Index

Note: Page numbers followed by "f" and "t" refer to figures and tables, respectively.

A	Antibipolar drugs, action mechanisms of,
Acute mood episodes, biomarkers for lithium	150-151
efficacy in, 299–305, 300t, 305t	Antibody-based methods, 460
Adaptive immune system, 194	Antidepressants, 492
Adenylate cyclase 2 (ADCY2) gene,	Aryl hydrocarbon receptor nuclear
295-296	translocator-like (ARNTL) gene,
ADRA2A, 492	296-297
ADRB3, 492	Atp1a3 gene, 69
Adrenocorticotropic hormone (ACTH), 314,	Attentional bias, 23
414	Atypical antipsychotics, 492
Affective cognition, 260–261	Auditory steady state response (ASSR), 226
Aging mechanism	Autonomic nervous system (ANS), 410
altered intercellular communication,	_
160-161	В
cellular senescence, 157-158	Base excision repair (BER), 364, 369-371
DNA damage, 158-159	Bdnf gene, 75
epigenetic alterations, 158-159	Betadiversity in BD, 417
genomic instability, 158-159	Big data, 115
hallmarks of biological aging, 162t	Biological processes and pathways, 475
mitochondria dysfunction, 159-160	Biomarker(s), 82, 459
telomere attrition in, 157-158	in bipolar disorder, 41–42
Allostatic load, 324	current limitations, 9-10
α-amino-3-hydroxy-5-methyl-4-	future directions in, 11–12
isoxazolepropionic acid receptors	categories, 5–9, 6f
(AMPARs), 227	diagnosis/trait, 6–7
Alpha-diversity in BD, 416-417	prognosis, 8
Alzheimer's disease (AD), 334–335,	risk, 5–6
414-415	stage, $7-8$
"Amoeboid" morphology, 196	state/acuity, 7
Amphetamines, 66	treatment response, 8–9
Amplitude of low-frequency fluctuation	definition of, $2-5$
(ALFF), 24	of lithium efficacy in bipolar disorders
Animal models	acute mood episodes, biomarkers for
of depression, 72–75	lithium efficacy in, 299-305
of mania, 65-70	lithium prophylaxis efficacy, biomarkers
mitochondrial dysfunction, 147-149	of, 294–299
of psychiatric disorders, 64	lithium's efficacy, 293–294
Ank3 gene, 69, 215-217	process of discovering and validating, 2, 3f
ANTI gene, 145	rationale for, in bipolar disorder, 2–5, 4f
Anterior cingulate cortex (ACC), 83, 86, 97	Black bile, 191–192

Blood-brain barrier (BBB), 405–406, 412 Brain-derived neurotrophic factor (BDNF),	Classical bowel toxemia theory, 385 Clinical Pharmacogenetics Implementation
419–420, 441–443	Consortium (CPIC), 489–490
Brain-derived neurotrophic factor (BDNF), 7,	Clock, 295–296
277, 281–285, 295, 304, 337–338,	Clock19, 215–216
492	Cognitive dysfunctions, 254–255
	Cognitive impairment, 253–254
C	Cognitive inhibition, 23
Cancer research and bipolar disorder,	Coheritability, 130
373-374	Collapsin response mediator protein-2
CACNA1C, 490-491	(CRMP2), 295
Calcium signaling, 331–333	Common variant heritability, 130
in cells, 143f	ConLiGen group, 297–298
Cambridge Neuropsychological Test	Corticosteroid-binding globulin (CBG),
Automated Battery, 258	320–321
cAMP response element-binding (CREB), 442	Corticosterone, 74
Canadian Rapid Treatment Center of	Corticotrophin-releasing hormone (CRH), 314
Excellence, 239–240	318-319, 321-322
Candidate gene, 296	C-reactive protein (CRP), 7
Cannabinoid receptor 1 (Cb1) gene, 75	Creatine, 101, 103 <i>f</i>
Capillary electrophoresis time-of-flight mass	Crohn's disease, 385, 404
spectrometry (CETOFMS), 43	Cyberball game, 22
Cellular senescence, 157–158	CYP1A2, 488
Cellular studies, 440–443	CYP2C9, 490
glycogen synthase kinase-3\beta, 442-443	CYP2C19, 487, 489-490
