bed rest and darkness, for rapid cycling, 678, 693nn61–62, 843
- Behavior
in bipolar depression, 66–68, 70–71, 72, 73t
in hypomania, 39
in mania, 33–37, 34f, 39–40, 60, 61t–62t
sexual, 35, 188, 189t, 348–49, 354n19
- Behavior facilitation system, 332
- Behavioral activation system, 332
- Behavioral disorders, in adolescent-onset bipolar disorder, 197, 203
- Behavioral sensitization. *See also* Kindling or sensitization model
in kindling or sensitization model, 470
protein kinase C activity and, 547
- Behavioral stabilization, initial, in acute mania/hypomania and mixed states, 723–24
- Behavioral therapy. *See* Cognitive-behavioral therapy
- Behavioral Treatment for Substance Abuse in Severe and Persistent Mental Illness (BTSAS), 945
- Bell's mania, 35–36
- Benzodiazepines
for acute hypomania, 728
for acute mania, 723, 727, 742
for anxiety disorders, 946
for maintenance treatment in pregnancy, 816t
pharmacology, 719
for suicidal patient, 960, 966–67
- Berlioz, Hector, 78
- Berryman, John, 401
- Biarylpropylsulfonamide LY392098, 513
- Binge eating, 225, 949
- Biographical studies, creativity, 383–89, 384t–388t, 390f
- Biological rhythms, 139, 661, 662f. *See also* Circadian rhythm
- Biological studies
in children of bipolar parents, 219
neurologic. *See* Neurobiology
- Biometrics, 413
- Bipolar Affective Disorder Dimension Scale, 371
- Bipolar depression. *See also* Depression
behavior in, 66–68, 70–71, 72, 73t
in children and adolescents, 178, 198–99, 200b
acute treatment, 911, 915, 929, 934nn4–6
treatment of first episode, 911
classic clinical descriptions, 65–68
clinical studies, 71–72
versus depressive aspect of borderline personality disorder, 108
misdiagnosis as unipolar depression, 104–6, 104b, 115nn14–17
pretreatment evaluation, 748–49
prodromal symptoms, 886
psychotic symptoms in, 58, 59t, 67–68, 71–72
versus schizophrenia or schizoaffective disorder, 103
seasonality, 254–55
subjective experiences of patients, 68–71
treatment, 747–92
in children and adolescents, 911, 915, 929, 934nn4–6
clinical management, 748–59
comorbidities and, 750
complex regimens, 757
first episode, in at-risk youth, 911
general considerations, 749–50
hospitalization, 749
pretreatment evaluation, 748–49
review of literature, 759–92, 759t, 760t
selection of approach, 751–59, 752f–753f
versus unipolar depression, 15–18, 16t–17t, 26–27nn30–35. *See also* Bipolar-unipolar distinction
- Bipolar disorders. *See also specific topics, e.g.,* Course and outcome
assessment, 355–78
in children and adolescents, 187–221
clinical description, 29–86
comorbidity, 223–45
course and outcome, 119–50
creativity and, 379–406
depressive dominance, 23–24, 27n48
diagnosis, 89–114
in DSM-IV, 91–92
dynamic nature, 31–32
epidemiology, 155–85
genetics, 411–61
historical roots, 3–8
history in, 112–13
interpersonal functioning and, 337–52
mania primacy, 15
neuroanatomy and neuroimaging, 609–54
neurobiology, 463–601
neuropsychology, 273–321
offspring studies, 206–20
personality and, 323–37
psychosis and, 57, 58, 59t, 431–33, 432t
risk assessment, 369–71, 370t
seasonal rhythms, 680–82, 681f
secondary, 109, 110b

- Bipolar disorders (*continued*)
 sleep in, 665
 spectrum. *See* Manic-depressive spectrum
 suicide and, 247–69, 953–76
 versus unipolar depression. *See*
 Bipolar-unipolar distinction
- Bipolar Disorders Information Center, 977
- Bipolar-I disorder, 21
 adoption studies, 422t
 family studies, 416t, 418
 maintenance treatment, 798–99
 most recent episode mixed, DSM-IV
 diagnostic criteria, 97, 97b
 prevalence, by demographic characteristics,
 165, 168t
 substance abuse in, 232
 twin studies, 419, 420t
- Bipolar-I versus bipolar-II disorder
 antidepressant-related switches, 776
 clinical differences, 18–19, 19t, 27nn36–38
 comparison to Angst' typology, 11–12
 original distinction, 9, 11
 short-term memory deficits, 294
 suicide, 250–51, 251t
- Bipolar-II disorder
 comorbidity
 anxiety disorders, 234
 migraine, 244
 obsessive-compulsive disorder, 238
 course and outcome, 146, 149
 diagnosis, 12, 114n6
 DSM-IV diagnostic criteria, 96, 96b, 114n7
 family studies, 416t, 418
 genetic studies, 433–34
 maintenance treatment, 799, 828, 829t, 830
 prevalence, 167
 treatment of depression, 767, 769b, 799
 twin studies, 419, 420t
 versus unipolar depression, 17
- Bipolar-III disorder, 19, 27n38
- Bipolar-III disorder, 21
- Bipolar Kids, 977
- Bipolar News, 977
- Bipolar-NOS
 in children, 159, 195–96
 DSM-IV diagnostic criteria, 98–99
- Bipolar Significant Others, 977
- Bipolar spectrum. *See* Manic-depressive spectrum
- Bipolar Spectrum Diagnostic Scale, 371
- Bipolar-unipolar distinction, 8–19
 in children, 190
 in children of bipolar parents, 915, 934n6
 clinical description and diagnosis, 104–6, 104b,
 115nn14–17
 clinical differences
 bipolar-I versus bipolar-II depression,
 18–19, 19t
 bipolar versus unipolar depression, 15–18,
 16t–17t, 26–27nn30–35
 encephalomalacia, 310–13, 311f, 312f
 family functioning, 350–52
 neuropsychological burden, 274–75, 275f,
 309–10
 overview, 9–13, 10t–11t, 26nn18–24
 personality, 330–32
 seasonal rhythms, 681, 694n70
 sleep deprivation therapy, 675
 spontaneous motor activity, 287, 288
 suicide, 250, 251t
 verbal and performance IQ, 278–79, 281f
- Bipolar/unipolar ratio, 12
- Birth defects, medication-induced, 815–17, 816t,
 817b, 817t
- Birth weight, in children of bipolar parents, 219
- Black bile, 3–4
- Bleuler, Eugene, 8, 26n17, 33, 67, 380
- Blood dyscrasia, from carbamazepine, 810
- Body temperature
 in circadian rhythm disturbances, 671–72
 regulation, NREM sleep and, 663
 rhythm of, REM sleep propensity and, 670–71
- Borderline personality disorder, 108–9, 115n18,
 202, 336, 949
- Botanicals, antidepressant effects, 792
- Brain. *See also* Neuroanatomical correlates;
 Neurobiology; Neurochemistry;
 Neuroimaging studies;
 Neuropsychology
 functional asymmetry, and localization of
 mood systems, 318–20
 gene expression in, 448–50, 449t
 lateralization of damage, 316–18, 317f, 610–11
 regulation of depression versus mania, 315–18,
 317f
 structural abnormalities, 310–13, 311f, 312f
- Brain-derived neurotrophic factor (BDNF),
 444–45
 antidepressants and, 582, 585f
 cellular actions, 568, 606n78
 versus ERK pathway, 583–84
 estrogen and, 531
 social defeat stress paradigm, 582–83
- Brain stimulation. *See also* Transcranial
 magnetic stimulation (TMS)
 affective states provoked by, 313–14
 for bipolar depression, 783–84
- Breakthrough symptoms, management, 818–19
- Breast-feeding women, maintenance treatment
 in, 817–18
- Brief psychotic disorder, 107, 107b
- Bromocriptine, 486, 784
- Bulimia, 240, 949
- Bupropion
 for bipolar depression, 755, 756, 760t, 767–69,
 770f, 794n37
 in children and adolescents, 915
 cycle acceleration with, 780
 pharmacology, 718
 response to, baseline cerebral activity and, 638
 for seasonal affective disorder, 685
 switches with, 777–78
 for weight loss in obese patients, 950
- Burden of disease
 bipolar disorder, 178, 180, 180t
 hippocampal atrophy and, 274
- Burnout, cycle length and, 131
- Burns, Robert, 78
- Buschke Selective Reminding Test, 306
- Byron, George Gordon, Lord, 78, 381, 382f, 383b
- Calcitonin, 535–36
 Calcitonin/CGRP α (CALCA) gene, 535–36
 Calcium/calmodulin (CaM) pathway, 537f
 Calcium channel blockers
 for acute mania, 743
 for maintenance treatment, 842–43
- Calcium signaling abnormalities, 548–52,
 549t–551t, 552f
 mitochondrial–endoplasmic reticulum
 regulation and, 568–69
- Calmodulin-dependent protein kinase II
 (CaMKII), presynaptic targets, 556–57,
 605–6nn70–71
- cAMP/CREB cascade, antidepressants and, 582,
 584f, 585f
- cAMP/protein kinase A signaling, 541–42
- cAMP response element binding protein (CREB)
 antidepressants and, 582, 584f, 585f
 lithium and, 543
- cAMP signaling pathway, 538, 540–45, 540f, 541t,
 542t, 550
- Canadian Network for Mood and Anxiety
 Treatments Algorithm, 713
- Candidate genes
 functional, 436, 443
 positional, 443
 promising, 443–45
- Carbamazepine
 acetylcholine and, 503
 for acute mania, 723, 725, 726
 in children and adolescents, 918t, 923, 927
 combinations with, 733
 dosages, 727
 efficacy, 730f, 730t, 731t, 733, 745nn12–16
 plus risperidone, 740
 adenylyl cyclase and, 544
 adherence to, 855, 856t
 for anxiety disorders, 946, 948
 for bipolar depression, 754, 759t, 763
 dopamine and, 488
 efficacy, strength of evidence, 838t
 glutamate and, 513
 for maintenance treatment, 809–10
 in breast-feeding women, 818
 differential response, clinical characteristics
 associated with, 828t
 efficacy, 830–31, 832t, 833t, 847nn64–69
 plus lithium, 839
 in pregnancy, 815, 816t, 817
 pretreatment evaluation and ongoing
 monitoring, 803t
 side effects, 807t, 810
 for mixed mania, 725
 norepinephrine and, 481
 pharmacology, 716–17, 720n17
 REM sleep and, 667
 response to, baseline cerebral activity and, 637
 serotonin and, 497–98
 somatostatin and, 533
 Stevens-Johnson syndrome and toxic
 epidermal necrolysis risk, 810t
 for substance abuse, 942t, 943
 teratogenicity, 815, 816t, 817
 vasopressin and, 533
- Cardiovascular disease, 146, 154n48, 240, 619, 949
- Carroll Depression Rating Scale-Revised, 362
- Catecholamine overdrive, psychomotor
 retardation and, 285
- Category Test, 298
- β -Catenin upregulators, 593t
- Caudate, volumetric studies, 625

- Cell survival pathways, regulation with antidepressants, 581–87, 584f, 585f
- Cellular plasticity cascades, 559–81, 597–99
N-acetylaspartate increased level with lithium, 579–80, 580f
atrophic changes, 559–68, 564b, 565t–566t
Bcl-2 overexpression with lithium and valproate, 572–74, 573f, 581, 583f
cell survival pathway regulation with antidepressants, 581–87, 584f, 585f
ERK MAPK, activation by lithium and valproate, 570–72, 571f
glial cell pathology, 562–63
glial cell type affected, 563–64, 567
gray matter volume increases with lithium, 580, 581f
hippocampal neurogenesis regulation by antidepressants, 586–87, 588f, 589f
hippocampal neurogenesis with lithium and valproate, 576, 578–79, 578f, 579f
long-term implications, 587–89, 590t–594t, 595f
mitochondria and, 570
morphometric brain findings, 559–62, 564b, 565t–566t
neuroprotective effects of lithium, 574–75, 574b, 575f, 606–7n82
neuroprotective effects of valproate, 575–76
neurotrophic actions of antidepressants, 582f, 584, 586, 586b, 587f
neurotrophic signaling cascades, 568, 606n78
neurotrophic signaling-mediated mitochondrial dysfunction, 568–70
retinal ganglion cell axon regeneration with lithium, 576, 577f
stress and, 525–27, 526f, 595f
treatment targets, 589, 590t–594t, 599–601, 600f
- Cellular resiliency, 595f
impairment, 567–68
treatment targets, 599
- Center for Epidemiologic Studies-Depression (CES-D) scale, 363
- Center for Mental Health Services, 978
- Centers for Disease Control and Prevention, National Center for Injury Control and Prevention, 977
- Central nervous system depressants, abuse, 228–29
- Central nervous system stimulation. *See also* Transcranial magnetic stimulation (TMS)
affective states provoked by, 313–14
for bipolar depression, 783–84
- Central nervous system symptoms, in lithium intoxication, 808
- Central obesity, 243
- Cerebellum
activity in depression, 636
activity in mania, 638–39
volumetric studies, 622
- Cerebral activity, 627–52, 653, 653b
baseline markers of treatment response, 637–38
in depression, 629–37, 630f–634f
in healthy subjects, 627–29, 629f
in mania, hypomania, and rapid cycling, 638–39
mood state effects, 637
specific. *See* Cerebral neurochemistry
subcortical hyperintensities and, 620
treatment effects, 637
- Cerebral asymmetry, 626
- Cerebral blood flow (CBF), 627
- Cerebral cortex
glial cell pathology, 562–63
morphological abnormalities, 559–62, 564b, 565t–566t
volumetric studies, 612–17, 612f, 613f, 615t, 621–25, 623f, 626
- Cerebral metabolic rate for glucose (CMRglu), 627
- Cerebral neurochemistry
dopaminergic system, 484–85
psychomotor retardation, 284
serotonergic system, 494, 495
specific, 639–52. *See also* Magnetic resonance spectroscopy
- Character, definition, 324
- Child
abuse, bipolar parents and, 217–18
antidepressant use in, adverse psychiatric events, 930–32, 960, 973–75
bipolar disorder in. *See* Adolescent-onset bipolar disorder; Childhood-onset bipolar disorder
of bipolar parents, 206–20, 350–52
biological studies, 219
bipolar disorder versus unipolar depression in, 915, 934n6
creativity, 396, 396t
early studies, 207, 208b
family life and environmental influences, 217–19, 218f
first episode of depression in, treatment, 911
mechanisms of risk, 217–20
methodological issues, 206–7
neurocognitive studies, 219
outcomes
controlled studies, 207–15, 209t–213t, 216b
parents' clinical and demographic features and, 219–20
recent studies with novel designs, 215, 217
treatment, 930
physical health surveys with mental health questions, 156–57
- Child- and Family-Focused Cognitive-Behavioral Therapy, 903
- Child and Adolescent Bipolar Foundation (CABF), 978
- Child Behavior Checklist (CBCL), 159
- Childbirth
bipolar disorder and, 184
in triggering episodes, 138
- Childhood-onset bipolar disorder, 188–96
aggression in, treatment, 913, 914t, 929
assessment and diagnosis, 195–96, 376–78, 377t, 910
challenges posed by, 907–9
clinical management, 909–17
comorbidity, 191–93, 192t, 193f, 203t, 909
course and outcome, 196
depression in, 190–91
acute treatment, 911, 915, 929, 934nn4–6
treatment of first episode, 911
- developmental issues, 194–95
diagnostic controversies, 191–95, 907–8
electroconvulsive therapy in, 912, 933
epidemiologic findings, 158–59, 176–78, 177t, 204–5
genetic concerns, 910–11
implications, 205–6
indistinct diagnostic boundaries, 191–93, 192t, 193f
maintenance treatment, 911–12, 915–16, 929–30
mania/ADHD in, 191–93, 192t, 193f
acute treatment, 910, 911, 912–13, 915
mania/hypomania in
acute treatment, 911, 912, 914t, 917–28, 918t, 934n2
diagnostic questions, 193–94, 912–13
features, 188, 189t
medical adverse events, 932–33
prevention in at-risk youth, 917
psychiatric adverse events, 930–32
psychoeducation in, 910, 916, 933
psychosocial treatments, 916
psychotherapy in, 902, 903, 933–34
review of literature, 917–34
summary of pharmacological studies, 933
symptoms and clinical presentation, 188–91, 190b
treatment, 907–34
- Children's Depression Inventory (CDI), 376
- Chile study, 173t, 174
- M-Chlorophenylpiperazine, for seasonal affective disorder, 685
- Chlorpromazine
for acute mania, 731t, 736
side effects, 813
- Cholecystokinin (CCK), 535
- Cholesterol, low, suicide and, 260–61
- Choline, magnetic resonance spectroscopy, 501, 641–43
- Choline bitartrate, 500
- Cholinergic agents, for acute mania, 743–44
- Cholinergic-aminergic balance hypothesis, 498, 501, 641
- Cholinergic system, 498, 500–503
lithium and, 502–3
neuroendocrine challenge studies, 501
sleep and, 667, 673, 676
summary of findings, 503, 503b
- Christchurch Psychiatric Epidemiology Study, 167
- Chromium, antidepressant effects, 792
- Chromosome(s)
in bipolar disorder, 427–30, 427f
schematic illustration, 426f
X-, 429
- Chromosome 4, 427–28
- Chromosome 6q16-22, 428
- Chromosome 8q24, 428–29
- Chromosome 12q24, 429
- Chromosome 13q31-33, 429
- Chromosome 16p12-13, 429
- Chromosome 18, 429
- Chromosome 21q22, 429
- Chromosome 22q11-13, 429
- Chronic mild stress paradigm, 468
- Chronicity
in childhood-onset bipolar disorder, 196
cognitive impairment and, 309–10