mitochondrial-mediated pathway, 440-441	CYP2D6, 487-490
neurotrophic factors and associated	CYP3A4, 488
pathway, 441-442	CYP3A5, 488
Central nervous system (CNS), 385-387,	Cytochrome P450 (CYP), 486-487
405-406, 410-413	Cytokines, pro-inflammatory, 161
Cerebrospinal fluid, mitochondrial	_
dysfunction, 144	D
C—G dinucleotides (CpG), 267–268, 277	Damage-associated molecular patterns
Cho, 100–101	(DAMPs), 175–176
Choline, 100–101, 103 <i>f</i>	Dbp gene, 70
Chronic mild stress, 73, 74 <i>t</i>	Default mode network (DMN), 445-446
Chronic progressive external ophthalmoplegia	Deficient social cognition, 21–23
(CPEO), 145	Deoxyribonucleic acid (DNA), 267–269
Chronic restraint stress, 73–74	Depression
Circadian biomarkers of bipolar disorder,	animal models of, 72–75
349–351	environmental models, 72–74
future research, 355–356	chronic mild stress, 73, 74 <i>t</i>
light sensitivity, 351	chronic restraint stress, 73–74
objectively measured sleep, activity/	maternal deprivation/separation, 72–73
circadian rhythms, 351–354	genetic models of, 75
circadian rhythms, 353–354	Bdnf and Trkb genes, 75
motor activity, 352–353	Cb1 gene, 75
sleep, 352	Tph2 gene, 75
endophenotypes for BD, 354–355	pharmacological models of, 74
sleep characteristics, 349–351	corticosterone, 74
Circadian locomotor output cycles protein	surgical model of, 74–75
kaput (CLOCK), 68	olfactory bulbectomy, 74–75

Depressive-like behavior assessment, in animals, 76–77, 78t	Environmental models of depression, 72–74 chronic mild stress, 73, 74 <i>t</i>
forced swimming test, 76	chronic restraint stress, 73–74
tail suspension test, 76	maternal deprivation/separation, 72–73
sweet food consumption test, 76–77 splash test, 77	Enzyme-linked immunosorbent assay (ELISA), 460
Dexamethasone suppression test (DST),	Epigenetic alterations, biological aging,
320-321, 322 <i>t</i>	158-159
Diacylglycerol (DAG), 333–335	Epstein—Barr virus, 295
Diffusion tensor imaging (DTI), 26, 83–84,	ERK/MAPK pathway, 441–442
444–445	Excellent lithium responders, 294–295
DNA damage and affective states, 367–369	Extensive or normal metabolizers, 485–486
DNA damage and repair mechanisms,	F
363–364	-
DNA damage, biological aging, 158–159	Fecal microbiota transplantation (FMT),
DNA damage markers, 364–366, 365 <i>f</i>	414–415, 419, 421–422
DNA damage/repair mechanisms, 363–364	Fever therapy, 191–192
DNA methylation, 268–269, 279 <i>t</i> , 284 <i>t</i>	Fine mapping, 129–130
analysis, sample source for, 269	5-HTTLPR, 492
and animal and preclinical model studies of, 283–285	Food and Drug Administration (FDA), 486–487, 491
and bipolar disorder diagnosis, 270-278	Forced swimming test, 76
global methylation studies, 270	Functional magnetic resonance imaging
whole-genome analyses, 270–276, 274t	(fMRI), 63
gene-specific analyses, 271t, 276-278	
measurement of, 268-269	G
role in bipolar disorder, 269–270 and treatment response in bipolar disorder,	Gamma-aminobutyric acid (GABA), 96–98, 99 <i>f</i> , 388–389
278-283	Gas chromatography-mass spectroscopy (GC
gene-specific studies, 281-283	MS), 40–41
global methylation, 278–281	Gastrointestinal dysfunction
whole-genome analyses, 281	and inflammation, 404, 405f
DNA repair markers, 369–372	in psychiatric disorders, 404-406
Dopamine transporter (DAT), 68	Gastrointestinal tract, 385–386
Dorsal PFC (DPFC), 257–258	Gclm, 215–217
DRD2, 492	Gene-specific analyses, 276-278, 281-283
Drug discovery research, mitochondrial	Genetic factors, 351
dysfunction, 149	Genetic models, of depression, 75
Drug metabolism, 486–490	Bdnf and Trkb genes, 75
Drugs development targeting gsk-3β, 447–449	cannabinoid receptor 1 (<i>Cb1</i>) gene, 75 tryptophan hydroxylase 2 (<i>Tph2</i>) gene, 75
DSM-5 classification, 167–168	Genetic models, of mania, 64, 68–70
Dysbiosis, 403–404	Ank3 gene, 69
E	Atpla3 gene, 69
	Clock gene, 68
8-oxo-dG, quantification of, 366–367 Electroencephalography (EEG), 63, 223–226,	Dat gene, 68 Dbp gene, 70
225t	Grik2 gene, 69
Endophenotype approach, 255–257, 354–355	Gsk-3 gene, 69–70
Enteric nervous system (ENS), 410–412	Shank3 gene, 68–69
Environmental animal models, 64–66 paradoxical sleep deprivation, 65–66	Genetics, mitochondrial dysfunction, 144–145

Genome-wide association studies (GWAS),	Harvard Brain Bank, 146
5-6, 126-127, 231, 296-298, 351,	Hayling Sentence Completion Task (HSCT),
461-472, 490-491	257-258
challenges and opportunities for next era,	Healthy controls (HC), 258-261, 472-474
134-135	High-dimensionality (H-D), 476
common variant heritability and	Hippocampus, 86–87
coheritability, 130	HLA-B*15:02 allele, 491
fine mapping, 129–130	Homocysteine, 7
heritability and family studies, 126	Homologous recombination, 364
Manhattan plot, 128f	Hormonal mechanisms, 350
missing heritability, 133	Hormones, 160
pharmacogenetics, 133-134	HTR2C, 492
polygenic risk scores, 131-133, 132f	Human genome, 126-127, 485
recent results of, 127-129	Human gut microbiota, 386-387, 406-410
Genomic instability, biological aging,	Human studies, 415-416
158-159	Humoral theory, 191
Germ-free (GF) animal studies, 413-414	Humors, 191
Germ-free mice (GFM), 389-390	Hydrophilic interaction liquid
Global methylation, 270, 278-281	chromatography-high resolution mass
Glucocorticoid receptors (GRs), 314-315	spectrometry (HILIC-HRMS), 43
GluD1, 215-217	Hypothalamus—pituitary—adrenal (HPA)
Glutamate decarboxylase-like protein	axis, 202, 203f, 313-316, 315f,
(GADL1), 296-297	322-325, 385-386, 410, 412
Glutamate receptor-based biomarkers,	dysregulation, 176-177
227–232, 228 <i>t</i>	
ionotropic, 227-231	I
metabotropic, 231-232	Iatrogenic poor phenotype, 488-489
Glutamate, 96–98	Iba1-IR microglia/macrophages, 28-29
Glutamate-based dysfunction	Illumina HumanMethylation, 268-269
clinical, 219–232	Immune system, 192–194, 193 <i>f</i>
electroencephalography, 223-226, 225t	Immunoassay methods, 460
glutamate receptor-based biomarkers,	Independent component analyses (ICA), 24
227-232	Induced pluripotent stem cells (iPSCs), 295
magnetic resonance spectroscopy,	Ingenuity pathway analysis (IPA), 461-472,
219–223, 221 <i>t</i>	475
positron emission tomography, 226-227	INSIG2, 492
preclinical, 215-219	Insulin signaling, 176–177
treatment, 233–241, 234t	Insulin-like growth factor binding protein
ketamine, 237–241	(IGFBP3 and IGFBP5), 473-474
lamotrigine, 233–236	Intercellular communication, 160-161
riluzole, 236–237	Intermediate metabolizers, 485-486
Glutamatergic hyperactivity, 96-98	Intermediate phenotype, 255–256
Glutamine, 96–98	
Glycogen synthase kinase-3β, 442–443	International Society for Bipolar Disorders
J	International Society for Bipolar Disorders Task Force, 240–241
GNB3, 492	
	Task Force, 240-241