- Chronicity (*continued*)
 subsyndromal
 in children of bipolar parents, 207, 214
 in long-term outcome, 145
- Chronobiological dysregulation, in seasonal affective disorder, 685–87
- Chronobiological effects of mood stabilizers, 672–73
- Chronobiological interventions, 673–78, 674t, 675b. *See also* Sleep deprivation therapy
- Cingulate cortex, anterior. *See* Anterior cingulate cortex
- Circadian clock, master, 660, 689nn3–12
- Circadian rhythm
 amplitude, 671–72
 beat phenomenon, 661, 661f, 669
 biological day and night/dusk and dawn in, 661, 662f
 disturbances, 667–73
 chronobiological interventions, 673–78, 674t, 675b
 clock genes and, 660, 673
 desynchrony and free-running hypothesis, 668–69
 extended rest-dark period and, 678, 693nn61–62
 hypothesized relationships, 668f
 interpersonal and social rhythm therapy related to, 901
 phase-advance hypothesis, 669–70, 670f, 692n43
 phase instability, 670–71
 temperature dysregulation hypothesis, 671–72
 in elderly person, 670
 free-running, 668–69
 in humans, 660–61, 689–90n13
 lithium and, 557, 562f
 molecular mechanisms, 557, 560f–561f
 mood stabilizers and, 672–73
 nonsleep, REM sleep and, 669
 phase response curve, 661, 690n14
 phase shift, for seasonal affective disorder, 686–87
 physiology, 659–61
 signaling pathway abnormalities and, 598–99
 temporal organization, 661, 662f
- Citalopram, for bipolar depression, 793n18
- Clinical assessment. *See* Assessment
- Clinical description, 29–86
 cyclothymia and manic-depressive temperaments, 82–86
 depressive states, 65–72
 manic states, 32–65
 mixed states, 72–82
 overview, 29–32
- Clinical Global Impressions Scale for Bipolar Illness (CGI-BP), 375
- Clinical studies
 cyclothymia and manic-depressive temperaments, 84–86
 depressive states, 71–72
 level I randomized controlled, challenges in interpreting, 707–12, 707b, 708t
 manic states, 40–65
 mixed states, 78–82, 79t, 80t
 neurobiology constraints, 464–66, 466b
 signaling pathways, 539t
 suicide-oriented, 961
- Clinician-Administered Rating Scale for Mania (CARS-M), 361
- Clinician attitudes and expectations, psychotherapeutic issues, 880–81
- Clinician factors, in medication adherence, 865
- Clock-controlled genes, 660
- Clock genes, 660, 673, 689nn5–7, 690n15
- Clonazepam
 for acute hypomania, 728
 for acute mania, 723, 727, 742
 pharmacology, 719
- Clonidine, noradrenergic response, 479
- Cloninger's Temperament Character Inventory, 115n18
- Clozapine
 for acute mania, 727, 731t, 737, 738t, 746nn29–30
 in children and adolescents, 912, 918t, 927
 versus chlorpromazine, 736
 for maintenance treatment, 813, 841
 efficacy, 833t, 836, 847n77
 pretreatment evaluation and ongoing monitoring, 805t
 side effects, 807t
 side effects, 813
 for suicidal patient, 975
 weight gain from, 793n13, 813
- Coate, M., 39
- Cocaine
 abuse, 228, 230, 944
 sensitization to, 470, 472
- Codon, 423
- Cognition
 assessment. *See* Neuropsychological evaluation
 changes, mood change and, 403
 in depression, 66, 69–70, 71–72
 factors affecting, 305–13
 “hot,” 304–5
 in hypomania, 32–33
 impaired. *See also* Memory deficits; Thought disorder
 antidementia agents for, 847n76
 in children of bipolar parents, 207, 219
 chronicity/developmental effects, 309–10
 comparisons across domains, 302–4, 303f
 differential, establishment, 274
 genetic subtypes and, 434–35
 lithium effects, 275, 306–8, 306f, 307f, 807
 long-term outcome and, 144–45
 meta-analysis of findings, 275–305, 322nn3–4
 profile, 302–4, 303f
 psychotic features and, 308–9
 state dependency, 273–74
 structural brain abnormalities and, 310–13, 311f, 312f
 subcortical hyperintensities and, 619
 summary, 321
 topography, 302–4, 303f
 in mania, 33, 37–38, 43–53, 44t, 46t–48t, 49f, 50f, 51t
- Cognitive-behavioral therapy
 for anxiety disorders, 947, 948
 efficacy, 892t–895t, 899–900
- Cognitive speed, 283–85
- “Cognitive triad,” 899
- Cohort studies, prospective, 141–44, 142t, 153nn44–45
- Combination therapy
 generalizability, 710
 rational, versus irrational polypharmacy, 750
- Combinatory thinking, creativity and, 397
- Commitment laws, 722
- Communication
 patterns, in mania
 versus depression, 52–53, 53t
 versus schizophrenia, 51–52, 52f
 of suicidal intent, 953–54
- Communication enhancement training, in family/couples therapy, 902
- Community samples, treatment effectiveness, 701
- Community surveys
 with adults, 162–76
 with children and adolescents, 176–78, 177t
 methodological issues, 157–62
- Comorbidity, 223–45
 in adolescent-onset bipolar disorder, 202–3, 202t, 203t
 anxiety disorders, 233–39, 234t–236t, 238t, 946–48
 attention-deficit/hyperactivity disorder, 239
 cardiovascular disease, 146, 240, 949
 in childhood-onset bipolar disorder, 191–93, 192t, 193f, 203t
 diabetes, 243–44
 eating disorders, 239–40, 241t, 948–49
 medical conditions, 240–44, 949–51
 migraine, 244
 National Comorbidity Study, 156, 165, 166t, 167t, 176, 185–86n2, 223
 overview, 223–25
 overweight and obesity, 242–43, 949–50
 personality disorders, 240, 334–37, 335t, 949
 adolescent-onset, 202–3
 suicide and, 266, 269n16
 in triggering episodes, 138
 psychiatric disorders, 224f, 225–40
 signaling pathway abnormalities and, 598
 substance abuse, 225–33, 226t–229t, 937–46, 940t–942t
 suicide and, 266
 thyroid dysfunction, 241–42, 950–51
 treatment, 937–51
- Completer analysis, 711
- Complex Figure Test, 275, 275f, 301
- Complex genetic disorders, 430, 462nn11–12
- Compliance. *See* Medications, adherence
- Composers. *See also* Creativity
 biographical studies, 383–89, 384t–389t, 390f
- Composite International Diagnostic Interview (CIDI), 156, 160
 University of Michigan modification, 160
- Comprehensive Psychopathological Rating Scale (CPRS), 369
- Computed tomography
 versus magnetic resonance imaging, 611
 single photon emission
 of dopaminergic system, 485
 of serotonergic system, 495
- COMT gene, 444
- Concordance, 419

- Conduct disorder, 191, 192t, 202, 203
- Confidentiality, 887, 962
- Confounding bias, 710
- Confusion, in mania, 43, 44t
- Congenital malformations, medication-induced, 815, 817
- Conners' Abbreviated Parent Questionnaire, 376, 377t
- Consent, informed, 883, 885
- Constant routine sleep, 668, 691n38
- "Constitutional cyclothymic," 83–84
- Continuation treatment
in acute mania/hypomania and mixed states, 724–25
definition, 702–3, 797, 844n1
versus true prophylaxis, 800
- Continuous Performance Test (CPT), 289
- Contraception
carbamazepine and, 809, 810
oxcarbazepine and, 810
- Controlled oral word association (COWA) tests, 300–301
- CORE measure of psychomotor disturbance, 286–87, 286b
- Corpus callosum, size, 626
- Correlates of bipolar disorder
epidemiological, 181–85
medication adherence, 859t–860t, 863–65
neuroanatomical, 310–13, 311f, 312f, 610–11
neurobiological, 284–85
- Cortical sulcal prominence, 612f, 614, 615t, 616, 617
- Cortic limbic dysregulation model of depression, 632, 633f
- Corticotropin-releasing factor (CRF), 521, 523–24
hypersecretion, 524
stress-induced morphometric changes and, 526, 602n44
suicide and, 261
- Corticotropin-releasing factor (CRF) receptor antagonists, 524, 527–28, 591t, 787
- Corticotropin-releasing factor (CRF) stimulation test, 524
- Corticotropin-releasing hormone/
dexamethasone test, combined, 524–25, 602n41
- Cortisol
agents lowering, antidepressant effects, 787
hypersecretion, 243, 244, 494, 521
in urine, 477
- Costs of manic-depressive illness, 699–700, 719nn2–5
- Countertransference, 880
- Couples therapy, 887, 897t–898t, 902
- Course and outcome, 119–50
adolescent-onset bipolar disorder, 199–204
age at onset and, 125, 151nn13–16
anxiety disorders and, 234, 236
bipolar-II disorder, 146, 149
charting, 373–74, 373f
childhood-onset bipolar disorder, 196
in children of bipolar parents
controlled studies, 207–15, 209t–213t, 216b
parents' clinical and demographic features and, 219–20
episode characteristics. *See* Episodes
family/marital functioning and, 347–48
hypothyroidism and, 242
kindling or sensitization model, 128f, 129–31, 151–52nn22–28
long-term, 141–47, 153nn44–46
cognitive impairment and, 144–45
prospective cohort studies, 141–44, 142t, 153nn44–45
quality of life, 145
subsyndromal morbidity and chronicity, 145
manic versus depressive, 134
mechanisms of recurrence, 149
methodological issues, 119–20
mortality, 146, 147t–148t
patient education on, 883, 884f, 885f
personality and, 332–33
polarity, 133–35, 152–53nn33–36
premorbid functioning and, 120
psychotic symptoms and, 57
questions on, 748
social predictors, 341, 342t–343t
substance abuse and, 232–33
suicide and, 267–69, 268t
- Cox regression, 711
- CP-154, 526, 528
- CRA 1000, 528
- Creatine, magnetic resonance spectroscopy, 645–46
- Creatinine, level, lithium and, 807
- Creativity, 379–406
biographical studies, 383–89, 384t–388t, 390f
characteristics of illness and, 397–401, 398t, 399f, 400t
experiences derived from illness and, 401–2
family studies, 394–96, 395f, 395t, 396t
historical background, 379–81
lithium effects on, 308, 857
living writer and artist studies, 389–93, 391t, 392f–394f
in mania, 39
methodological issues, 381–83
during mood states, 400–401, 400t
positive aspects, importance of studying, 402–6
seasonal patterns, 393, 393f
- CREB. *See* cAMP response element binding protein (CREB)
- CREB₁ gene, 431
- Crepuscular rhythm, 659, 689n2
- CRF. *See* Corticotropin-releasing factor (CRF)
- Cronholm-Ottoson Depression Scale, 365
- Cross-National Collaborative Group, 156, 157, 157t, 165–67, 169t–172t, 171, 182–83
- Crossover research design, 707
- Crying, pathological, 316, 317f
- Cultural differences
bipolar disorder, 182–83
suicide, 262
- Cushing's disease, 521, 533
- Custance, John, 37, 38–39, 69
- Cycle acceleration, antidepressant-related, 750, 778–81, 779t, 780f
in children and adolescents, 930–31
- Cycle length (frequency of episodes), 128–33, 151–52nn22–31
age at onset and, 131, 152nn30–31
burnout and, 131
definition, 128
episode number and, 128–31, 128f, 151–52nn22–28
as familial trait, 128
rapid cycling pattern. *See* Rapid cycling
- Cyclic AMP. *See* cAMP entries
- Cyclicity, circadian rhythms and, 669. *See also* Circadian rhythm
- Cycloid personality, 82
- Cycloid psychosis, 107–8
- Cyclothymia, 87n25, 330
in children of bipolar parents, 214
classic clinical descriptions, 82–84
clinical studies, 84–86
DSM-IV diagnostic criteria, 98, 98b
in manic-depressive spectrum, 22, 23, 27n43
operational criteria, 84–85, 85b
predominantly depressed, 85
pure, 85
subtypes, 85
- Cyclothymic scale, 21–22
- Cyproterone acetate, 529
- Cytogenetics, 451
- Dacrystic epilepsy, 316, 317
- Darkness, bed rest and, for rapid cycling, 678, 693nn61–62, 843
- Death
causes, in Global Burden of Disease (GBD) study, 178, 179t
in manic-depressive illness, 146, 147t–148t
from suicide, impact on family and therapist, 965–66
- Deep white matter hyperintensities
in bipolar disorder, 618f, 619
in major depression, 310, 311f, 312f, 618–19, 618f
- Deficit states, mood disorders as, 313–14
- Dehydroepiandrosterone (DHEA)
antidepressant effects, 528, 787
hypomanic effects, 728
- Delirious depression, 68
- Delirious mania, 35–36, 722, 744n1
- Delirium
drug-induced, in elderly person, 815, 815f
DSM-IV diagnostic criteria, 109–10, 110b
- Delusions
assessment, 53
in bipolar disorder, 58, 59t
depressive, 67, 68, 71–72
hypochondriacal, 68
manic, 33, 54t–56t, 57–58, 59t
in mixed states, 80
suicide and, 267
- Dementia, DSM-IV diagnostic criteria, 110–12, 111b
- Dementia praecox. *See* Schizophrenia
- Demographic variables. *See* Epidemiology
- Denial
medication adherence and, 862
as psychotherapeutic issue, 874–75, 876
suicide and, 953–54
- Depressants, central nervous system, abuse, 228–29
- Depression. *See also* Bipolar depression;
Bipolar-unipolar distinction;
Depressive states; Major depressive disorder; Unipolar depression
animal models, 467–68

- Depression (*continued*)
 atypical, 17
 cerebral activity in, 629–37, 630f–634f
 childhood-onset, 190–91
 in children of bipolar parents, 207, 915
 chronic subsyndromal, 145, 149
 cognition in, 66, 69–70, 71–72
 cognitive-behavioral therapy for, 899
 delirious, 68
 double, 149
 excited, 74, 75t
 with flight of ideas, 76t
 functional neuroimaging studies in, 629–37, 630f–634f
 historical dichotomies, 8
 linguistic and communication patterns, 52–53, 53t
 mania as defense against, 326, 353n3
 morbidity, 700
 obesity and, 243
 phase-advance hypothesis, 669–70, 670f, 692n43
 recurrent brief, 23, 27n44
 seasonal rhythms, 680–81, 693–94nn67–70
 secondary, 21, 611
 self-perceptions during, 327–29, 328f
 suicide and, 263–64
 summer, 680
 vascular subtypes, 653
 winter, 665, 679, 758
- Depression Adjective Check Lists (DACL), 363
- Depression and Bipolar Support Alliance (DBSA), 978
 advance directives, 887b
 self-help groups, 887–88
- Depression and Related Affective Disorders Association (DRADA), 978
- Depression scales, 358–61, 360t, 366, 366f, 367f, 376–78
- Depressive-catastrophic reactions, during Wada procedure, 314
- Depressive insanity, 67–68
- Depressive mania, 40, 41t, 43, 74, 75t, 79
- Depressive mixed state, 14–15, 97, 98
- Depressive pseudodementia, 110–11
- Depressive states
 classic clinical descriptions, 65–68
 clinical studies, 71–72
 subjective experiences of patients, 68–71
- Depressive stupor, 68
- Depressive temperament, 82
- Dermatologic problems
 from carbamazepine, 810
 from lamotrigine, 811, 812f, 845nn27–28
 from lithium, 807, 844n14
 serious, risk, with anticonvulsants and antibiotics, 810t
- Descriptive epidemiology, 155
- Desipramine
 for bipolar depression, 759t, 760t, 768, 794n37
 switches with, 777–78
- Despair syndrome, in primate separation paradigm, 467
- Destabilizing factors, breakthrough symptoms from, 818–19
- Desynchronization hypothesis, circadian rhythm disturbances, 668–69
- Deterministic chaos model, 149
- Developmental effects, cognitive impairment and, 309–10
- Developmental issues, in childhood-onset bipolar disorder, 194–95
- Developmental tasks, dealing with, 879
- Dexamethasone, protein kinase C activity and, 548
- Dexamethasone/corticotropin-releasing hormone (DEX/CRH) test, 524–25, 602n41
- Dexamethasone suppression test (DST), 521–23
 somatostatin and, 533
 suicide and, 261
- Dextroamphetamine, for mania/ADHD, 928
- Diabetes, 243–44
 antipsychotic-related, 814, 846n36
 lithium and, 807–8
- Diagnosis, 89–114. *See also* Clinical description criteria for, 93–100. *See also* Diagnostic and Statistical Manual-IV (DSM-IV) criteria differential, 102–12. *See also* Differential diagnosis
 in epidemiologic studies, 157–58, 157t, 160
 future directions, 457
 issues
 age-specific, in epidemiologic studies, 158–59
 bipolar versus unipolar depression, 104–6, 104b, 115nn14–17
 childhood-onset bipolar disorder, 191–95, 907–8
 childhood-onset mania, 193–94
 hypomania, 12, 158
 suicide, 247–48
- Diagnostic and Statistical Manual-I (DSM-I), 90–91
- Diagnostic and Statistical Manual-II (DSM-II), 91
- Diagnostic and Statistical Manual-III-R (DSM-III-R), 91–92
- Diagnostic and Statistical Manual-IV (DSM-IV), 89, 90b
 limitations, 9, 91–92
 organization, 91–92, 91f
 revisions in, 92–93
- Diagnostic and Statistical Manual-IV (DSM-IV) criteria, 93–100
 application problems, 100
 bipolar disorder in children, 908
 bipolar-II disorder, 96, 96b, 114n7
 bipolar-NOS, 98–99
 cyclothymia, 98, 98b
 delirium, 109–10, 110b
 dementia, 110–12, 111b
 hypomania, 95–96, 95b
 major depressive disorder, 96, 97b
 mania, 93–95, 94b
 mixed states, 93, 96–98, 97b
 schizoaffective disorder, 99–100, 103b
- Diagnostic and Statistical Manual-V (DSM-V), 93, 94f
 “Diagnostic drift,” 846n52
- Diagnostic hierarchy concept, 107
- Diagnostic Interview for Genetic Studies (DIGS), 160
- Diagnostic Interview Schedule (DIS), 156, 160
 for Children (DISC), 377
- Diagnostic Inventory for Depression (DID), 363
- Diagnostic shifting, 92
- Diagnostic systems, development, 89–93
- Diet, as component of treatment, 705
- Differential diagnosis, 102–12, 703
 attention-deficit/hyperactivity disorder, 106–7
 borderline personality disorder, 108–9, 115n18
 brief psychotic disorder, 107, 107b
 cycloid psychosis, 107–8
 epilepsy, 111
 organic brain disorders, 109–12
 psychotic disorder-NOS, 108
 schizoaffective disorder, 102–4
 schizophrenia, 7–8, 102–4
 unipolar depression, 104–6, 104b, 115nn14–17
- Diffusion tensor imaging, of subcortical hyperintensities, 620–21
- Disability
 causes, in Global Burden of Disease (GBD) study, 178, 180, 180t
 in manic-depressive illness, 699–700
 Disability-adjusted life years (DALYs), 178
- Disappointment, as psychotherapeutic issue, 877
- DISC-1* gene, 451
- Disease burden
 bipolar disorder, 178, 180, 180t
 hippocampal atrophy and, 274
- Disease model, 8
- Disinhibition, in children of bipolar parents, 214
- Disruptive behavioral disorders, in adolescent-onset bipolar disorder, 203
- Distractibility. *See also* Attention and attention deficits
 assessment, 289
 in attention-deficit/hyperactivity disorder versus mania, 106
 in mania, 43, 44t
- Disulfiram, for alcohol abuse, 944
- Diuretics, lithium and, 804
- Divalproex. *See* Valproate
- Dm bipolar subgroup, 126
- DMI (depression-mania-interval) sequence, antidepressant-related switches and, 774, 776
- DMP696, 528
- DNA markers, microsatellite, 423, 424
- Docosahexaenoic acid (DHA), antidepressant effects, 791
- Donepezil, 498, 500
 for acute mania, 744
 for cognitive impairment, 847n76
- Dopamine agonists, for bipolar depression, 784–85
- Dopamine receptors, 444
- Dopaminergic system, 481–82, 484–88
 association studies, 438t–439t
 augmentation studies, 485–86
 carbamazepine and, 488
 catecholamine depletion strategies, 484
 CSF homovanillic acid levels, 482, 484
 lithium and, 486–87
 neuroreceptor imaging studies, 484–85
 protein kinase C activity and, 547
 seasonal affective disorder and, 685
 sleep and, 676
 summary of findings, 488, 488b–490b
 in switch process, 484
 valproate and, 487–88

- Dorsolateral prefrontal cortex. *See* Prefrontal cortex
- Double depression, 149
- Double Trouble in Recovery (DTR), 945
- Droperidol, intramuscular, 744n2
- Drosophila*, circadian cycle, 557, 560f–561f
- Drug abuse. *See* Substance abuse
- Drugs. *See* Medications
- DSM. *See* Diagnostic and Statistical Manual entries
- Duloxetine
for bipolar depression, 770
pharmacology, 718–19
- Dynorphin A, lithium and, 532, 603n49
- Dysphoric mania, 42f, 42t, 80, 97, 98, 782
- Early age at onset. *See also* Adolescent-onset bipolar disorder; Childhood-onset bipolar disorder
in alcoholism, versus adolescent-onset bipolar disorder, 938
genetics, 434
versus late, 124
in psychotic mania, 205
in recurrent depression, 431
suicide attempts and, 268–69
- Eating disorders, 239–40, 241t, 948–49
- Ebstein's anomaly, lithium and, 815
- Echo-plantar magnetic resonance spectroscopic imaging (EP-MRSI), for bipolar depression, 783
- Edmonton Survey of Psychiatric Disorders, 166
- Education. *See* Psychoeducation
- Educational level, bipolar disorder and, 182
- Effect-size estimates, 709
- Effortful processing, memory and, 296–98
- Eicopentanoic acid, suicide and, 254
- Elation. *See* Euphoria
- Elderly
bipolar disorder in, 159, 227, 283–85
circadian rhythm in, 670
depression in
 electroconvulsive therapy for, 758
 encephalomalacia and, 310–11, 312f
 maintenance treatment in, 814–15, 815f
- Electrocardiogram, lithium effects, 807
- Electroconvulsive therapy
for acute mania, 724, 731t, 742–43, 744n3
in children and adolescents, 912
anticonvulsant effect, 315
antidepressant effects, 314–15, 315f
for bipolar depression, 758, 782–83, 795n59
 plus lamotrigine, 764
cerebral activity and, 637
in childhood-onset bipolar disorder, 912, 933
learning and memory deficits, 295, 295f
for maintenance treatment, 841–42
for mixed states, 743
REM sleep and, 667
for suicidal depression, 960, 967
- Electroencephalography, sleep, 662–63, 691n29
- E.M. Power +, antidepressant effects, 792
- Emergency management of acute mania/hypomania and mixed states, 723
- Emotions
characteristics, 609, 610t
facial, activation studies, 628
- Encephalomalacia
in bipolar disorder, 312–13
in major depressive disorder, 310–12, 311f, 312f
- Endler, Norman, 874–75
- Endophenotype, 435, 465. *See also* Genetic subtypes
circadian/sleep disturbances, 666
SERT function, 496
as strategy, 435, 596, 597f
- P-Endorphin, antidepressant effects, 532, 603n47
- Energy loss, in depression, 69
- Environment-gene interactions, 457
- Environmental factors
in children of bipolar parents, 217–19, 218f
in medication adherence, 864–65
- Epidemiologic Catchment Area (ECA) study, 156, 163–65, 164t, 167t, 185–86n2
- Epidemiology, 155–85
alcohol abuse/dependence, 226–27, 226t, 227f
application to psychiatric disorders, 155–57
bipolar spectrum, 175–76, 176t
childhood- and adolescent-onset bipolar disorder, 204–5
in children of bipolar parents, 214–15
community surveys
 with adults, 162–76
 with children and adolescents, 176–78, 177t
correlates of bipolar disorder, 181–85
genetic, 413–22, 458–59
international comparisons, 165–67, 169t–173t, 171–75
medication adherence, 863
methodological issues, 157–62
 age at onset, 161–62
 age-specific diagnostic issues, 158–59
 diagnostic methods, 160
 functional impairment, 161
 incidence and prevalence rates, 161
 nonresponse or refusal to participate bias, 160
 sample size, 161
 variable diagnostic criteria, 157–58, 157t
substance abuse, 227–28, 228t
WHO studies, 178–81, 179t, 180t
- EPIDEP study, 31
- Epigenetic factors, 596–97
- Epilepsy
versus bipolar disorder, 111
dacrystic, 316, 317
gelastic, 316, 317, 317f
lithium-pilocarpine model of seizures, 502–3
- EPIMAN study, 31, 60
- Episodes
duration, 133
in children, 194
fetal and newborn risk during, 817b
first, in childhood-onset depression, 911
frequency. *See* Cycle length (frequency of episodes)
number, 126–28, 127t, 151nn17–21. *See also* Recurrence; Relapse
onset, 133
 polarity, 133–34
 pattern, 135
precipitants, 135–41, 138b
 drugs and medical conditions, 138–40, 139t–140t, 231–32
- life events, 135–38, 136t–137t
season, 140–41
sexual abuse, 153n42
sleep loss, 140, 883, 886f
stress, 870
- Epistasis, 427, 430
- Equilib, antidepressant effects, 792
- ERK MAPK signaling cascade
activation by lithium and valproate, 570–72, 571f
versus BDNF pathway, 583–84
- Estrogen
brain-derived neurotrophic factor and, 531
neuromodulatory effects, 530–31, 602–3n45
replacement, for bipolar depression, 788
- Ethnic differences
in adolescent-onset bipolar disorder, 198
in bipolar disorder, 182–83
in seasonal affective disorder, 682, 694n72
- Ethyl-eicosapentaenoate (EPA), antidepressant effects, 791
- Eugenics, 413
- Euphoria
addictive-like qualities, 403
in adolescent-onset bipolar disorder, 197
in childhood-onset bipolar disorder, 188, 189t
creativity and, 398, 398t
in mania, 37, 41t, 725, 725f
- Euthymic state, self-perceptions during, 328, 328f
- Evidence-based medicine, 706–7, 707b
- Evoked potential, P300, as endophenotype, 435
- Excited depression, 74, 75t
- Executive dysfunction
in bipolar disorder, 298–300, 299f, 300f
suicide risk and, 259
- Exercise
for bipolar depression, 758–59
as component of treatment, 705
- Exon, 423
- Experimental design, constraints for, 464–66, 466b
- Experimental epidemiology, 155
- Expert Consensus Guideline Series, 978
- Extracellular receptor-coupled kinase signaling pathway. *See* ERK MAPK signaling cascade
- Extrapyramidal side effects
atypical antipsychotics, 812–13, 845nn31–33, 848n90
typical antipsychotics, 720n18, 845n29
- Extraversion-introversion
bipolar-unipolar differences, 331
remitted bipolar patients and normal groups, 329–30
- Eysenck Personality Inventory (EPI), 329
- Facial emotion, activation studies, 628
- Factorial studies
of hypomania, 60, 64, 65t
of mania, 60, 63t–64t, 64–65, 65t
- Falret, Jean Pierre, 7, 32–33, 40, 73
- False unipolar depression, 14–15, 14t, 106, 133, 152–53nn33–34, 163
- Family
functioning
bipolar disorder and, 350–52
in children of bipolar parents, 217–19, 218f

- Family (*continued*)
 clinical outcome predictors, 347–48
 psychotherapeutic issues, 879
 impact of suicide on, 965–66
 involvement
 in diagnosis of bipolar disorder, 113
 in medication adherence, 852
 in suicide prevention, 964
 psychoeducation, 885–87, 902
 Family history
 age at onset and, 125, 150n11, 151n12
 bipolar disorder and, 185
 questions on, 749
 suicide risk and, 255, 256f
 Family studies
 associational, 436, 436f
 of creativity, 394–96, 395f, 395t, 396t
 of manic-depressive illness, 414–19, 415t–418t
 of schizophrenia and psychotic affective disorder, 432–33, 432t
 Family therapy, 887, 897t–898t, 902, 916, 933–34
 Fantastic melancholia, 67–68
 Fatty acids, omega-3. *See* Omega-3 fatty acids
 Fears
 irrational, in depression, 69–70
 of recurrence, 873, 879
 Fenfluramine
 for antipsychotic-related weight gain, 814
 challenge test, 493
 Fetal risks
 during affective episode, 817b
 from teratogens, 815–17, 816t, 817b, 817t
 Ficinus, Marsilius, 25n5
 Financial behavior, in mania, 39–40
 FIND approach to childhood-onset bipolar disorder, 910
 Fish oil
 antidepressant effects, 790–91, 795n68
 for maintenance treatment, 843
 Fitzgerald, F. Scott, 69, 70–71
 Flexibility of thought, creativity and, 397
 Florence, Italy study, 172, 173t, 174
 Fluency of thought, creativity and, 397
 Fluoxetine
 for bipolar depression, 759t, 767, 793n18
 lithium augmentation, 762
 for maintenance treatment
 in breast-feeding women, 818
 efficacy, 832t
 plus olanzapine, 781, 918t
 response to, baseline cerebral activity and, 637
 plus sleep deprivation therapy, 677
 Flupenthixol, for maintenance treatment, 833t, 836
 Fluphenazine, for acute mania, 723
 Fluvoxamine, pharmacology, 718
 Forced desynchrony sleep, 668, 691n37
 Forced swim test, 468
 Frontal lobe
 activation studies, 636
 activity in depression, 630–34, 630f–634f
 activity in mania, 638
 subcortical hyperintensities, 618, 621
 volumetric studies, 559–61, 565t, 621–22, 623f
 stress and, 525, 602n43
 Frustration, as psychotherapeutic issue, 877
 Functional impairment, 161, 699–700
 Functional neuroimaging studies. *See* Neuroimaging studies, functional
 Functional status assessment, in children of bipolar parents, 216b
 Furor, 4
 G protein signaling, 538, 540–41, 540f, 541t. *See also* G_s/cAMP-generating signaling pathway
 calcium abnormalities and, 550
 lithium and, 543, 604n59
 G-protein-coupled receptor kinase, dopamine and, 488
 G72/G30 genes, 445
 GABA (gamma aminobutyric acid)
 in cerebrospinal fluid, 504–5
 circadian rhythms and, 660
 magnetic resonance spectroscopy, 646–47
 in plasma, 505
 GABA synthetic enzymes, in postmortem brain, 505–6
 GABAergic system, 237, 503–8
 lithium and, 506–7
 regulatory processes, 504f
 summary of findings, 507–8, 508b
 valproate and, 507, 943
 Gabapentin
 for acute mania, 724, 735
 in children and adolescents, 927
 for anxiety disorders, 946, 947
 for bipolar depression, 754, 765, 794n28
 versus lamotrigine, 764
 for maintenance treatment, 835
 pharmacology, 717
 REM sleep and, 667
 Galantamine, for cognitive impairment, 847n76
 Galen of Pergamon, 4–5
 Gamma aminobutyric acid (GABA). *See* GABA (gamma aminobutyric acid); GABAergic system
 Garner, Alan, 69
 Gastric bypass surgery, 950
 Gastrointestinal effects
 lithium, 804
 valproate, 809
 Gelastic epilepsy, 316, 317, 317f
 Gender differences
 antidepressant-related cycling, 778
 antidepressant-related switches, 774
 bipolar disorder, 181
 cerebral metabolic rate for glucose, 627
 in children of bipolar parents, 214–15
 hallucinations, 60
 manic activity and behavior, 60
 mixed states, 80
 neuroimaging studies, 612
 polarity pattern, 134
 Gene, 413
 Gene-environment interactions, 457
 Gene expression, 447–52, 460
 in brain, 448–50, 449t
 future directions, 456–57
 sleep deprivation studies, 469–70
 testing gene- and allele-specific function, 451–52
 in white blood cells, 451
 Gene therapy, 457
 General Behavioral Inventory (GBI), 21–22, 27n40, 369–70, 370t, 372–73
 Genetic anticipation, 121, 446
 Genetic concerns
 in childhood-onset bipolar disorder, 910–11
 as psychotherapeutic issue, 873–74, 879–80
 Genetic counseling, 453–55, 460–61
 Genetic disorders, complex, 430, 462nn11–12
 Genetic engineering, 452
 Genetic heterogeneity, 430
 Genetic homogeneity, 456
 Genetic subtypes
 of bipolar disorder, 431–35
 age at onset, 125, 434
 bipolar-II as, 433–34
 cognitive impairment, 434–35
 comorbid attention-deficit/hyperactivity disorder, 434
 comorbid panic and anxiety disorders, 434
 psychosis, 431–33, 432t
 rapid cycling, 435
 of major depressive disorder, 430–31
 Genetics, 411–61, 595–96
 adoption studies, 421–22, 422t
 alternative genetic mechanisms, 460
 anticipation and trinucleotide repeats, 446
 parent-of-origin effect, 446–47
 alternative phenotypic definitions, 430–35, 459, 462nn13. *See also* Genetic subtypes
 association studies, 436–46, 437t–442t. *See also* Association studies
 endophenotype strategy, 435, 596, 597f
 epidemiological studies, 413–22, 458–59
 epigenetic factors, 596–97
 family studies, 414–19, 415t–418t
 future directions, 455–57, 461
 historical framework, 412–13
 linkage studies, 423–30. *See also* Linkage studies
 pitfalls, 458
 psychiatric, 413
 research directions, 455–57
 research sequence, 414f
 seasonal affective disorder, 684
 suicide risk, 255–59, 256f, 257t, 258t
 twin studies, 419–21, 420t–421t, 461n4
 Geniuses, 383. *See also* Creativity
 Genome, human, 422–23, 459
 Genome scans, 426, 428t
 Genomewide scan, 424–25
 Genomic imprinting, 447
 Genotype to phenotype pathway, 448f
 German school of psychiatric genetics, 413
 Glial cells
 pathology, 562–63
 subtypes affected, 563–64, 567
 Global Assessment of Functioning (GAF) scale, 375
 Global Burden of Disease (GBD) study, 178–80, 179t, 180t
 Global cerebral activity
 in depression, 629–30
 in mania, 638
 Global cerebral volumes, 626
 Global cortical gray matter volumes, 626
 Global intellectual functioning, 276–78, 277f
 Glucocorticoid receptor (GR), 452, 523
 Glucocorticoid receptor (GR) antagonists, 528–29, 591t, 787

- Glucocorticoids, 525–27
 hippocampal neurogenesis impairment and, 527
 protein kinase C activity and, 547–48
 stress-induced morphometric changes and, 526–27, 526f
- Glutamatergic system, 508–16
 as antidepressant target, 513–14, 514f, 515f
 carbamazepine and, 513
 hippocampal atrophy and, 510–11, 511f
 lithium and, 512–13
 magnetic resonance spectroscopy, 509–10, 647–48
 plasma and CSF glutamate levels, 508–9
 positron emission tomography, 510
 postmortem studies, 510–11, 511f
 regulatory processes, 508f–509f
 somatic treatments and, 511–12
 valproate and, 512, 513
- Glutamic acid decarboxylase (GAD), in postmortem brain, 506
- Glycogen synthase kinase-3 (GSK-3), as target, 557–59, 558f, 559b, 563f, 593t, 606nn72–74
- Glycogen synthase kinase-3 (GSK-3) inhibition circadian rhythm and, 557, 560f–561f, 692n49
 neuroprotective effects, 559b
- Glycogen synthase kinase-3-β, 244
- Goldstein-Scheerer Object-Sorting Test, 45
- Gonadal steroids
 monoamine oxidase inhibitors and, 531, 602–3n45
 neuromodulatory effects, 529–31
- Gorham Proverbs Test, 45
- Grandiose thoughts
 in childhood-onset bipolar disorder, 188, 189t
 in mania, 37–38, 43, 44t
- Gray matter volume, lithium and, 580, 581f
- Grief, in interpersonal and social rhythm therapy, 901
- Griesinger, Wilhelm, 7, 35
- Group therapy
 multifamily, 902–3
 for substance abuse, 945–46
- Growth hormone (GH), challenge studies, 479–80, 493, 501
- G_s/cAMP-generating signaling pathway, 538, 539t, 540–45, 540f, 541t
 antidepressants and, 544–45
 valproate and, 544
- GSK-3. *See* Glycogen synthase kinase-3 (GSK-3)
- Gynecological problems, from valproate, 809
- Hair loss
 from lithium, 807
 from valproate, 809
- Hallucinations
 assessment, 53
 in bipolar disorder, 58, 59t, 71
 depressive, 67, 68
 gender differences, 60
 manic, 54t–56t, 58–59, 59t
 in mixed states, 80
 suicide and, 267
- Haloperidol, for acute mania, 723, 727, 731t, 736–37, 740, 744n5
 versus amisulpiride, 741
- versus aripiprazole, 737, 741
 in children and adolescents, 912
 versus clonazepam, 742
 versus lorazepam, 742
 versus oxcarbazepine, 735
 plus phenytoin, 736
 versus risperidone, 740
- Hamilton Depression Inventory, 362–63
- Hamilton Depression Rating Scale (Ham-D), 25, 192, 364, 847n82
- Handedness, 286
- Handwriting, in mania, 34–35, 34f
- Haplotype, 445
- Harm avoidance
 bipolar-unipolar differences, 331
 suicide and, 262
- Hazard ratio, 711
- Health belief model of nonadherence, 862
- Hearing loss, nonsyndromic, 462n11
- Helplessness, learned, 467–68
- Hematologic monitoring, during carbamazepine treatment, 810
- Hepatic effects
 carbamazepine, 810
 valproate, 809
- Heterogeneity
 diagnostic and illness, 325
 genetic, 430
- High-risk studies, 206–20. *See also* Child, of bipolar parents
- Hippocampus
 atrophy, 622–25
 antidepressants and, 584
 burden of illness and, 274
 cellular mechanisms, 510–11, 511f
 duration of illness and, 567
 long-term outcome and, 144
 stress and, 510–11, 511f, 525, 602nn42–43
 glial cell pathology, 563
 neurogenesis
 with lithium and valproate, 576, 578–79, 578f
 reduced
 in pathophysiology of depression, 623–24
 stress and, 527
 regulation by antidepressants, 586–87, 588f, 589f
 shape, 624
- Hippocrates, 3, 25n3
- Historical roots of manic-depressive illness, 3–8
 Kraepelinian synthesis, 7–8, 25–26nn10–11
 nineteenth century ideas, 5, 7, 25n9
 post-Kraepelinian developments, 8, 26nn12–17
 pre-nineteenth century ideas, 3–5, 6b, 25nn2–8
- Histrionic personality disorder, 336
- Homelessness, bipolar disorder and, 183–84
- Homovanillic acid levels
 in cerebrospinal fluid, 482, 484
 lithium and, 487
 sleep and, 676
 valproate and, 487
- Hopelessness
 in depression, 71
 suicide and, 261–62, 957, 963
- Hormonal agents, for bipolar depression, 785–88
- Hormones. *See* Neuroendocrine systems
- Hospitalization
 in acute mania, 722–23, 912
- in bipolar depression, 749
 of children and adolescents, 912
 as marker of episode, 126, 151n20
 suicide after, 268
 for suicide prevention, 964–65
- HPA axis. *See* Hypothalamic-pituitary-adrenal (HPA) axis
- HPG (hypothalamic-pituitary-gonadal) axis, 788
- HPT (hypothalamic-pituitary-thyroid) axis, 241–42, 517–20, 520b, 785–87
- Human Genome Project, 423
- Humiliation, as psychotherapeutic issue, 874
- Humoral theory of mental disorders, 3, 5
- Hungary study, 172, 173t
- Huntington's disease, 282–83
- 5-Hydroxyindolacetic acid (5-HIAA)
 alcoholism and, 267
 carbamazepine and, 497–98
 in cerebrospinal fluid, 490–91
 lithium and, 496
 suicide and, 259
- Hyperactivity. *See also* Attention-deficit/hyperactivity disorder (ADHD)
 in adolescent-onset bipolar disorder, 197
 animal models, 469–70
 extreme, 725, 725f
 in hypomania, 96
- Hyperacusis, 399
- Hyperalert state, in mania, 39
- Hypercortisolemia, 243, 244, 494, 521
- Hypericum, antidepressant effects, 790
- Hyperintensities, subcortical, 310–13, 311f, 312f, 612f, 617–21, 618f
- Hypermethylation, 450
- Hypersomnia, 665, 667
- Hyperthymia, 85, 330
- Hyperthymic temperament, 22, 85–86
- Hyperthyroidism, 242, 517
- Hypofrontality, in depression, 630, 630f
- Hypoglycemia, reactive, 705
- Hypomania, 43. *See also* Manic states
 activity and behavior in, 39
 acute treatment, 727–28, 729f
 from atypical antipsychotics, 757, 793n12
 cerebral activity in, 638–39
 childhood-onset
 acute treatment, 911, 912, 914t, 917–28, 918t, 934n2
 comorbidity with ADHD, 191–93, 192t, 193f, 910, 911, 912–13, 915
 diagnostic issues, 193–94, 912–13
 features, 188, 189t
 cognition and perception in, 32–33
 creativity and, 397–402
 diagnostic criteria
 DSM-IV, 95–96, 95b
 variable, 157–58
 diagnostic issues, 12, 158
 duration threshold, 18–19
 dysphoric, 727
 factorial studies of, 60, 64, 65t
 familial vulnerability, 21
 hyperactivity in, 96
 mood in, 32
 positive aspects, 402–6, 857, 878
 pretreatment evaluation, 722
 recurrent brief, 23, 27n44, 175, 225