GNB3, 492	Task Force, 240–241 Intracellular signaling abnormalities, 102–104
GNB3, 492 Graph theory model, 24	Task Force, 240–241 Intracellular signaling abnormalities, 102–104 myo-inositol, 102–104, 105 <i>f</i>
GNB3, 492 Graph theory model, 24 <i>Grik</i> 2 gene, 69, 215–217	Task Force, 240–241 Intracellular signaling abnormalities, 102–104 myo-inositol, 102–104, 105f Intracellular signaling cascades brain-derived neurotrophic factor, 337–338 calcium signaling, 331–333
GNB3, 492 Graph theory model, 24 <i>Grik</i> 2 gene, 69, 215–217 <i>Gsk</i> -3 gene, 69–70 GSK3- β/Wnt pathways, 335–337	Task Force, 240–241 Intracellular signaling abnormalities, 102–104 myo-inositol, 102–104, 105f Intracellular signaling cascades brain-derived neurotrophic factor, 337–338
GNB3, 492 Graph theory model, 24 <i>Grik</i> 2 gene, 69, 215–217 <i>Gsk-</i> 3 gene, 69–70	Task Force, 240–241 Intracellular signaling abnormalities, 102–104 myo-inositol, 102–104, 105f Intracellular signaling cascades brain-derived neurotrophic factor, 337–338 calcium signaling, 331–333

mitochondrial dysfunction, 338–339	intracellular signaling abnormalities,
iPS cell model, mitochondrial dysfunction,	102-104
149–150	mitochondrial dysfunction and neuronal
Irritable bowel disease (IBD), 404, 415–416,	alterations, 98–102
419–420	proton Mrs, 95–96
Irritable bowel syndrome (IBS), 404–405,	Magnetoencephalography (MEG), 63
412	Major depressive disorder (MDD), 22,
Isobaric tags for relative and absolute	200–201, 350–353, 355, 414–417,
quantitation (iTRAQ)	461, 473–475, 485, 488–490
K	Malaria therapy, 191–192
	Mania, animal models of, 65–70
Ketamine, 237–241	environmental models, 65–66
Kindling theory, 169	genetic models, 68–70
defined, 67–68	pharmacological models, 66–67
KIT-ligand (KITLG), 473–474	surgical model, 67–68 Mania-like behavior assessment, in animals,
L	70-72
Lactate, 101–102, 103 <i>f</i>	delayed discounting task, 71
Lactate, 101–102, 103 <i>y</i> Lamotrigine, 233–236	open-field test, 70–71
carbamazepine, 491	hyperactivity, 70
LARS2 (mitochondrial leucyl-tRNA	risk-taking behavior, 71
synthetase), 146–147	sexual behavior, 71
Lateral hypothalamic kindling model,	stereotypy, 70
67–68	resident—intruder test, 71
Light sensitivity, 351	sexual behavior test, 72
Linkage disequilibrium (LD), 127	Mass spectrometry (MS), 460–461
Lipopolysaccharide (LPS), 405–406	Maternal deprivation/separation, 72–73
Liquid chromatography-mass spectroscopy	Matrix-assisted laser desorption/ionization-
(LC-MS), 40–41, 461	time of flight (MALDI-TOF/TOF),
Lithium (Li), 491	461
for BD treatment, 63	MC4R, 492
efficacy, 293-294	Metabolic fingerprinting, 40
Lithium prophylaxis efficacy, biomarkers of,	Metabolite abnormalities, in BD, 96-104
294-299	glutamatergic hyperactivity, 96-98
Lymphocytes, 197	intracellular signaling abnormalities,
	102-104
M	myo-inositol, 102-104, 105f
Machine learning model, 115–116, 116 <i>t</i> , 117 <i>f</i>	mitochondrial dysfunction and neuronal
for suicidality prediction, 119	alterations, 98–102
supervised learning, 121	choline, 100–101, 103 <i>f</i>
for treatment selection, 120	creatine, 101, 103 <i>f</i>
unsupervised learning, 121	lactate, $101-102$, $103f$
Macrophages, 28–29	N-acetyl-aspartate, 98–100, 103f
Magnetic resonance imaging (MRI),	Metabolomics
444–445, 447	in bipolar disorder, 42–51