- Hypomania (*continued*)
 secondary, 109, 110b
 sleep in, 665–66
 structure, 60, 64, 65t
 “Hypomanic alert,” 133
 Hypomanic Personality Scale, 370–71, 373
 Hyponatremia, from oxcarbazepine, 734
 Hypothalamic-pituitary-adrenal (HPA) axis,
 520–29
 bipolar depression and, 787–88
 cortisol hypersecretion, 521
 CRF and, 523–24
 DST abnormalities, 521–23
 stress-induced morphometric changes and,
 525–27, 526f
 suicide and, 261
 summary of findings, 529, 530b
 as treatment target, 527–29
 Hypothalamic-pituitary-gonadal (HPG) axis, 788
 Hypothalamic-pituitary-thyroid (HPT) axis,
 241–42, 517–20, 520b, 785–87
 Hypothyroidism, 241, 242, 517, 950–51
 from lithium, 487, 518, 804, 806, 808, 842,
 845nn20–21, 932
 rapid cycling and, 242, 518, 951
- Icelandic study, 171, 173t
 Illness acceptance/denial, medication adherence
 and, 862
 Imaginal exposure therapy, for post-traumatic
 stress disorder, 948
 Imipramine
 for bipolar depression, 759t, 760t
 lithium augmentation, 762
 versus moclobemide, 767
 versus tranlycypromine, 766
 for maintenance treatment, efficacy, 833t
 Immune function, seasonal affective disorder
 and, 681–82, 694n68
 Imprinting, genomic, 447
 Impulsivity
 in mania, 94–95
 suicide risk and, 258
 Incidence rates
 in epidemiologic studies, 161. *See also*
 Epidemiology
 methodological issues, 155–62
 Income, bipolar disorder and, 182
 Informed consent, 883, 885
 Inhibited mania, 76t
 Inositol, antidepressant effects, 764, 791
 Inositol depletion hypothesis, 545, 546t, 550–53,
 553f, 604nn62–66
 Inositol monophosphatase (IMPase), 451
 Inpatient Multidimensional Psychiatric Scale, 365
 Insanity, depressive, 67–68
 Insight
 lack of, medication adherence and, 863–64
 nature of episode and, 876
 Insomnia
 breakthrough symptoms and, 819
 in childhood-onset bipolar disorder, 188, 189t
 in depression, 666–67
 suicide and, 266
 in triggering episodes, 140, 883, 886f
 Institutionalized samples, epidemiologic
 findings, 184
- Insulin resistance, from hypercortisolemia, 244
 Integrated Group Therapy (IGT), for substance
 abuse, 945–46
 Intellectual functioning
 fluid versus crystallized, 282
 global, 276–78, 277f
 Intelligence quotient (IQ)
 full-scale, 276–78, 277f
 verbal-performance discrepancy, 278–82,
 279f–281f
 Intensive clinical management (ICM), versus
 interpersonal and social rhythm
 therapy, 901–2
 Intent-to-treat analysis, 711
 Internal State Scale (ISS), 368–69
 International Classification of Diseases-6
 through 9 (ICD-6 through ICD-9),
 90–91
 International Classification of Diseases-10
 (ICD-10), 89, 90b, 92
 International epidemiological comparisons,
 165–67, 169t–173t, 171–75
 International Foundation for Research and
 Education on Depression (iFred), 978
 Internet educational material, 883
 Interpersonal functioning, 337–52
 family functioning, 350–52
 marriage, 343–50
 social functioning, 337–43
 Interpersonal therapy, 678, 693n63, 896t,
 900–902, 903
 Interviewers, lay, interpretative problems, 163
 Intron, 423
 Introversion-extraversion
 bipolar-unipolar differences, 331
 remitted bipolar patients and normal groups,
 329–30
 Inventory of Depressive Symptomatology
 clinician-administered (IDS-C), 364
 self-report version (IDS-SR), 363
 Inventory to Diagnose Depression, 363
 Ireland study, 173t, 174
 Irritability
 in adolescent-onset bipolar disorder, 197
 in childhood-onset bipolar disorder, 188
 in depression, 71
 in mania, 41t
 in mixed states, 80
 Irritable temperament, 83
 Israel study, 173t, 174
- James, William, 380
 Jaspers, K., 32, 74, 77
 Journal, 750, 793n4
 Juvenile Bipolar Research Foundation (JBRF), 978
- Kahlbaum, Karl Ludwig, 7
 Ketamine, 511–12, 513–14
 Ketoconazole, antidepressant effects, 787
 Khlebnikov, Velimir, 38
 Kiddie Schedule for Affective Disorders and
 Schizophrenia (KSADS), 159, 376
 Washington University version
 (WASH-U-KSADS), 159, 376
 Kindling or sensitization model, 128f, 129–31, 149,
 151–52nn22–28
 animal studies, 470–72
- behavioral sensitization in, 470
 extreme sensitization in, 472
 protein kinase C activity and, 547
 rapid cycling in, 131, 132f
 substance abuse in, 230–31
 Knockout/knockin mouse model, 452
 Korean Epidemiologic Study of Mental
 Disorders, 167
 Kraepelin, Emil
 on alcohol dependence in manic-depressive
 illness, 226
 biographical note, 24–25nn
 on depression, 66, 67–68
 as founder of German school of psychiatric
 genetics, 413
 on manic-depressive spectrum, 19–20
 on manic states, 32, 33, 34–35, 34f, 36–37, 40,
 57–58, 86n3, 380
 on mixed states, 73–74, 75t–76t, 96–97, 114n8
 Kraepelinian synthesis, 7–8, 25–26nn10–11
 Kraepelin’s classification of psychotic disorders,
 101, 101t
- Labiality of mood, in mania, 40–41, 41t
 Lamb, Charles, 380
 Lamotrigine, 511–12
 for acute mania, 735, 745n21
 in children and adolescents, 918t
 for anxiety disorders, 948
 for bipolar depression, 754, 759t, 763–64,
 794nn23–26
 in children and adolescents, 915, 929, 934n4
 versus olanzapine-fluoxetine combination,
 781
 for bipolar-II depression, 769b
 efficacy, strength of evidence, 838t
 for maintenance treatment, 811
 in bipolar-II disorder, 799
 in breast-feeding women, 818
 in children and adolescents, 916
 differential response, clinical characteristics
 associated with, 828t
 efficacy, 831–35, 832t, 834f, 847nn70–74
 in elderly person, 814–15
 plus lithium, 839
 versus lithium, 822–23
 in pregnancy, 816t, 817
 pretreatment evaluation and ongoing
 monitoring, 803t
 in rapid cycling, 832t, 834–35
 side effects, 807t, 811
 pharmacology, 717
 rash from, 811, 812f, 845nn27–28
 REM sleep and, 667
 Stevens-Johnson syndrome and toxic
 epidermal necrolysis risk, 810t, 932–33
 for substance abuse, 942t, 943, 944
 switches with, 764
 teratogenicity, 816t, 817
 Late age at onset, 124
 very, 124–25, 150n10
 Lateral ventricular enlargement, 612–17, 612f,
 615t
 Lateralization of brain damage, 316–18, 317f,
 610–11
 Latitude, seasonal affective disorder and, 682
 Laughing, pathological, 316, 317f

- Learned helplessness, 467–68
- Learning deficits, 291–98. *See also* Memory deficits
- Lecithin, for acute mania, in children and adolescents, 928
- Leucopenia, from carbamazepine, 810
- Leukocytes, gene expression in, 451
- Level I randomized controlled trials, challenges in interpreting, 707–12, 707b, 708t
- Levels of evidence, 706–7, 707b
- Levels of processing, memory and, 296–98
- Levetiracetam, for acute mania, 724, 736, 746nn23–24
- Liability threshold model, 421
- Life Chart Method (LCM), 373–74, 881–82
- Life events, in triggering episodes, 135–38, 136t–137t
- Life Goals Program, 903–4
- Lifestyle changes, 705
- Light
 - phase response curve, 661, 690n14
 - sensitivity to, 671–72
 - seasonal affective disorder and, 687–88
 - suicide and, 254
- Light therapy. *See* Phototherapy
- Limbic basal ganglia–thalamocortical circuits, 610, 610f
- Limbic regional cerebral blood flow (rCBF), 628–29, 629f
- Limit setting, 745n7
- Linguistic patterns
 - in mania versus depression, 52–53, 53t
 - in mania versus schizophrenia, 51–52, 52f
- Linkage disequilibrium studies, 445
- Linkage studies, 423–30, 459
 - affected sibling pair method, 426
 - complex disorders, 430, 462nn11–12
 - findings, 426, 427f
 - future directions, 455
 - LOD score approach, 425–26, 461–62n9
 - meta-analyses, 426–27, 428t
 - method, 423–25, 425f
 - promising chromosomal regions, 427–30, 427f
- Lithium
 - for acute hypomania, 728
 - for acute mania, 723, 725, 725f, 726, 740
 - plus carbamazepine, 733
 - in children and adolescents, 912, 917–23, 918t, 920t–922t, 934n2
 - versus clonazepam, 742
 - combination therapy, 928
 - dosages, 726
 - efficacy, 729–33, 730f, 730t, 731t, 732f
 - plus haloperidol, 733, 736
 - versus lamotrigine, 735
 - versus olanzapine, 739
 - versus oxcarbazepine, 735
 - plus quetiapine, 740
 - plus risperidone, 740
 - versus risperidone, 740
 - versus valproate, 734
 - versus verapamil, 743
 - plus ziprasidone, 741
 - adenyl cyclase and, 543–44, 604n60
 - adherence to, 849–68. *See also* Medications, adherence
 - for aggression, 913, 914t, 929
 - Bcl-2 overexpression, 572–74, 573f, 581, 583f
 - for bipolar depression, 751, 753, 759, 759t, 760t, 761–62
 - versus antidepressants, 759, 760t, 761, 761t
 - augmentation of antidepressants, 761–62, 762t, 793nn16–19
 - plus carbamazepine, 763
 - in children and adolescents, 911, 929
 - plus topiramate, 765
 - plus valproate, 763, 794n22
 - blood levels
 - in acute mania, 726
 - instant test, 804
 - in maintenance, 802, 804, 844n7
 - cardiovascular mortality and, 949
 - cholinergic system and, 502–3
 - chronobiological effects, 672–73
 - circadian rhythms and, 557, 562f
 - cognitive impairment from, 275, 306–8, 306f, 307f, 807
 - in comorbid conditions
 - anxiety disorders, 948
 - cardiovascular disease, 949
 - eating disorders, 949
 - substance abuse, 939, 940t, 941t, 943
 - creativity and, 403–5, 405f, 405t
 - CREB and, 543
 - dermatologic problems from, 807, 844n14
 - diabetes and, 243–44
 - discontinuation
 - relapse after, 824–25
 - suicide risk after, 971
 - dopaminergic system and, 486–87
 - effects on normal mood, 824
 - efficacy, strength of evidence, 838t
 - G protein signaling and, 543, 604n59
 - GABAergic system and, 506–7
 - glucocorticoids and, 494
 - glutamate and, 512–13
 - hippocampal neurogenesis with, 576, 578, 578f
 - historical perspective, 798
 - for hyperkinesia in children of bipolar parents, 930
 - hypothyroidism from, 487, 518, 804, 806, 808, 842, 845nn20–21, 932
 - inositol-deficient diet and, 732–33
 - intoxication, 808–9
 - intrinsic qualities, adherence and, 865
 - magnetic resonance spectroscopy, 651–52, 652f
 - maintenance. *See* Lithium maintenance
 - marital functioning and, 349–50
 - for mixed mania, 725, 725f
 - monitoring, 716, 720nn15–16, 726
 - as “mood normalizer,” 798
 - neuroprotective effects, 557, 574–75, 574b, 575f, 581, 606–7n82
 - neurotrophic effects, 580, 580f–582f, 586b, 587–89
 - norepinephrine and, 480
 - opiates and, 532, 603n49
 - personality and, 333–34
 - pharmacogenetics, 453
 - pharmacology, 715–16
 - phosphoinositide cycle and, 550–53, 553f, 604nn62–66
 - precautions/medical issues, 753
 - productivity and, 404, 405t
 - prophylaxis. *See* Lithium maintenance
 - protein kinase C and, 554, 554f
 - psychopharmacological revolution initiated by, 699, 719n1
 - REM sleep and, 667
 - renal effects, 807–8, 844nn15–19
 - responsiveness to
 - as endophenotype, 435
 - offspring studies, 215, 219
 - retinal ganglion cell axon regeneration with, 576, 577f
 - serotonergic system and, 496–97
 - sexual behavior and, 349
 - side effects, adherence and, 862–63
 - plus sleep deprivation therapy, 677
 - suicide and, 254, 762
 - teratogenicity, 815, 816t
 - vasopressin and, 533
 - weight gain from, 806, 844nn11–12, 932
- Lithium maintenance, 802, 804, 806–9
 - plus anticonvulsants, 839, 848nn87–88
 - plus antidepressants, 839, 840t, 841
 - plus antipsychotics, 841
 - blood levels, 802, 804, 844n7
 - breakthrough depression on, 750
 - in breast-feeding women, 817–18, 846n45
 - versus carbamazepine, 830–31, 831f
 - in children and adolescents, 911, 916, 929–30
 - differential response, clinical characteristics
 - associated with, 828t
 - efficacy, 819–29, 832t, 833t
 - in bipolar-II disorder, 828, 829t
 - contemporary studies using lithium as comparator, 821–23, 846nn49–52
 - placebo-controlled studies prior to 1980, 820–21, 821f
 - predictors, 825, 827–28, 828t, 846nn56–59
 - in rapid cycling, 825–27, 826t–827t
 - in recurrent unipolar depression, 800, 828–29
 - renewed controversies, 821–23
 - in treating mania versus depression, 823–24
 - in elderly person, 814–15
 - versus lamotrigine, 831–34, 834f
 - versus olanzapine, 837
 - perceived losses associated with, 877–78
 - in pregnancy, 815, 816t
 - pretreatment evaluation and ongoing monitoring, 803t
 - recurrence rate bias, 126, 128
 - side effects, 804, 806–8, 807t
 - before sleep deprivation, 789
 - for suicide prevention, 960, 967–71, 968f, 969f, 970t, 972–73, 976n5
 - toxicity treatment, 808–9
 - versus valproate, 829–30
- Living alone, medication adherence and, 864
- Localization of mood systems, brain functional asymmetry and, 318–20
- Locomotor activity, baseline, 469
- LOD score approach, linkage studies, 425–26, 461–62n9
- Lofepramine, for bipolar depression, 762
- Logan, Joshua, 875, 879
- Lombroso, C., 383
- Longitudinal Interval Follow-Up Evaluation (LIFE), 373