Magnetic resonance spectroscopy (MRS),	blood/urine metabolomic analyses,
glutamate-based dysfunction,	44–49, 45 <i>t</i> , 50 <i>f</i>
219–223, 221 <i>t</i>	brain tissue/cerebrospinal fluid
brain regions involved in cognitive and	metabolomics analysis, 42–44 future directions of, 51–53
affective regulation, 104–106, 106 <i>t</i> metabolite abnormalities in, 96–104	defined, 39
glutamatergic hyperactivity, 96–98	in psychiatric disorders, 39–41
gratamatergic hyperactivity, 90-98	iii psycillaute disorders, 39–41

Metabolomics (Continued)	N-acetyl-aspartate, 98–100, 103f
targeted, 39-40	Mitochondrial permeability transition pore
untargeted, 39-40	(mPTP), 149
Methylation DNA immunoprecipitation	Mitochondrial-mediated pathway, 440-441
(MeDIP), 270–276	Monoamine dysregulation, 66
Microbiome and bipolar disorder	Monocyte to lymphocyte ratio (MLR),
microbiota-gut-brain axis, 385-396	197-198
and mental health, 388-389	Montgomery Åsberg Depression Rating Scale
biomarker of treatment response in,	233-236
395-396	Motor activity, 352–353
consequences of, 387–388	Multisystem inflammatory disease, 403-404
diagnostic biomarker for, 391-394	Myo-inositol, 102–104, 105f
differential diagnosis biomarker for,	
394-395	N
mood state biomarker for, 394	N-acetyl-aspartate (NAA), 98–100
tools, 389–391	The National Center for Biotechnology
Microbiome-gut-brain (MGB) axis, 410-413,	Information (NCBI), 485-486
411 <i>f</i> , 416	Near infrared spectroscopy (NIRS), 63
Microbiota-gut-brain axis (MGBA), 385-396,	Neuregulin (NRG1) gene, 295-296
387f, 390f	Neurocognitive endophenotypes, 257–263
Microglia, 28–29	affective cognition, 260-261
Microglial activation, 196-197	cognitive dysfunctions, 253-255
Micro-RNA (miR), 298	endophenotypes, concept of, 255-257
Mineralocorticoid receptors (MRs), 314-315	limitations of, 261–263
glucocorticoid receptors, 316-320, 318f,	Neurocognitive studies, of suicidal behavior,
318t, 319t	20-27
Mismatch negativity (MMN), 224-226	cognitive processes, 23
Mismatch repair, 364	deficient social cognition, 21-23
Missing heritability, 133	neuroimaging studies for classification, 26
Mitochondria dysfunction, 159-160	pharmacological neuroimaging studies, 25
Mitochondrial DNA (mtDNA), 141-142	resting state neuroimaging studies, 24-25
damage and repair, 372-373	risky decision-making, 20-21
Mitochondrial dysfunction	structural neuroimaging studies, 25-26
action mechanisms of antibipolar drugs,	tentative neuroanatomical summary of
150-151	suicidal acts, 26-27
animal models, 147–149	Neurodegeneration vs. neuroplasticity,
cellular models, 142-144	173-174
cerebrospinal fluid, 144	Neuroendocrine and stress pathways
drug discovery research, 149	hypothalamus—pituitary—adrenal axis,
genetics, 144–145	314-316
iPS cell model, 149–150	mineralocorticoid receptors/glucocorticoid
molecular and cellular pathogenesis in	receptors, 316–320
PVT, 150–151	neuroendocrine function test, 320-323
neural circuits around PVT, 151	psychoneuroendocrine progression of, 324t
postmortem brains, 146-147	steroid hormones, 316
proposal of mitochondrial hypothesis,	stress, 324–325
141-142	Neuroendocrine function test, 320–323
Mitochondrial dysfunction and neuronal	Neuroimaging markers, in psychiatry, 82
alterations, 98-102	Neuroimaging studies, 444-447
choline, 100–101, 103f	diffusion tensor imaging, 444-445
creatine, 101, 103f	drugs development targeting gsk- 3β ,