- Lorazepam
for acute mania, 723, 727, 742
versus clonazepam, 742
versus olanzapine, 739
pharmacology, 719
- Low-resolution electromagnetic tomography (LORETA), 691n55
- Lowell, Robert, 401, 402, 874, 875, 879
- Lunar cycles, suicide and, 253
- Lysergic acid diethylamide (LSD), as precipitant, 231
- Magnesium sulfate, for acute mania, 743
- Magnetic resonance imaging
in adolescent-onset bipolar disorder, 204
versus computed tomography, 611
functional, in psychomotor retardation, 284
hyperintensities, 310–13, 311f, 312f, 612f, 617–21, 618f. *See also* Encephalomalacia
- Magnetic resonance spectroscopy
N-acetylaspartate, 639–41
choline, 501, 641–43
creatine, 645–46
echo-planar, for bipolar depression, 783
GABA, 646–47
glutamatergic system, 509–10, 647–48
lithium, 651–52, 652f
myoinositol, 644–45
phosphorous (³¹P), 648–51, 651f
proton (¹H), 639–48
- Maintenance treatment, 797–844
for bipolar depression, efficacy of antidepressants, 770–71, 794nn38–41
breakthrough symptom management, 818–19
in breast-feeding women, 817–18
in children and adolescents, 911–12, 915–16, 929–30
clinical management, 798–819
complex regimens, 839–41
definition, 703, 797
in elderly person, 814–15, 815f
generalizability of research, 709–10
guidelines, 800, 801b
medications for
adverse effects, 807t
combination, 839–41, 840t
efficacy tables, 832t, 833t, 838t
prescription data, 801
review of literature, 819–43
selection, 801–14
teratogenicity, 815–17, 816t, 817b, 817t
overview, 798–800
perceived losses associated with, 877–78
in pregnancy, 815–17, 816t, 817b, 817t
pretreatment evaluation and monitoring, 803t–806t
psychotherapy in, 869–905. *See also* Psychotherapy
in rapid cycling, 826t–827t
successful, resources for, 800–801
transition to, in acute mania/hypomania and mixed states, 724–25
- Major depressive disorder. *See also* Bipolar-unipolar distinction; Unipolar depression
in children of bipolar mothers, 207
cholinergic sensitivity, 524
DSM-IV diagnostic criteria, 96, 97b, 247
encephalomalacia in, 310–13, 311f, 312f, 618f, 619
family studies, 416t–417t, 418
gender-specific, 431
genetic subtypes, 430–31
recurrent, early onset, 431
sleep in, 666–67
twin studies, 419, 420t–421t
- Malformations, congenital, medication-induced, 815, 817
- Managed care constraints, 704, 720n9
- Mania. *See also* Hypomania; Manic states
acute treatment
in children and adolescents, 911, 912, 914t, 917–28, 918t, 934n2
clinical features modifying, 725–26, 725f
clinical management, 721–28
continuation treatment and transition to maintenance therapy, 724–25
emergency management, 723
hospitalization, 722–23
initial behavioral stabilization, 723–24
medical, 721–44
medication dosages and therapeutic monitoring, 726–27
mood stabilization, 724
pretreatment evaluation, 722
psychological issues, 728
recommendations, 729f
review of literature, 729–44, 730f, 730t, 731t, 732f
adolescent-onset, 197–98
animal models, 469–70
from atypical antipsychotics, 757, 793n12
Bell's, 35–36
cerebral activity in, 638–39
childhood-onset
acute treatment, 911, 912, 914t, 917–28, 918t, 934n2
comorbidity with ADHD, 191–93, 192t, 193f, 910, 911, 912–13, 915
diagnostic issues, 193–94, 912–13
features, 188, 189t
chronic, 36–37
cognitive-behavioral therapy, 899
delirious, 35–36, 722, 744n1
depressive, 40, 41t, 43, 74, 75t, 79
DSM-IV diagnostic criteria, 93–95, 94b
dysphoric, 782
euphoric versus mixed, 725, 725f
versus hypomania, 95–96
incidence, after puberty, 176, 186n7
induction, with antidepressants
in DSM-IV, 93
substance abuse and, 233, 245n3
with poverty of thought, 75t
primacy, 15
prodromal symptoms, 886
psychoanalytic perspective, 326, 353n3
psychotic. *See* Psychosis/psychotic symptoms, in mania
pure, 13–14, 32, 94
versus schizophrenia or schizoaffective disorder, 103, 114–15n13
seasonal rhythms, 681
secondary, 21, 109, 110b, 611
sleep deprivation therapy and, 675, 677
sleep in, 665–66
sleep loss as precipitant, 140, 883, 886f
stages, 41–42, 42f, 42t, 86n3
structure, 60, 63t–64t
temporal variations, 181
unipolar, 13–14, 26nn26–27
vascular subtypes, 653
- Mania scales, 358–61, 360t, 366, 366f, 367f, 376, 377t
- Manic-depressive spectrum
emergence, 19–24, 23f
epidemiologic studies, 175–76, 176t
illustration, 22–23, 23f
incidence, 12
proposed definition, 20, 20b
“soft,” 175
comorbidity, 224–25
- Manic-depressive temperament, 82–86. *See also* Cyclothymia
- Manic Depressiveness Scale, 371
- Manic Diagnostic and Severity Scale (MADS), 361
- Manic State Rating Scale (MSRS), 359, 360t
- Manic states
chronic subsyndromal, in children, 145
classic clinical descriptions, 32–37
clinical studies, 40–65
self-perceptions during, 327–29, 328f
subjective experiences of patients, 37–40
- Manic stupor, 76t, 77
- Manic temperament, 22, 82–83
- MAOIs. *See* Monoamine oxidase inhibitors (MAOIs)
- MAP kinase. *See* Mitogen-activated protein (MAP) kinase *entries*
- Marijuana abuse, 229, 233
- Marital functioning
assortative mating and, 349
bipolar disorder and, 344–47
clinical outcome predictors, 347–48
and risk to children of bipolar parents, 217–18
sexual behavior, 348–49
treatment effects, 349–50
unipolar depression and, 343–44
- Marital status
bipolar disorder and, 183
medication adherence and, 864
- Maternal deprivation paradigm, 467
- Mating, assortative, 349
- Md and mD bipolar subgroups, 12, 126
- MECA (Methods for the Epidemiology of Child and Adolescent Mental Disorder) study, 156, 176–77
- Meclobemide, for bipolar depression, 759t
- Medial frontal gyrus, activation studies, 628
- Medical adverse events, in childhood-onset bipolar disorder, 932–33
- Medical Care Outcomes Study (MOS) Screener, 363
- Medical classification models, categorical versus dimensional, 20
- Medical conditions
comorbid, 240–44, 949–51
in triggering episodes, 138, 139t–140t
- Medical pretreatment evaluation. *See* Pretreatment evaluation

- Medications. *See also* Pharmacotherapy
- adherence, 849–68
 - breakthrough symptoms and, 818
 - clinical management, 850–52
 - clinician attitudes, 850–51
 - definitions, 854
 - empirical correlates, 859t–860t, 863–65
 - factors associated with, 852, 853t
 - measurement, 855
 - psychotherapy, 852, 865, 866t–867t, 870, 889
 - rates, 855–57, 856t
 - reasons for nonadherence, 857–63, 859t–860t, 861f
 - review of literature, 852–65
 - in schizophrenia, 853–54, 854b
 - self-help groups, 852, 888
 - side effects and, 862–63
 - substance abuse and, 233
 - suggestions for facilitating, 851–52, 851b
 - dosages, in treatment of acute mania/hypomania and mixed states, 726–27
 - rational development, 457
 - in triggering episodes, 138–40, 139t–140t
- Medscape Psychiatry & Mental Health, 978
- Melancholic patients, psychomotor disturbance, 283, 286–87
- Melancolie anxieuse, 73
- Melatonin
 - for acute mania, in children and adolescents, 928
 - circadian rhythms and, 660
 - phase response curve, 661
 - secretion
 - antidepressants and, 673
 - in bipolar disorder, 671
 - light sensitivity, 671
 - seasonal rhythms, 680, 694n69
- Melatonin duration hypothesis, in seasonal affective disorder, 685–86, 695n79
- Memantine, 514
- Memory deficits, 291–98
 - bipolar-unipolar differences, 274–75, 275f
 - lithium-induced, 306–7, 307f, 322n22
 - long-term, 294–95, 295f, 296f
 - mediational processes, 295–98
 - attention, effort, and levels of processing, 296–98
 - mood congruence, 298
 - storage versus retrieval, 295–96
 - short-term, 293–94, 294f
- Men. *See* Gender differences
- Mendelian traits, 412–13
- Menopause, bipolar disorder and, 184
- Mental health services, rate of use, 164–65
- Meta-analysis of research, limitations, 710
- Meta-regression, 710
- Metabolic syndrome
 - from atypical antipsychotics, 813, 845–46n35
 - drug-induced, 243
- Methylphenidate
 - for bipolar depression, 785
 - for maintenance treatment, 843
 - for mania/ADHD, 928
- Metyrapone, 529
- Meyer, Adolph, 8, 26n12
- MHPG (3-methoxy-4-hydroxy-phenylglycol)
 - in cerebrospinal fluid, 475–76
 - in plasma, 473, 475
 - in postmortem brain, 476
 - in urine, 476–77
- Microarray studies, 450
- Microsatellite DNA markers, 423, 424
- Mifepristone (RU-486), antidepressant effects, 528–29, 787
- Migraine, 244
- Mineral supplements, antidepressant effects, 792
- Mineralocorticoid receptor (MR), 523
- Minnesota Multiphasic Personality Inventory (MMPI), 327, 327f
- Mirror-image studies, 846n48
- Mirtazapine
 - for bipolar depression, 762
 - for suicidal patient, 967
- Mitochondrial dysfunction, neurotrophic signaling-mediated, 568–70
- Mitochondrial inheritance, 446–47
- Mitogen-activated protein (MAP) kinase phosphatase inhibitors, 593t
- Mitogen-activated protein (MAP) kinase signaling cascade, neurotrophins and, 570–72, 571f
- Mixed states
 - acute treatment, 725, 725f
 - adolescent-onset, 198
 - antidepressant-related switches, 776, 974
 - antipsychotics in, 782
 - childhood-onset, 196
 - classic clinical descriptions, 72–77
 - clinical studies, 78–82, 79t, 80t
 - definition, 72
 - depressive, 14–15, 97, 98
 - DSM-IV diagnostic criteria, 93, 96–98, 97b
 - electroconvulsive therapy for, 743
 - Kraepelin's classification, 73–74, 75t–76t, 96–97, 114n8
 - pretreatment evaluation, 722
 - versus pure mania, 94
 - rates, 78, 79t
 - versus schizophrenia or schizoaffective disorder, 103
 - serotonergic system in, 491
 - subjective experiences of patients, 77–78
 - substance abuse and, 232
 - suicide and, 263, 269n11, 957–58, 959–60
 - symptoms, 79–80, 80t
- MK-801, 513
- MK-869, 533–34, 591t
- Moclobemide, for bipolar depression, 767, 794n33
- Modafinil, for bipolar depression, 785
- Mode of inheritance models, 418–19
- Modified Manic Rating Scale (MMRS), 359
- Monitoring
 - hematologic, during carbamazepine treatment, 810
 - lithium, 716, 720n15–16, 726
 - in maintenance treatment, 803t–806t
 - in treatment of acute mania/hypomania and mixed states, 726–27
- Monoamine metabolism, association studies, 439t–440t
- Monoamine oxidase A (MAOA) gene, 443
- Monoamine oxidase inhibitors (MAOIs)
 - augmentation with, 485–86
 - for bipolar depression, 755–56, 766–67
 - lithium augmentation, 761, 793n17
 - gonadal steroids and, 531, 602–3n45
 - pharmacology, 717–18
- Montgomery-Asberg Depression Rating Scale (MADRS), 364, 365, 750
- Mood
 - cerebral activity and, 637
 - characteristics, 609, 610t
 - cognitive effects on, 403
 - creativity and, 400–401, 400t
 - cycles and fluctuations, treatment
 - considerations, 749–50
 - in depression, 66, 68–69, 71
 - elevation
 - in borderline personality disorder, 108
 - nonadherence and, 863
 - in hypomania, 32
 - learning to discriminate, 879
 - in mania, 32, 37, 40–43, 41t
 - in movement disorders, 282–83
 - self-perceptions, 327–29, 328f
- Mood chart, 750, 793n4, 844n6, 881–82, 882f
- Mood congruence effects, 298, 305
- Mood Disorder Questionnaire (MDQ), 105–6, 115n15, 175, 371
- Mood disorders
 - as deficit states, 313–14
 - diagnostic classification systems, 89–93, 90b, 91f
 - DSM-IV diagnostic criteria, 93–100
 - neuropsychological conceptualizations, 313–21
 - personality and, 324–25
 - proposed classification, 93, 94f
 - release model, 314–15, 315f
 - sleep disturbances in, time course, 664–65
 - substance abuse and, 226–27, 226t, 227f
- Mood Garden, 978
- Mood morbidity, 795n55
- “Mood normalizer,” lithium as, 798
- Mood stabilization, in acute mania/hypomania and mixed states, 724
- Mood stabilizers. *See also* Carbamazepine; Lamotrigine; Lithium; Oxcarbazepine; Valproate
 - adherence to, 849–68, 856t
 - antidepressant-related cycling and, 780, 780f
 - antidepressant-related switches and, 774, 795n48
 - chronobiological effects, 672–73
 - definition, 797
 - efficacy, strength of evidence, 838t
 - for maintenance treatment
 - breakthrough depression on, 750
 - in children and adolescents, 916, 929–30
 - differential response, clinical characteristics associated with, 828t
 - pretreatment evaluation and ongoing monitoring, 803t–804t
 - in recurrent unipolar depression, 800
 - perceived losses associated with, 877–78
 - REM sleep and, 667
 - for substance abuse, 939–44, 940t–942t
 - U.S. prescribing patterns, 714b
 - weight gain from, 243
- Mood systems, localization of, brain functional asymmetry and, 318–20

- Moore, Thomas, 400–401
- Mortality rates in manic-depressive illness, 146, 147t–148t
- Motor abnormalities, 285–86, 285f. *See also* Psychomotor functioning
- Motor activity, spontaneous, 286–88, 286b
- Motor speed
- disturbances, 283–85
 - lithium effects, 306, 306f
- Mouse model, 452
- Movement disorders, mood disturbances in, 282–83
- MRI. *See* Magnetic resonance imaging
- MRS. *See* Magnetic resonance spectroscopy
- Multifamily psychoeducation, 902, 903
- Multiple Visual Analog Scales of Bipolarity (MVAS-BP), 359–60
- Multiplicative multilocus model, 419
- Munich Follow-up Study, 167
- Muscarinic agonists, 500
- Muscarinic receptors, lithium and, 502
- Myoinositol, magnetic resonance spectroscopy, 644–45
- Naloxone, antimanic effects, 532, 603n46
- Naltrexone, for alcohol abuse, 944
- National Alliance for Research on Schizophrenia and Depression (NARSAD), 978
- National Alliance on Mental Illness (NAMI), 978
- National Comorbidity Study (NCS), 156, 165, 166t, 167t, 176, 185–86n2, 223
- National Institute of Mental Health (NIMH), 978
- National Institute on Alcohol Abuse and Alcoholism (NIAAA), 978
- National Institute on Drug Abuse, 978
- National Mental Health Association (NMHA), 978
- National Suicide Prevention Lifeline, 979
- Naturalistic studies, 706
- Nefazodone
- for bipolar depression, 770
 - pharmacology, 719
 - for suicidal patient, 967
- Negative affectivity, 326
- Negative self-esteem, 899
- Neonate
- lithium toxicity in, 815
 - risk to, during affective episode, 817b
- Nephropathy, lithium, 807–8, 844nn15–19
- Netherlands study, 173t, 174
- Neuroanatomical correlates, 310–13, 311f, 312f, 610–11
- Neurobiology, 463–601
- animal models, 466–73
 - of bipolar disorder, 468–73
 - of depression, 467–68
 - constraints for clinical studies, 464–66, 466b
 - correlates, 284–85
 - levels of analysis, 464, 465f
 - suicide, 254, 259–62
- Neurochemistry
- dopaminergic system, 484–85
 - psychomotor retardation, 284
 - serotonergic system, 494, 495
 - specific, 639–52. *See also* Magnetic resonance spectroscopy
- Neurodevelopmental aspects, in
- adolescent-onset bipolar disorder, 203–4
- Neuroendocrine systems, 516–29
- combined dexamethasone/corticotropin-releasing hormone test, 524–25, 602n41
 - corticotropin-releasing factor, 521, 523–24
 - dexamethasone suppression test, 521–23
 - glucocorticoids and, 525–27
 - gonadal steroids, 529–31
 - HPA axis, 520–29, 530b
 - HPT axis, 517–20, 520b
 - stress and, 525–27, 526f
 - thyrotropin-releasing hormone, 519–20
 - as treatment targets, 527–29
- Neuroimaging studies. *See also* Computed tomography; Magnetic resonance imaging; Positron emission tomography; *specific anatomical locations*
- in affective processing, overview, 609–11, 610f
 - age and, 611–12
 - age at onset and, 612
 - executive function, 300
 - functional, 627–52, 653, 653b
 - baseline markers of treatment response, 637–38
 - in depression, 629–37, 630f–634f
 - in healthy subjects, 627–29, 629f
 - in mania, hypomania, and rapid cycling, 638–39
 - mood state effects, 637
 - in psychomotor retardation, 284
 - of sleep, 664, 691n27
 - of specific cerebral neurochemistry, 639–52. *See also* Magnetic resonance spectroscopy
 - treatment effects, 637
 - future directions, 653–54
 - gender and, 612
 - MRI versus CT, 611
 - sleep deprivation therapy, 676
 - structural, 611–27, 626t, 652–53
 - subcortical hyperintensities, 310–13, 311f, 312f, 612f, 617–21, 618f
- Neurokinin-1 (NK-1) antagonists, 533–34, 591t
- Neuroleptic drugs. *See* Antipsychotics
- Neuropeptide Y (NPY), 534–35
- Neuropeptide Y (NPY) receptor agonists, 591t
- Neuropeptides, 531–36. *See also individual neuropeptides*
- Neuroplasticity. *See* Cellular plasticity cascades
- Neuroprotective effects
- Bcl-2, 572
 - glycogen synthase kinase-3 (GSK-3) inhibition, 559b
 - lithium, 557, 574–75, 574b, 575f, 581, 606–7n82
- Neuropsychological burden, documentation, 274–75
- Neuropsychological evaluation, 273–305
- attention, 289–91, 290f, 291f
 - contributions, 273–75
 - executive functions, 298–300, 299f, 300f
 - global intellectual functioning, 276–78, 277f
 - learning and memory, 291–98
 - long-term memory, 294–95, 295f, 296f
 - mediational processes, 295–98
 - short-term memory, 293–94, 294f
 - psychomotor functioning, 282–89
 - cognitive and motor speed, 283–85
 - motor skills, 285–86, 285f
 - speech rate, 288–89
 - spontaneous activity, 286–88, 286b
 - verbal and performance IQ, 278–82, 279f–281f
 - verbal and visuospatial skills, 300–302, 301f, 302f
- Neuropsychology, 273–321. *See also* Cognition and conceptualization of mood disorders, 313–21
- normal findings in bipolar patients, 321
- Neurotensin, 535
- Neuroticism
- bipolar-unipolar differences, 330
 - during remission, 326
 - remitted bipolar patients and normal groups, 329
 - vulnerability and, 333
- Neurotransmitter system(s), 473–536
- cholinergic, 498, 500–503, 503b
 - circadian rhythms and, 660
 - dopaminergic, 481–82, 484–88, 488b–490b
 - GABAergic, 503–8, 504f, 508b
 - glutamatergic, 508–16, 508f–509f, 511f, 514f–515f, 516b
 - gonadal steroids, 529–31
 - neuroendocrine systems, 516–29
 - neuropeptides, 531–36
 - noradrenergic, 473–81, 474f, 482b, 483b–484b
 - seasonal affective disorder and, 684–85
 - serotonergic, 490–98, 492f, 498b–500b
 - sleep and, 663–64, 691n26
- Neurotrophic effects
- antidepressants, 582f, 584, 584b, 586, 587f
 - lithium, 580, 580f–582f, 586b, 587–89
 - valproate, 587–89
- Neurotrophic signaling cascades, 568–70, 606n78
- Neurotrophins. *See also specific agents, e.g.,*
- Brain-derived neurotrophic factor (BDNF)
 - MAP kinase signaling cascade and, 570–72, 571f
- New Haven Survey, 162
- Newcastle Rating Scales, 365
- NIMH prospective Life Chart Method (NIMH LCM-p), 881–82
- Nimodipine
- for acute mania, 743
 - in children and adolescents, 928
 - for maintenance treatment, 842
 - response to, baseline cerebral activity and, 637
- NMDA receptor(s), 510
- NMDA receptor antagonists, 513–14, 514f, 515f, 592t, 602n32
- Nomifensine, 486
- Nonadherence. *See* Medications, adherence
- Nonresponse bias, in epidemiologic studies, 160
- Noradrenergic system, 473–81
- Norepinephrine, 473–81
- adrenergic receptor studies, 478–79
 - association studies, 439t
 - carbamazepine and, 481
 - catecholamine depletion challenges, 480
 - in cerebrospinal fluid, 475–76
 - lithium and, 480
 - pharmacological challenge strategies, 479–80

- in plasma, 473, 475
- in postmortem brain, 476
- regulatory processes, 474f
- seasonal affective disorder and, 685
- suicide and, 261
- summary of findings, 481, 482b–484b
- treatment targets, 590t
- in urine, 476–78
- valproate and, 481
- Norepinephrine reuptake inhibitors, selective, 718–19, 770
- Norepinephrine/serotonin reuptake inhibitors, 769–70
- Norfluoxetine, 718
- Normetanephrine, in urine, 477
- Norway study, 173t, 174
- Nottingham, England study, 173t, 174
- Novelty seeking
 - bipolar-unipolar differences, 331
 - suicide and, 262
- Nutritional psychiatry, 792
- Nutritional supplements
 - for bipolar depression, 790–92
 - for maintenance treatment, 843
- Obesity, 242–43, 949–50. *See also* Weight gain
- Observational studies, 706
- Observer rating scales
 - advantages and disadvantages, 357–58
 - depressive symptoms, 363–65
 - manic states, 359–61, 360t
- Obsessive-compulsive disorder, 234, 237–38, 947
- Off-on, on-off research designs, 707, 708t
- Offspring studies, 206–20. *See also* Child, of bipolar parents
- Olanzapine
 - for acute mania, 723, 725, 727, 730f, 730t, 731t, 738–39, 738t, 746nn31–36
 - in children and adolescents, 918t, 927, 928
 - versus haloperidol, 736–37
 - for anxiety disorders, 947
 - for bipolar depression, 756–57, 759t, 781
 - for eating disorders, 949
 - efficacy, strength of evidence, 838t
 - plus fluoxetine, 781, 918t
 - intramuscular formulation, 739
 - for maintenance treatment, 813, 841
 - in children and adolescents, 916
 - efficacy, 832t, 833t, 837–38, 847–48nn79–84
 - pretreatment evaluation and ongoing monitoring, 805t
 - side effects, 807t
 - manic/hypomanic symptoms from, 757, 793n12
 - for mixed mania, 725
 - side effects, 813
 - for suicidal patient, 975
 - weight gain from, 813, 814
- Olfaction, seasonal affective disorder and, 688
- Oligodendroglia, 564
- Oligogenic, 430
- Omega-3 fatty acids
 - antidepressant effects, 790–91, 795n68
 - bipolar disorder and, 184–85
 - for maintenance treatment, 833t, 843
 - mania and, 743
 - protein kinase C and, 555
 - role, 555–56, 605n68
 - suicide and, 254
- On-off research designs, 707, 708t
- Onset of illness. *See also* Age at onset
 - suicide and, 267–68
- Opiate analogs, antidepressant effects, 532, 603n47
- Opiate antagonists, in mania, 532, 603n46
- Opiates
 - abuse, 228–29, 230
 - antidepressant effects, 532, 603n47
 - in cerebrospinal fluid, 532–33, 603n48
 - lithium and, 532, 603n49
 - postmortem brain studies, 532
- Opioid system, endogenous, 531–32
- Opposite states, ability to reconcile, 400–401, 407n8
- Oppositional defiant disorder, 191, 192t, 913
- Oral contraceptives
 - carbamazepine and, 809, 810
 - oxcarbazepine and, 810
- Oregon Adolescent Depression Project, 370, 373
- Orexin/hypocretin, 664, 691n26
- ORG 34517, 529
- Organic brain disorders, versus bipolar disorder, 109–12
- Orlistat, for antipsychotic-related weight gain, 814
- Orthomolecular psychiatry, 792
- Oscillator, versus pacemaker, 689n3
- Outcome. *See* Course and outcome
- Overweight and obesity, 242–43, 949–50. *See also* Weight gain
- Oxcarbazepine
 - for acute mania, 724, 727, 731t, 734–35
 - in children and adolescents, 918t, 927, 935n8
 - for bipolar depression, 754, 763
 - for maintenance treatment, 810–11
 - efficacy, 831, 833t
 - in pregnancy, 816t
 - pretreatment evaluation and ongoing monitoring, 804t
 - side effects, 807t, 811
 - pharmacology, 717
- Oxytocin, 535
- p values, 707
- P300 evoked potential, as endophenotype, 435
- Pacemaker, versus oscillator, 689n3
- Pair-wise concordance, 419
- Pancreatitis, from valproate, 809
- Panic attacks, suicide and, 959
- Panic disorder, 167, 171, 171t, 234, 236–37, 946–47
- Paralimbic structures, anterior, activation studies, 628–29, 629f, 636
- Parent-of-origin effect, 446–47
- Parents. *See also* Family
 - bipolar, offspring of. *See* Child, of bipolar parents
 - clinical and demographic features, children's outcomes and, 219–20
- Parents Med Guide, 978
- Paroxetine
 - for bipolar depression, 755, 767
 - plus lamotrigine, 764
 - for suicidal patient, 967
- Pathophysiology. *See also* Neurobiology
 - dissociating therapeutics and, 320–21
- Patient and Family Education Program, 889, 899
- Patient education. *See* Psychoeducation
- Patient factors, in medication adherence, 852, 853t, 863–64
- Patient perspectives, psychotherapeutic issues, 872–75
- Patient subjective experiences
 - depressive states, 68–71
 - manic states, 37–40
 - mixed states, 77–78
- PCOS (polycystic ovary syndrome), from valproate, 809, 932
- PCP (phencyclidine), as precipitant, 231
- Pedigree, extended bipolar, offspring studies, 215
- Pedunculopontine and laterodorsal tegmental nuclei (PPT-LDT), 690n22
- Pendulum Resources, 978
- Penetrance, 430
- Perception
 - in hypomania, 33
 - in mania, 38–39, 53–60
 - self-, in affective states, 327–29, 328f
- Performance IQ, 278–82, 279f–281f
- Pergolide, for bipolar depression, 784
- Periventricular hyperintensities
 - in bipolar disorder, 618f, 619
 - in major depression, 310, 311f, 312f, 618f, 619
- Personality, 323–34
 - clinical outcome and, 332–33
 - comparisons between bipolar and unipolar patients, 330–32
 - comparisons between manic-depressive episodes and periods of remission, 326–27, 327f
 - comparisons between remitted bipolar patients and normal groups, 329–30
 - conceptual issues, 324, 352n11
 - cyclothymia and, 330
 - definition, 324
 - hyperthymia and, 330
 - medication effects on, 333–34
 - methodological issues, 325–26
 - psychoanalytic perspectives, 326, 352–53nn2–7
 - qualities, 324
 - relationship to mood disorders, 324–25
 - self-perceptions across affective states, 327–29, 328f
- Personality disorders, 240, 334–37, 335t. *See also specific disorders*
 - in adolescent-onset bipolar disorder, 202–3
 - medication adherence and, 864
 - suicide and, 266, 269n16
 - treatment, 949
 - in triggering episodes, 138
- Personality traits, in children of bipolar parents, 216b
- PET. *See* Positron emission tomography
- Petterson Scale, 359
- pH differences, magnetic resonance spectroscopy, 650–52
- Pharmacogenetics, 453, 454t, 457, 460
- Pharmacological bridge, 473
- Pharmacology, 715–19
- Pharmacotherapy. *See also* Medications
 - adequacy of trials, 749, 793n3
 - focus on monotherapy, 796n71

- Pharmacotherapy (*continued*)
 rational combined, versus irrational polypharmacy, 750
 “real-world,” 701–2
- Phencyclidine, as precipitant, 231
- Phenobarbital, Stevens-Johnson syndrome and toxic epidermal necrolysis risk, 810t
- Phenocopy, 430
- Phenotype. *See also* Endophenotype; Genetic subtypes
 alternative definitions, 430–35, 459, 462n13
- Phenytion
 for acute mania, 724, 730t, 731f, 736
 for maintenance treatment, 836
 Stevens-Johnson syndrome and toxic epidermal necrolysis risk, 810t
- Phobia, social, 237, 947
- Phonological loop, 293
- Phosphate, inorganic, magnetic resonance spectroscopy, 650
- Phosphocreatine, magnetic resonance spectroscopy, 650, 651f
- Phosphodiesterase 4 (PDE4) inhibitors, 592t
- Phosphodiesterases, magnetic resonance spectroscopy, 650
- Phosphoinositide, calcium abnormalities and, 550
- Phosphoinositide signaling pathway, 545, 546t, 550–53, 553f, 604nn62–66
- Phospholipase C (PLC) pathway, 537f
- Phosphomonoesters, magnetic resonance spectroscopy, 648–50
- Photoperiodic systems, 679–80
- Photostasis, 687
- Phototherapy, 674t, 675b, 684, 694n76
 for bipolar depression, 758, 789–90
 side effects, 793n14
 plus sleep deprivation therapy, 677
 timing, 670, 686–87
- Phrenitis, 3
- Physicians’ Global Assessment Scale (GAS), 365
- Pilocarpine, 501, 743–44
- Pindolol, after sleep deprivation, 789
- Piquer, Andres, 5
- Pituitary gland, volumetric studies, 626
- Placebo responses, in children, 915, 934n4
- Plasticity. *See* Cellular plasticity cascades
- Plath, Sylvia, 68–69, 70
- Plato, 226
- Platter, Felix, 5
- Poe, Edgar Allen, 225–26
- Poets, 386t–389t, 402. *See also* Creativity
- Polarity. *See also* Bipolar-unipolar distinction versus cyclicality, 9, 13
 polyphasic, 134
- Polarity-specific model of mood states, 332
- Polycystic ovary syndrome (PCOS), from valproate, 809, 932
- Polyuria, from lithium, 808
- Porsolt test, 468
- Positive aspects of manic-depressive illness, 402–6, 857, 878
 clinical considerations, 403–5, 405f, 405t
 social and ethical considerations, 405–6
 theoretical considerations, 402–3
- Positive finding bias, 710–11
- Positron emission tomography
 of dopaminergic system, 484–85
 of glutamatergic system, 510
 in psychomotor retardation, 284
 of serotonergic system, 494, 495
 of sleep, 664, 691n27
- Post-traumatic stress disorder, 238–39, 238t, 948
- Postpartum psychosis, 107
- Postpartum relapse, 815
- Power, statistical, 456
- Pramipexole
 augmentation with, 486
 for bipolar depression, 760t, 784–85
- Precipitants of episodes, 135–41, 138b
 drugs and medical conditions, 138–40, 139t–140t, 231–32
 life events, 135–38, 136t–137t
 season, 140–41
 sexual abuse, 153n42
 sleep loss, 140, 883, 886f
 stress, 870
- Prefrontal cortex
 activation studies, 636
 activity in depression, 630–34, 630f–634f
 atrophy, 559–61, 565t
 volumetric studies, 621–22, 623f
 stress and, 525, 602n43
- Pregabalin, for anxiety disorders, 946
- Pregnancy
 bipolar disorder and, 184
 FDA drug safety categories, 817t
 maintenance treatment in, 815–17, 816t, 817b, 817t
 in triggering episodes, 138
- Premorbid functioning, 120, 150nn1–3
- Preoptic nucleus, ventrolateral, 690n23
- Prescription data
 maintenance medications, 801
 mood stabilizers in U.S., 714b
- Present State Examination (PSE)—Catego, 89
- Pressured speech, in adolescent-onset bipolar disorder, 197
- Presynaptic proteins, as treatment targets, 556–57, 605–6nn70–71
- Presynaptic release machinery, pathological alterations, 556, 605n69
- Pretreatment evaluation, 703
 of acute mania/hypomania and mixed states, 722
 of bipolar depression, 748–49
 in maintenance treatment, 803t–806t
- Prevalence rates
 in epidemiologic studies, 161. *See also* Epidemiology
 methodological issues, 155–62
- Prevention
 in at-risk youth, 917
 future directions, 457–58
 suicide. *See* Suicide, prevention
- Primate separation paradigm, 467
- Proband, 415
- Proband-wise concordance, 419
- Problem-solving techniques
 in childhood-onset bipolar disorder, 903, 933–34
 in family/couples therapy, 902
- Prodromal patterns, education on, 883, 886, 886f
- Productivity, lithium effects, 857
- Progesterone, neuromodulatory effects, 531, 602–3n45
- Prolactin
 atypical antipsychotics and, 932
 challenge studies, 493
- Prophylactic efficacy
 in definition of mood stabilizer, 797
 strength of evidence for, 838t
- Prophylactic treatment. *See* Maintenance treatment
- Prophylaxis
 research design, 709
 true, versus continuation treatment, 800
- Prospective cohort studies, 141–44, 142t, 153nn44–45
- Protein kinase A/cAMP signaling, 541–42
- Protein kinase C
 calcium abnormalities and, 549
 dopamine and, 547
 glucocorticoids and, 547–48
 lithium and, 554, 554f
 omega-3 fatty acids and, 555
 valproate and, 554–55, 554f
- Protein kinase C inhibitors, 593t
 antimanic effects, 553–55, 554f
- Protein kinase C signaling, 545, 547–48, 547b
- Proton (¹H) magnetic resonance spectroscopy, 639–48
- “Prototype” phenomenon, 105
- Pseudodementia, depressive, 110–11
- Psoriasis, from lithium, 807, 844n14
- Psychiatric adverse events, in childhood-onset bipolar disorder, 930–32
- Psychiatric disorders
 comorbid, 224f, 225–40
 epidemiologic methods, 155–57
- Psychiatric genetics, 413
- Psychiatric pretreatment evaluation. *See* Pretreatment evaluation
- Psychiatric Status Rating (PSR) scale, 373
- Psychiatry, nutritional, 792
- Psychoanalytic model, 8
- Psychoanalytic perspectives on personality, 326, 352–53nn2–7
- Psychoeducation, 889, 890t–891t, 899
 Barcelona program, 900, 900b
 in childhood-onset bipolar disorder, 910, 916, 933
 family, 885–87, 902
 Life Goals Program, 903–4
 on medication adherence, 851–52
 multifamily, 902, 903
 patient, 882–85, 884f–886f, 887b
 recommended readings, 979–80
- Psychological issues, in treatment of acute mania, 728
- Psychological traits, suicide and, 261–62
- Psychomotor activation, in mania, 60
- Psychomotor disturbance, CORE measure of, 286–87, 286b
- Psychomotor functioning, 282–89
 cognitive and motor speed, 283–85
 motor skills, 285–86, 285f
 speech rate, 288–89
 spontaneous activity, 286–88, 286b
- Psychomotor retardation, neuropsychological evaluation, 273

- Psychosis/psychotic symptoms. *See also*
 Delusions; Hallucinations
 in adolescent-onset bipolar disorder, 198
 age at onset and, 53, 125
 in bipolar depression, 58, 59t, 67–68, 71–72
 bipolar disorder and, 57
 in childhood-onset bipolar disorder, 188
 cognitive impairment and, 308–9
 cycloid, 107–8
 drug-induced, 230
 in DSM-IV diagnostic criteria for mania, 94
 genetic subtypes and, 431–33, 432t
 in mania, 42f, 42t, 43, 53–60, 54t–56t, 59t, 725
 in children and adolescents, 205, 912
 thought disorder and, 51, 51t
 in mixed states, 80
 mood-incongruent, lithium efficacy and, 827
 postpartum, 107
 suicide and, 267
- Psychosocial adjustment, assessment, 374–76
- Psychosocial stress, breakthrough symptoms
 from, 818
- Psychosocial treatments
 in childhood-onset bipolar disorder, 916
 for substance abuse, 945–46
- Psychostimulants
 behavioral sensitization to, 470
 for bipolar depression, 785
 hyperactivity from
 animal model, 469
 lithium and, 487
 increased use, age at onset and, 205, 206
 for maintenance treatment, 843
 for mania/ADHD
 in children and adolescents, 913
 combination therapy, 928
 rebound on, 913
- Psychotherapeutic issues, 871–81
 ambivalence, 876–77
 anger, 875–76
 clinician attitudes and expectations, 880–81
 dealing with developmental tasks, 879
 denial, 874–75, 876
 disappointment, 877
 family/relationship concerns, 879
 fears of recurrence, 873, 879
 frustration, 877
 genetic concerns, 873–74, 879–80
 learning to discriminate moods, 879
 losses associated with medication, 877–78
 patient perspectives, 872–75
 shame and humiliation, 874
- Psychotherapy, 869–905
 for anxiety disorders, 947, 948
 in childhood-onset bipolar disorder, 933–34
 for children and adolescents, 902–3
 clinical management, 871–88
 cognitive-behavioral therapy, 892t–895t,
 899–900
 effectiveness studies, 889, 898t, 903–4
 family/couples therapy, 887, 897t–898t, 902
 historical context, 871, 905nn2–3
 interpersonal and social rhythm therapy, 896t,
 900–902
 medication adherence, 852, 865, 866t–867t,
 870, 889
 meta-analyses, 904, 904f
 mood charting, 881–82, 882f
 psychoeducation. *See* Psychoeducation
 review of literature, 888–904
 suicide-oriented, 961
 support associations, 887–88
 unstructured, for substance abuse, 946
- Psychotic disorder
 brief, 107, 107b
 separate or continuous classification, 100–102,
 101t
- Psychotic disorder-NOS, versus bipolar disorder,
 108
- Psychotic exhaustion, 725, 725f
- Psychotic symptoms. *See* Psychosis/psychotic
 symptoms
- Puberty issue, in adolescent-onset bipolar
 disorder, 203–4
- Puerto Rico Study of Psychiatric Disorders, 167
- Pure cyclothymia, 85
- Pure mania, 13–14, 32, 94
- Putamen, volumetric studies, 625
- Pyridostigmine, growth hormone response, 501
- Quality-adjusted life years (QALYs), 178
- Quality of life, literature on, 145
- Quetiapine
 for acute mania, 727, 730f, 730t, 731t, 738t, 740
 in children and adolescents, 918t, 928,
 934nn9–10
 versus haloperidol, 737
 versus lithium, 731–32
 plus valproate, 928
 for bipolar depression, 782
 in children and adolescents, 929, 934n4
 efficacy, strength of evidence, 838t
 for maintenance treatment, 813
 pretreatment evaluation and ongoing
 monitoring, 805t
 side effects, 807t
 in offspring of bipolar parents, 930
 for substance abuse, 942t, 944
- R-121919, 528
- Race. *See* Ethnic differences
- Racing thoughts
 in childhood-onset bipolar disorder, 188, 189t
 in mania, 37–38, 43, 44t
 in mixed states, 79
- Rage, in childhood-onset bipolar disorder, 188
- RAINBOW program, 903
- Rapid cycling, 108, 131–33, 132b, 132f, 435
 acute treatment, 725–26
 adolescent-onset bipolar disorder, 198
 antidepressant response to lithium and, 751, 753
 antidepressant use and, 140
 carbamazepine and, 733
 cerebral activity in, 639
 extended rest-dark period for, 678,
 693nn61–62
 genetic subtypes and, 435
 hypothyroidism and, 242, 518, 951
 maintenance treatment, 826t–827t
 antidepressants for, 827
 calcium channel blockers for, 842–43
 lamotrigine for, 832t, 834–35
 lithium for, 825–27
 valproate for, 827
- panic disorder and, 237
 sleep and, 666
 substance abuse and, 232
 suicide and, 264–65, 265t
 treatment-resistant
 antidepressant discontinuation and, 827
 extended bed rest and darkness for, 843
- Rapid eye movement (REM) sleep. *See* Sleep,
 REM
- Ras pathway, 537f
- Rash
 from carbamazepine, 810
 from lamotrigine, 811, 812f, 845nn27–28
 from oxcarbazepine, 810t
- Rating scales. *See also* Assessment
 observer
 advantages and disadvantages, 357–58
 depressive symptoms, 363–65
 manic states, 359–61, 360t
 self
 advantages and disadvantages, 357, 357f
 depressive symptoms, 361–63
 manic states, 358–59
- “Raving maniac,” 36
- Reaction time, 285–86, 285f
- Reality, heightened sense of, in mania, 37
- Reasoning
 measures, 298, 300f
 preservation, 303
- Reasons for Living scale, 958
- Reboxetine
 for bipolar depression, 770
 pharmacology, 719
- Recombination, 423–24, 425f
- Recovery
 from bipolar depression, assessment of
 progress, 750, 793n4
 versus outcome studies, 143
 “sawtooth”-like pattern, 749, 793n3,
 882, 882f
- Recovery phase, 875
- Recurrence. *See also* Relapse
 antidepressant use and, 126
 fears of, 873, 879
 mechanisms, 149
 medication adherence and, 857
 patient education on, 883, 884f, 885f
 rates, 126–28, 127t, 151nn17–21
- Recurrent brief depression, 23, 27n44
- Recurrent brief hypomania, 23, 27n44, 175, 225
- Recurrent unipolar depression, 9
 early age at onset in, 431
 highly, 750
 maintenance treatment, 799–800, 828–29
 REM sleep and, 665
- Reelin deficiency, 601–2n29
 in hippocampus and cerebellum, 506
 in postmortem brain, 505–6
- Referral bias, 709
- Referral centers, treatment effectiveness, 701
- Refusal to participate bias, in epidemiologic
 studies, 160
- Regional cerebral blood flow (rCBF), limbic,
 628–29, 629f
- Regional cerebral metabolism, in depression,
 631f, 632f
- Regression model, 710