lactate, 101–102, 103 <i>f</i>	447-449

neuroinflammation, 446-447	Noninvasive functional imaging technologies,
resting-state functional magnetic resonance	63
imaging, 445–446	Nonsteroidal antiinflammatory drugs, 204
structural magnetic resonance imaging, 444	Nuclear magnetic resonance (NMR)
Neuroimmune pathways	spectroscopy, 40–41
evidence of immune dysfunction,	Nucleotide excision repair (NER), 364
194-200	1 (),
circulating levels of immune markers,	0
199-200	O-desmethylvenlafaxine, 489
clinical evidence, 195-196	Olfactory bulbectomy, 74–75
genetic evidence, 194-195	"OMICS", 475–476
immune cells (total count, phenotype,	Operational taxonomic unit (OTU), 410
and function), 197–199	Orbitofrontal cortex, 86
inflammatory markers in central nervous	Ouabain (OUA), 67
system, 196–197	Oxidative stress, 362–363
microglial activation, 196-197	
immune-based strategies, 204-205	P
immune (cerebrospinal fluid and blood)	Paradoxical sleep deprivation, 65-66
markers of diagnosis, 200-201	Paraventricular thalamic nucleus (PVT),
immune markers as predictors, 205	147–148, 148 <i>f</i>
immune system, 192–194, 193 <i>f</i>	molecular and cellular pathogenesis in,
integrating immune dysfunction with of	150-151
bipolar disorder, 201-204	neural circuits around, 151
Neuroinflammation, 446-447	Parkinson's disease (PD), 147-148, 414-415
Neuroprogression, in bipolar disorder	Peripheral blood, proteome characterization
biological basis of, 171-177	of, 461–472
hypothalamic—pituitary—adrenal axis	Pharmacodynamics, 133–134
dysregulation, 176–177	Pharmacogenetics, 133-134
insulin signaling, 176–177	Pharmacogenomics
molecular changes associated with	of drugs commonly used in bipolar
progression of illness, 175–176	disorder, 490–492
neuroanatomical changes, 171-173	antidepressants, 492
neurodegeneration vs. neuroplasticity,	atypical antipsychotics, 492
173-174	lamotrigine and carbamazepine, 491
clinical evidence of, 169–171	lithium, 491
clinical features, 169-170	valproic acid, 490-491
functioning, 171	and genetic variation, 485–486
neurocognitive changes, 170–171	pharmacokinetic, 486–490
evidence of, 168	CYP2C19, 489-490
future perspectives, 177–178	CYP2C9, 490
Neuropsychiatric disorders, microbiome-gut-	CYP2D6, 487–489
brain-axis findings in, 413–415	Pharmacokinetic, 133–134, 486–490
Neurotrophic factors/associated pathway,	Pharmacological animal models, 64
441-442	amphetamines, 66
Neurotrophins, 337	ouabain, 67
Neutrophil to lymphocyte ratio (NLR),	Pharmacological models, of depression, 74
197–198	corticosterone, 74
Neutrophils, 197	Pharmacological neuroimaging studies, 25
NIMH Family Study, 353–355, 355 <i>t</i>	Pharmacometabolomics of bipolar disorder,
N-methyl-D-aspartate receptors (NMDARs),	49–51
196, 227	Plasticity, 439–440, 440 <i>f</i>
Nonhomologous end-joining (NHEJ), 364	Platelet to lymphocyte ratio (PLR), 197–198

Pneumoencephalography, 81–82 Polygenic risk scores (PRS), 131–133, 132 <i>f</i>	Quantitative trait loci (QTL) mapping studies, 129–130
Polymorphism XBP1—116 C/G, 490–491 Poor metabolizers, 485–486	R
Positron emission tomography (PET), 22–23, 63, 447	Radioimmunoassay (RIA), 320–321 Rapid and ultrarapid metabolizers, 485–486
glutamate-based dysfunction, 226–227	Rapid eye movement (REM) sleep, 224–226
Postmortem brain research, exploring cellular/	Receiver operative characteristic area under