- Relapse. *See also* Recurrence
 after antidepressant discontinuation, 755, 793nn9–10
 life events and, 138
 after lithium discontinuation, 824–25
 negative self-esteem as predictor, 899
 postpartum, 815
 prevention, research design, 709–10
 rates, 126–28, 127t, 151nn17–21, 883, 884f, 885f
 true, 819
 “Relapse drill,” 886–87
 Relative risk, 418
 Release model of mood disorders
 versus deficit state model, 313–14
 therapeutic implications, 314–15, 315f
 Religious beliefs, suicide and, 262
 REM sleep. *See* Sleep, REM
 Renal effects, lithium, 807–8, 844nn15–19
 Reproduction
 seasonal rhythms, 680
 valproate effects, 934n3
 Research Diagnostic Criteria (RDC), 91, 114n2
 Research literature. *See* Treatment research literature
 Reserpine-induced depression, 115n19
 Resiliency, cellular, 595f
 impairment, 567–68
 treatment targets, 599
 Resources
 information, 977–80
 for successful maintenance treatment, 800–801
 Restriction enzymes, 423
 Restriction fragment length polymorphisms (RFLPs), 423
 Retinal ganglion cell axon regeneration, with lithium, 576, 577f
 Reverse tolerance, 470. *See also* Kindling or sensitization model
 Reviews of research, limitations, 710, 720n11
 Reward dependence, bipolar-unipolar differences, 331
 Reynolds Depression Screening Inventory, 362–63
 Riluzole, for bipolar depression, 764–65
 Risk assessment
 bipolar disorder, 369–71, 370t. *See also* Correlates of bipolar disorder
 suicide
 acute versus chronic risk factors, 956b, 957–58, 957t
 evaluation of patient history, 956
 goals and timing, 954–55, 954b, 955b, 956b
 protective factors, 956b, 958
 suicidal intent, 953–54
 Risperidone
 for acute mania, 727, 730f, 730t, 731t, 738t, 739–40, 746nn37–39
 versus amisulpiride, 741
 in children and adolescents, 918t, 927
 versus haloperidol, 737
 for aggression, 913, 914t, 929
 for anxiety disorders, 947
 for bipolar depression, 760t
 versus adjunctive lamotrigine, 764
 for maintenance treatment, 813, 841
 efficacy, 836–37, 847n78
 pretreatment evaluation and ongoing monitoring, 805t
 side effects, 807t
 RNA (ribonucleic acid), 423
 Roethke, Theodore, 37
 Role transitions/deficits, in interpersonal and social rhythm therapy, 901
 Ropinirole, for bipolar depression, 784
 “Roughening” concept, 780, 795n55
 RU-486, antidepressant effects, 528–29, 787
 Rural/urban comparisons
 bipolar disorder, 183
 seasonality of suicide, 253
 Rush, Benjamin, 33, 35, 379, 965
 Ruskin, John, 37
 SAD. *See* Seasonal affective disorder (SAD)
 St. John’s wort
 antidepressant effects, 790
 hypomanic effects, 728
 Sample size, in epidemiologic studies, 161
 Sao Paulo, Brazil study, 173t, 174
 Scale for the Assessment of Thought, Language, and Communication, 45
 Schedule for Affective Disorders and Schizophrenia (SADS), 160
 Schizoaffective depressed patients, 49, 100, 114n12
 Schizoaffective disorder
 versus bipolar disorder, 102–4
 DSM-IV diagnostic criteria, 99–100, 103b
 epidemiologic studies, 102
 family studies, 417t, 418
 thought disorder, 49
 Schizomaniac patients, 100
 Schizophrenia
 versus bipolar disorder, 102–4
 linguistic and communication patterns, 51–52, 52f
 versus manic-depressive illness, 7–8
 medication adherence in, 853–54, 854b
 neuroimaging studies, 652
 premorbid functioning, 120
 thought disorder in, 45–50, 46t–48t, 49f, 50f
 ventricular enlargement, 617
 Schizophrenia–affective disorder continuum, 101t, 102
 Schneiderian first-rank symptoms, in schizoaffective disorder, 99, 114n11
 Schott, A., 36
 Screening assessment
 adults, 371–72, 372t
 children and adolescents, 372–73
 Screening Assessment of Depression–Polarity (SAD-P), 371–72
 Screening for Mental Health, Inc., 978–79
 Seasonal affective disorder (SAD), 679
 atmospheric temperature and, 688
 bipolar disorder and, 682
 chronobiological dysregulation, 685–87
 circadian phase-shift hypothesis, 686–87
 diagnostic criteria, 682, 694n71
 dual-vulnerability hypothesis, 683–84
 epidemiology, 682–83
 genetic factors, 684
 light sensitivity and, 687–88
 melatonin duration hypothesis, 685–86, 695n79
 neurotransmitter dysfunction, 684–85
 olfaction and, 688
 pathophysiology, 684–88
 sleep in, 665
 summer form, 680
 syndromal versus subsyndromal, 683–84
 winter form, 665, 679
 Seasonal instability, 153n43
 Seasonal rhythms, 251–55, 678–88
 allergens/immune function and, 681–82, 694n68
 bipolar disorder, 254–55
 creativity, 393, 393f
 depression, 680–81, 693–94nn67–70
 mania, 681
 manic-depressive illness, 680–82, 681f
 melatonin secretion, 680, 694n69
 mixed states, 80
 neurobiological factors, 254
 physiological mechanisms, 679–80
 suicide, 251–55, 252f
 in triggering episodes, 140–41
 Secondary mood disorders, 21, 109, 110b, 611
 Sedation, from valproate, 809
 Sedative hypnotics, breakthrough symptoms and, 819
 Segregation analysis, 418
 Seizures. *See* Epilepsy
 Selection bias, in outcome studies, 119
 Selegiline, for bipolar depression, 756, 767
 Self-esteem
 inflated, in adolescent-onset bipolar disorder, 197
 negative, 899
 Self-help, as component of treatment, 705
 Self-help groups, 852, 887–88
 Self-medication hypothesis of substance abuse, 230–31
 Self-perceptions of affective states, 327–29, 328f
 Self-rating scales
 advantages and disadvantages, 357, 357f
 depressive symptoms, 361–63
 manic states, 358–59
 Self-Report Mania Inventory (SRMI), 358
 Sensitivity analysis, 720n12
 Sensitization. *See* Kindling or sensitization model
 Separation models of depression, 467
 Serial analysis of gene expression (SAGE), 450
 Serotonergic system, 490–98
 association studies, 437t–438t
 carbamazepine and, 497–98
 CSF metabolite levels, 490–91
 lithium and, 496–97
 longitudinal studies, 491
 in mixed state, 491
 neuroendocrine challenge studies, 493
 in postmortem brain, 491
 receptor studies, 493–96
 sleep and, 676
 summary of findings, 498, 498b–500b
 treatment targets, 590t
 tryptophan depletion challenge studies, 492–93
 valproate and, 497
 in well state, 491
 Serotonin
 in bipolar disorder, 237
 platelet uptake, 491
 seasonal affective disorder and, 684–85
 suicide and, 254, 259–60

- Serotonin 1A/1B receptor antagonists, 590t
- Serotonin 1A receptor, 493–94
- Serotonin 2A receptor, 494–95, 684
- Serotonin/norepinephrine reuptake inhibitors, for bipolar depression, 769–70
- Serotonin receptor subtypes, suicide and, 259–60
- Serotonin reuptake inhibitors, selective
- for anxiety disorders, 946, 947, 948
 - for bipolar depression, 755, 767, 768t, 769b
 - in children and adolescents, 915
 - plus lamotrigine, 764
 - lithium augmentation, 762, 793nn18–19
- cycle acceleration with, 780
- pharmacogenetics, 453, 454t
- pharmacology, 718
- for seasonal affective disorder, 685
- for suicidal patient, 960, 967
- suicide risk and, 960, 973–75
- switches with, 777
- Serotonin transporter gene, 443, 495–96
- Serotonin transporter gene promoter
- seasonal affective disorder and, 684
 - SSRI responsiveness and, 453, 454t
 - suicide and, 260
- Serotonin transporter genotype, hippocampal volume and, 624
- Sertraline
- for bipolar depression, versus bupropion or venlafaxine, 768–69, 77of
 - pharmacology, 718
 - response to, baseline cerebral activity and, 637–38
- Severity
- of depression, suicide and, 264
 - of mania, psychotic symptoms and, 53
- Sexton, Anne, 401, 402
- Sexual abuse
- in children of bipolar parents, 217–18
 - as precipitant, 153n42
- Sexual behavior, 35, 188, 189t, 348–49, 354n19
- SF-36 (Short Form Health Survey), 376
- SHAGGY gene, 691n49
- Shame, as psychotherapeutic issue, 874
- Shantin (Hong Kong) study, 172, 173t
- Sibutramine, for weight loss in obese patients, 950
- Signaling pathway(s), 536–89, 536f, 537f
- calcium, 548–52, 549t–551t, 552f
 - cellular plasticity cascades, 559–81. *See also* Cellular plasticity cascades
 - clinical studies, 539t
 - fatty acids and, 555–56, 605n68
 - glycogen synthase kinase-3 as target, 557–59, 558f, 559b, 563f, 606nn72–74
 - G_s /cAMP-generating, 538, 539t, 540–45, 540f, 541t
 - phosphoinositide, 545, 546t, 550–53, 553f, 604nn62–66
 - protein kinase C, 545, 547–48, 547b
 - putative roles, 538b, 598–99
 - synaptic vesicle proteins and, 556–57, 605–6nn69–71
- Single nucleotide polymorphisms (SNPs), 423
- Single photon emission computed tomography (SPECT)
- of dopaminergic system, 485
 - of serotonergic system, 495
- Sinistrality, 286
- Slater's fallacy, 129, 151–52n22
- Sleep. *See also* Circadian rhythm
- in affective disorders, 664–67
 - in bipolar disorder, 665
 - cholinergic system and, 667, 673, 676
 - chronobiological interventions, 673–78, 674t, 675b
 - constant routine, 668, 691n38
 - in depression, 67, 666–67
 - disturbances
 - in affective disorders, time course, 664–65
 - circadian, 666, 667–73. *See also* Circadian rhythm, disturbances
 - in depression, 70–71
 - noncircadian mechanisms, 673
 - suicide and, 266 - duration, physiology, 664, 691nn30–31
 - electroencephalography, 662–63, 691n29
 - excessive, 665, 667
 - experimental alterations, 673–78, 674t, 675b
 - forced desynchrony, 668, 691n37
 - functional neuroimaging studies, 664, 691n27
 - genetic factors, 663, 690nn19–21
 - loss
 - breakthrough symptoms and, 819
 - in childhood-onset bipolar disorder, 188, 189t
 - in depression, 666–67
 - suicide and, 266
 - in triggering episodes, 140, 883, 886f - in mania/hypomania, 93, 665–66
 - neural substrates, 663–64, 690–91nn22–26
 - NREM, 662, 663f
 - thermoregulation and, 663 - physiology, 662–64
 - REM, 662, 663f
 - amygdala activation, 691n28
 - cholinergic-induced, 501
 - cholinergic sensitivity and, 667
 - medication effects, 667
 - and nonsleep circadian rhythms, 669
 - recurrent depression and, 665
 - suppression, in sleep deprivation therapy, 677, 693n58
 - temperature rhythm and, 670–71 - in seasonal affective disorder, 665
 - stages, 662–63, 663f
 - two-process model, 31, 664, 673, 691nn29
- Sleep debt, 691n30
- Sleep deprivation models, 469–70
- Sleep deprivation therapy, 659, 674–78, 674t, 675b, 688n1
- for bipolar depression, 757–58, 788–89
 - bipolar-unipolar differences, 675
 - combination therapy, 677
 - lack of interest in, 674
 - mania and, 675, 677
 - mechanisms, 676–77
 - neuroimaging studies, 676
 - partial, 670, 67of
 - plus phase advance, 670, 692n43
 - REM sleep suppression, 677, 693n58
 - response predictors, 675–76
 - switches with, 789
 - timing, 677–78, 677f
 - TSH response, 519
- Sleep hygiene, 705
- Sleep phase advance, 677–78, 677f
- SMIT, 551
- Smoking, bipolar disorder and, 184
- Social Adaptation Self-Evaluation Scale (SASS), 375–76
- Social Adjustment Scale–Self Report (SAS–SR), 375
- Social anxiety disorder, 237, 947
- Social class, bipolar disorder and, 181–82
- Social defeat paradigm, 468, 582–83
- Social factors, in suicide, 262
- Social functioning, 337–43
- assessment, 374–76
 - clinical predictors of, 340–41
 - conceptual and methodological issues, 341, 343
 - impairment despite remission and treatment, 339–40
 - impairment during mania and depression, 337–39
- Social phobia, 237, 947
- Social predictors of clinical outcomes, 341, 342t–343t
- Social Rhythm Metric, 882, 901
- Social rhythm therapy, 678, 693n63, 896t, 900–902
- Social support
- medication adherence and, 864
 - outcome and, 341
- Socrates, 379
- “Soft bipolar spectrum,” 21
- Somatic symptoms, in bipolar depression, 72, 73t
- Somatostatin, 533, 603n50
- Soranus of Ephesus, 4, 226
- Span tasks, 293, 294f
- SPECT. *See* Single photon emission computed tomography (SPECT)
- Spectrum models, 20–21, 24. *See also* Manic-depressive spectrum
- Speech
- in mania versus depression, 52–53, 53t
 - in mania versus schizophrenia, 51–52, 52f
 - rate, 288–89
- Speech pause time, 289
- Speed of thought, creativity and, 397
- Spontaneous flexibility, creativity and, 397
- SSR125543A, 528
- Stanley Medical Research Institute, 979
- State, trait versus, 325
- State dependency, neuropsychiatric deficits, 273–74
- Steroids, gonadal
- monoamine oxidase inhibitors and, 531, 602–3n45
 - neuromodulatory effects, 529–31
- Stevens-Johnson syndrome, risk with anticonvulsants and antibiotics, 810t
- lamotrigine and, 932–33
- Stigma, 458
- Stimulants. *See* Psychostimulants
- Storage deficits, versus retrieval deficits, 295–96
- Stratification model, 710
- Stress
- hippocampal atrophy and, 510–11, 511f, 525, 602nn42–43
 - hippocampal neurogenesis impairment and, 527

- Stress (*continued*)
- marital, and risk to children of bipolar parents, 217–18
 - mechanisms underlying morphometric changes, 525–27, 526f, 595f
 - medication adherence and, 864
 - models of depression, 468
 - neural plasticity and, 525–27, 526f, 595f
 - post-traumatic, 238–39, 238t, 948
 - as precipitant, 870
 - prefrontal cortex volume and, 525, 602n43
 - psychosocial, breakthrough symptoms from, 818
 - social defeat paradigm, 468, 582–83
 - Stress-diathesis model of suicide, 257–59
 - Stroke, depression after, 319–20
 - Stroop test, 289
 - Structured Clinical Interview for DSM (SCID), 160
 - Structured Psychopathological Interview and Rating of the Social Consequences of Psychiatric Disturbances for Epidemiology (SPIKE), 160
 - Stupor
 - depressive, 68
 - manic, 76t, 77
 - Subcortical hyperintensities, 310–13, 311f, 312f, 612f, 617–21, 618f
 - Subjective experiences of patients
 - depressive states, 68–71
 - manic states, 37–40
 - mixed states, 77–78
 - Substance abuse, 225–33
 - in adolescent-onset bipolar disorder, 202, 203
 - age at onset and, 121
 - alcohol. *See* Alcohol abuse/dependence
 - antidepressant-related switches and, 776
 - in childhood-onset bipolar disorder, 191, 192t
 - cocaine, 228
 - functional outcome, 700
 - hypothetical relationships, 229–33, 229t
 - international comparisons, 171, 172t
 - marijuana, 229
 - medication adherence and, 864
 - methodological issues, 225
 - mixed states, 80
 - modification of course, 232–33
 - mood disorders, 226–27, 226t, 227f
 - opiates and central nervous system depressants, 228–29
 - as precipitant of illness, 231–32
 - questions on, 748
 - rates, 227–28, 228t
 - self-medication hypothesis, 230–31
 - suicide and, 232, 266–67
 - treatment, 937–46, 940t–942t
 - Substance Abuse and Mental Health Services, 979
 - Substance P, 533–34
 - Substance P receptors, 533–34, 591t
 - Subsyndromal morbidity and chronicity
 - in children of bipolar parents, 207, 214
 - in long-term outcome, 145
 - Succinate semialdehyde dehydrogenase (SSADH), 507
 - Suicide, 247–69, 953–76
 - acamprosate and, 944
 - adolescent-onset bipolar disorder and, 199, 200b
 - antidepressants and, 254, 931–32, 960, 973–75, 976n3
 - anxiety/agitation and, 265–66, 957–58, 959–60
 - attention deficits and, 303
 - bipolar disorder and, 167, 170t, 254–55
 - in bipolar-I versus bipolar-II disorder, 250–51, 251t
 - bipolar-unipolar distinction, 250, 251t
 - causes, 255–62
 - cholesterol and, 260–61
 - clinical correlates, 262–69
 - comorbidity and, 266
 - course of illness and, 267–69, 268t
 - depression and, 67, 70, 263–64
 - diagnostic and methodological issues, 247–48
 - in elderly person, 253
 - gender differences, 251, 253
 - genetic and family transmission, 255–59, 256f, 257t, 258t
 - history of suicide attempts and, 262–63
 - HPA axis hyperactivity and, 261
 - impact on family and therapist, 965–66
 - intent to commit, communication of, 953–54
 - manic-depressive illness and, 146, 153–54n47, 249–50
 - in MECA study, 177
 - mixed states and, 80, 263, 269n11, 957–58, 959–60
 - neurobiological factors, 254, 259–62
 - norepinephrine and, 261
 - obesity and, 243
 - prevention
 - acute management, 959–60, 966–67
 - clinician availability and attitudes, 963–64
 - communicating information, 962–63, 962b
 - follow-up care, 965
 - hospitalization, 964–65
 - involvement of family and friends, 964
 - long-term management, 960, 967–75
 - medication monitoring, 963
 - providing reassurance, 961–62
 - psychological aspects, 961–64
 - public health perspective, 953
 - suicide-oriented clinical trials, 961
 - therapeutic style and, 961
 - protective factors, 956b, 958
 - psychological traits and temperament, 261–62
 - psychosis and, 267
 - rapid cycling and, 264–65, 265t
 - rates, 248f, 249–55, 269n11
 - risk assessment
 - acute versus chronic risk factors, 956b, 957–58, 957t
 - evaluation of patient history, 956
 - goals and timing, 954–55, 954b, 955b, 956b
 - protective factors, 956b, 958
 - suicidal intent, 953–54
 - seasonality, 251–55, 252f
 - serotonin and, 254, 259–60
 - social factors and, 262
 - stress-diathesis model, 257–59
 - substance abuse and, 232, 266–67
 - violent, 253
 - Suicide Awareness Voices of Education, 979
 - Suicide Prevention Action Network USA (SPAN USA), 979
 - Sulfonamides, Stevens-Johnson syndrome and toxic epidermal necrolysis risk, 810t
 - Sumatriptan, challenge test, 493
 - Summer depression, 680
 - Sunlight, suicide and, 254
 - Support group, as component of treatment, 705
 - Supportive Treatment for Addiction Recovery (STAR), 945
 - Suprachiasmatic nuclei (SCN), 660, 689n3
 - in seasonal rhythms, 679–80
 - Surgeon General of the United States, 979
 - Survival analysis, 711–12
 - Switch process
 - antidepressant-related, 750, 771–78, 773t–776t, 794–95nn42–54, 974
 - in children and adolescents, 930–31
 - versus spontaneous switches, 776–77
 - dopaminergic system in, 484
 - lamotrigine-related, 764
 - medical treatments and, 771, 771f
 - sleep deprivation and, 789
 - Symbyax, 781, 918t
 - Synapsin, 556–57, 605–6nn70–71
 - Synaptic vesicle proteins, 556–57, 605–6nn69–71
 - Synaptobrevin, 556
 - Synaptojanin, 556
 - Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), 898t, 899–900, 903–4, 979

T tests, 709

T₃ (triiodothyronine), antidepressant effects, 757, 786, 950

T₄. *See* Thyroxine

Tail suspension test, 468

Taiwan Epidemiology Project, 167

Tamoxifen, antimanic effects, 554, 555, 743

Temperament. *See also* Cyclothymia

 - characteristics, 609, 610t
 - cycloid, 82
 - cyclothymic, 83–84
 - definition, 324
 - depressive, 82
 - hyperthymic, 22, 85–86
 - irritable, 83
 - manic, 22, 82–83
 - manic-depressive, 82–86
 - and manifestations of mixed states, 80
 - suicide and, 262
 - vulnerability and, 332–33

Temperament scale of Memphis, Pisa, Paris, and San Diego (TEMPPS), 22, 27n41

Temperature

 - atmospheric, seasonal affective disorder and, 688
 - body
 - in circadian rhythm disturbances, 671–72
 - regulation, NREM sleep and, 663
 - rhythm of, REM sleep propensity and, 670–71

Temporal domains of affects, 609, 610t

Temporal lobe

 - activity in depression, 634–35
 - activity in mania, 638
 - epilepsy, psychosis associated with, 111
 - volumetric studies, 625

Temporal variations in bipolar disorder, 181

- Teratogenicity, 815–17, 816t, 817b, 817t
- Testosterone
 neuromodulatory effects, 530
 replacement, for bipolar depression, 788
- Texas Medication Algorithm, 713, 720n13, 889, 899
- Thalamus
 activity in depression, 635–36
 volumetric studies, 625–26
- Therapeutic alliance, 703–5, 854, 865, 872
- Third ventricular enlargement, 612f, 615t, 616–17
- Thought disorder
 assessment, 45
 in depression, 69, 71
 in mania, 43–51, 44t, 46t–48t, 49f, 50f, 51t
 longitudinal studies, 49–51, 50f, 51t
 versus schizophrenia, 45–50, 46t–48t, 49f, 50f
 in schizoaffective disorder, 49
 working definition, 44
- Thought Disorder Index, 45, 49, 49f
- Thoughts
 characteristics, creativity and, 397
 grandiose
 in childhood-onset bipolar disorder, 188, 189t
 in mania, 37–38, 43, 44t
 mania with poverty of, 75t
 racing
 in childhood-onset bipolar disorder, 188, 189t
 in mania, 37–38, 43, 44t
 in mixed states, 79
- Thrombocytopenia, from valproate, 809
- Thyroid dysfunction, 241–42, 517–20, 520b, 950–51. *See also* Hyperthyroidism; Hypothyroidism
 rapid cycling and, 242, 518, 951
- Thyroid hormones
 antidepressant effects, 518–19, 757, 785–87
 for lithium-induced hypothyroidism, 842, 848n92
 regulation, 517
- Thyroid peroxidase antibodies (TPO Abs), during lithium treatment, 808
- Thyroid-stimulating hormone (TSH), 517
 during lithium treatment, 808
 sleep deprivation and, 519
- Thyrotropin-releasing hormone (TRH), 517
 antidepressant effects, 519–20
- Thyrotropin-releasing hormone (TRH)
 stimulation test, 519
- Thyroxine
 antidepressant effects, 518–19, 757, 786
 for hypothyroidism, 842, 848n92, 950–51
- Tiagabine
 for acute mania, 736
 for bipolar depression, 765
 for maintenance treatment, 835, 847n75
 pharmacology, 717
- Tianeptine, 584
- Timeless* gene, 689n5
- TMS. *See* Transcranial magnetic stimulation (TMS)
- Tolerance, reverse, 470. *See also* Kindling or sensitization model
- Topiramate
 for acute mania, 724, 735, 745nn18–20
 in children and adolescents, 918t, 927
 for bipolar depression, 754, 760t, 765, 793n7, 794n27
 for eating disorders, 949
 for maintenance treatment, 835–36
 pharmacology, 717
 for substance abuse, 943
 weight loss effects, 806, 809, 814, 950
- Tower of London, 298
- Toxic epidermal necrolysis risk, with anticonvulsants and antibiotics, 810t
- Trait(s)
 premorbid, vulnerability and, 332
 state versus, 325
- Transcranial magnetic stimulation (TMS)
 for acute mania, 743
 baseline cerebral activity and, 638
 for bipolar depression, 783, 795nn60–61
 for depression, 320
- Transmission disequilibrium test, 436, 436f
- Tranlycypromine
 augmentation with, 485–86
 for bipolar depression, 760t, 766
- Treatment
 of acute mania/hypomania and mixed states, 721–44
 acute phase
 definition, 702
 tapering off and discontinuation after, 802
 adherence. *See* Medications, adherence
 of bipolar depression, 747–92
 of comorbidity, 937–51
 continuation phase
 in acute mania/hypomania and mixed states, 724–25
 definition, 702–3, 797, 844n1
 versus true prophylaxis, 800
 effectiveness, “real-world” pharmacotherapy and, 701–2
 general considerations, 703–5, 704b
 guidelines and algorithms, 712–15, 714b
 history, questions on, 748–49
 lifestyle changes in, 705
 maintenance. *See* Maintenance treatment
 managed care constraints, 704, 720n9
 pharmacology of medications, 715–19
 prophylaxis phase. *See* Maintenance treatment
 resistance
 baseline cerebral activity and, 638
 episode number and, 130
 subcortical hyperintensities and, 620
 response
 baseline cerebral activity markers, 637–38
 pharmaceutical, “sawtooth”-like pattern, 749, 793n3
 stages, 702–3
 of suicidal patient, 953–76
 therapeutic alliance in, 703–5
- Treatment effects
 on cerebral activity, 637
 on marital functioning, 349–50
 neuropsychological, 275, 305–8, 306f, 307f
 on personality, 333–34
 on prefrontal cortex volume, 559–61, 565t
- Treatment research literature, 706–12
 bias against off-on, on-off and crossover designs, 707, 708t
 challenges in interpreting, 707–12, 708t
 levels of evidence, 706–7, 707b
 observational (naturalistic) studies, 706
 reviews of, limitations, 710, 720n11
 “Treatment-resistant depression,” 771
- Treatment targets(s)
 glucocorticoid, 523
 glutamatergic, 513–14, 514f, 515f
 glycogen synthase kinase-3 as, 557–59, 558f, 559b, 563f, 593t, 606nn72–74
 neuroendocrine systems as, 527–29
 “plasticity-enhancing,” 589, 590t–594t, 599–601, 600f
 presynaptic proteins as, 556–57, 605–6nn70–71
 summary, 590t–594t
- Tremor
 from lithium, 807
 from valproate, 809
- TRH. *See* Thyrotropin-releasing hormone (TRH)
- Tricyclic antidepressants
 for bipolar depression, 755, 765–66
 versus lithium, 761, 761t
 lithium augmentation, 761, 762t
 cycle acceleration with, 778–80, 779t, 780f
 for maintenance treatment, in breast-feeding women, 818
 pharmacology, 718
 switches with, 777–78
- Tridimensional Personality Questionnaire, 331
- Triiodothyronine, antidepressant effects, 757, 786, 950
- Trimethoprim-sulfamethoxazole, Stevens-Johnson syndrome and toxic epidermal necrolysis risk, 810t
- Trinucleotide repeat-containing genes, 441t–442t, 443, 446
- Tryptophan
 depletion challenge studies, 492–93
 seasonal affective disorder and, 684–85
 neuroendocrine challenge studies, 493
 for seasonal affective disorder, 684
- Tryptophan depletion problem, with antidepressants, 586–87, 589f
- Tryptophan hydroxylase (TPH) polymorphisms, suicide and, 259
- TSH. *See* Thyroid-stimulating hormone (TSH)
- Tuke, D.H., 33, 35
- Twin studies
 of manic-depressive illness, 419–21, 420t–421t, 461n4
 of schizophrenia and psychotic affective disorder, 433
 of suicide risk, 256, 257t
- Two-entities tradition, in classification of psychotic disorders, 101, 101t
- Tyrosine hydroxylase (TH) gene, 443–44
- Unipolar depression. *See also* Bipolar-unipolar distinction; Depression; Major depressive disorder
 adoption studies, 422t
 burden of disease, 178, 180, 180t
 in child of bipolar parents, 915, 934n6
 differential diagnosis, 104–6, 104b, 115nn14–17
 in DSM-IV, 9
 false, 14–15, 14t, 106, 133, 152–53nn33–34, 163
 marital functioning, 343–44
 prevalence, 162–63

- Unipolar depression (*continued*)
 psychotherapy, 905n2
 recurrent, 9
 early age at onset in, 431
 highly, 750
 maintenance treatment, 799–800, 828–29
 REM sleep and, 665
 relapse in, 126
 switch to bipolar diagnosis, 777
- Unipolar mania, 13–14, 26nn26–27, 319
- United States, mood stabilizer prescribing patterns, 714b
- University of Michigan modification of Composite International Diagnostic Interview (UM-CIDI), 160
- Urban/rural comparisons
 bipolar disorder, 183
 seasonality of suicide, 253
- Urinalysis, in substance abuse, 938
- Urinary osmolality, lithium and, 808
- Vagus nerve stimulation, for bipolar depression, 783–84
- Valproate
 for acute mania, 723, 739
 plus carbamazepine, 733
 in children and adolescents, 912, 918t, 923, 924t–926t, 927, 928, 934n3
 combination therapy, 928
 dosages and monitoring, 726–27
 efficacy, 730f, 730t, 731t, 733–34
 versus lithium, 725, 725f, 731, 732f
 versus olanzapine, 739
 versus oxcarbazepine, 735
 plus quetiapine, 740
 plus risperidone, 740, 928
 adherence to, 855, 856t
 for aggression, 913, 914t, 929
 for anxiety disorders, 946, 948
 Bcl-2 overexpression, 572–74, 573f, 581, 583f
 for bipolar depression, 754, 759t, 760t, 763, 794nn21–22
 plus topiramate, 765
 for bipolar-II depression, 769b
 chronobiological effects, 673
 dopaminergic system and, 487–88
 efficacy, strength of evidence, 838t
 extended-release form, 734
 GABAergic system and, 507
 glutamate and, 512, 513
 G_s /cAMP-generating signaling pathway and, 544
 hippocampal neurogenesis with, 578–79, 579f
 plus lamotrigine, 811
 for maintenance treatment, 809
 in bipolar-II disorder, 799, 830
 in breast-feeding women, 818
 in children and adolescents, 929–30
 differential response, clinical characteristics associated with, 828t
 efficacy, 829–30, 832t, 833t, 846–47nn60–63
 in elderly person, 814
 plus lithium, 839
 versus lithium, 822, 827
 plus olanzapine, 841
 versus olanzapine, 837
 in pregnancy, 815, 816t, 817
 pretreatment evaluation and ongoing monitoring, 803t
 in rapid cycling, 827
 side effects, 807t, 809
 for mixed mania, 734
 versus lithium, 725, 725f
 neurotrophic effects, 587–89
 norepinephrine and, 481
 in offspring of bipolar parents, 930
 PCOS from, 809, 932
 pharmacology, 716
 protein kinase C and, 554–55, 554f
 REM sleep and, 667
 response to, baseline cerebral activity and, 637
 serotonergic system and, 497
 Stevens-Johnson syndrome and toxic epidermal necrolysis risk, 810t
 for substance abuse, 940t, 941t, 943
 teratogenicity, 815, 816t, 817
 weight gain from, 932
 Vanillyl-mandelic acid (VMA), in urine, 477
 Vasoactive intestinal polypeptide (VIP), 535
 Vasopressin, 533, 603–4n51
 Venlafaxine
 for bipolar depression, 769–70, 793n18
 versus bupropion or sertraline, 768–69, 770f
 lithium augmentation, 762
 pharmacology, 718
 response to, baseline cerebral activity and, 637, 638
 for suicidal patient, 967
 switches with, 778
 Ventricular enlargement, 612–17, 612f, 615t, 620
 Ventrolateral preoptic nucleus, 690n23
 Verapamil
 for acute mania, 743
 in children and adolescents, 928
 for maintenance treatment, 843, 848n93
 Verbal IQ, 278–82, 279f–281f
 Verbal skills, 300–302, 301f
 preservation of, 303–4
 Vesicular monoamine transporter protein (VMAT₂), 485
 Vigilance, 289
 Visual analogue scales, 881, 882f
 combined assessment, 368–69
 self-reported depressive symptoms, 363
 self-reported manic symptoms, 359–60
 Visuospatial scratch pad, 293
 Visuospatial skills, 300–302, 302f
 Vitamins, antidepressant effects, 792
 Voxel-based morphometry, 621
- Wada procedure, depressive-catastrophic reactions during, 314
- Weather, seasonal affective disorder and, 682, 694n73
- Wechsler Adult Intelligence Scale, 45
- Weight gain
 from antidepressants, 793n13
 from antipsychotics, 243, 813–14, 845–46nn35–38
 in bipolar disorder, 242–43
 drug-induced
 in children and adolescents, 932
 treatment, 949–50
 from lithium, 806, 844nn11–12
 from valproate, 809
- Weight loss
 lamotrigine and, 811
 topiramate and, 806, 809, 814, 950
 treatments used for, 950
- Weissman Social Adjustment Scale, 376
- Wertham, F.I., 36
- Weygandt, W., 77
- White blood cells, gene expression in, 451
- White matter hyperintensities
 deep, in major depression, 310, 311f, 312f, 618–19, 618f
 as endophenotype, 435
- WHO studies, 178–81
 Global Burden of Disease (GBD) study, 178–80, 179t, 180t
 world mental health study, 2000, 180–81
- Whole-brain volumes, 626
- Winter depression, 665, 679, 758
- Wisconsin Card Sort Test, 298
- Wolf, Hugo, 69
- Women. *See also* Gender differences
 breast-feeding, maintenance treatment in, 817–18
 pregnant. *See* Pregnancy
- Wolf, Virginia, 875
- Word-association task, 398, 399f
- Working memory, 289
- World mental health study, 2000, 180–81
- Writers. *See also* Creativity
 biographical studies, 383–89, 384t–389t, 390f
 living, studies, 389–93, 391t, 392f–394f, 394, 395t
- Writing, in mania, 34–35, 34f
- Xanomeline, 500
- Years lived with disease (YLDs), 178
- Yellow bile, 3
- Yohimbine, noradrenergic response, 479
- Young Mania Rating Scale (YMRS), 358, 359–60, 376
- Zeitgebers
 entrainment, 672
 phase response curve, 661, 690n14
 sensitivity, 671–72, 692n46
- Ziprasidone
 for acute mania, 723, 727, 730f, 730t, 738t, 740–41
 in children and adolescents, 918t, 928
 intramuscular formulation, 741
 for maintenance treatment
 pretreatment evaluation and ongoing monitoring, 806t
 side effects, 807t
 pharmacology, 719
- Zonisamide
 for acute mania, 736
 for bipolar depression, 765, 794nn30–31
 for eating disorders, 949
 for weight loss in obese patients, 950
- Zotepine
 for acute mania, 741
 side effects, 813
- Zung Self-Rating Depression Scale, 362
- Zurich, Switzerland study, 173t, 174