molecular roots of suicide, 27-30	the curve (ROC-AUC), 473
evidence of activated microglia/	Red blood cells (RBC), 331–332
macrophages, 28–29	Reducing the noise, 256–257
inflammation/cognition, 30	Refining the genetic signal, 256–257
molecular evidence of increased	Renin—angiotensin—aldosterone system
inflammation in depression/suicide, 29	(RAAS), 313
Postmortem brains, mitochondrial	Resting state neuroimaging studies, 24–25
dysfunction, 146–147	Resting-state functional magnetic resonance
Prebiotics, 420–421	imaging (rs-fMRI), 445-446
Precision Medicine Initiative, 483	Ribonucleic acid-based (RNA), 267–268
Precision psychiatry, 484f	Riluzole, 236–237
in bipolar disorder	Risk biomarkers, 5–6
diagnosis and differential diagnosis, 116–118	Risky decision-making, in suicide attempters, 20–21
prognosis prediction, 118-119	Rodent sexual behavior test, 72
suicidality prediction, 119	
treatment selection, 120-121	S
supervised/unsupervised learning, 121 Prednisolone, 322	Schizophrenia (SZ), 200–201, 461, 473, 475 <i>vs.</i> bipolar disorder, 84–85
Prednisolone suppression test (PST), 322, 322t	SCN2A, 490-491
Prefrontal cortex (PFC), 440-441, 444	Search engines, 460–461
Prognostic biomarkers, 8	Second-generation antipsychotics (SGA), 50
Protein kinase C (PKC), 333-335, 337	Selective serotonin reuptake inhibitors
Proteome, 459-460	(SSRIs), 489–490
Proteomic biomarkers for bipolar disorder	Senator, Hermann, 385
biological processes and pathways, 475	Shank3, 68-69, 215-217
blood serum and plasma-based	Short-chain fatty acids (SCFAs), 412-413,
investigations of, 462t	420-421
current status, 472-473	Shotgun proteomics, 460–461
differentially abundant proteins, 473–475 "OMICS," future of, 475–476	Single-nucleotide polymorphisms (SNPs), 8, 295–298, 485–486
peripheral blood, proteome characterization of, 461–472, 462 <i>t</i>	Single-photon emission computed tomography (SPECT), 22–23
proteomic techniques, development of,	16S rRNA gene, 390-391
460-461	SLC6A4, 492
Proton magnetic resonance spectroscopy (¹ H-	Sleep, 352
Mrs), 95–96	characteristics, 349–351
Psychiatric disorders, gastrointestinal	Sleep-wake cycle, 350
dysfunction in, 404–406	SNAP25, 492
The Psychiatric Genomics Consortium, 8	Sodium, potassium-activated adenosine
- -	triphosphatase (Na/K-ATPase), 67
Q	Splash test, 77
Quantitative Insights Into Microbial Ecology	Stage biomarkers, 7–8
(QIIME), 390–391	State/acuity biomarker, 7

Steroid hormones, 316 Structural magnetic resonance imaging, 444 Structural neuroimaging markers, in bipolar disorder, 82–84 bipolar disorder vs. schizophrenia, 84–85 vs. unipolar depression, 85–87 biomarker, 82 diffusion tensor imaging, 83–84 existing literature, overview of, 83 in high-risk populations, 87–88 neuroimaging markers, in psychiatry, 82 as tool to improve diagnostic accuracy, 84–87 Subclinical trait, 255–256 Suicidality, 24–25 Suicide attempters, risky decision-making in, 20–21 Supervised learning, 121 Surgical models of depression, 74–75 olfactory bulbectomy, 74–75 of mania, 64 lateral hypothalamic kindling, 67–68 Sweet food consumption test, 76–77 Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study, 171, 492	Taxonomic level analyses, 417–418 Telomere attrition, 157–158 Thyroid-stimulating hormone (TSH), 295 Timeless circadian clock (TIM) gene, 296–297 Toll-like receptors (TLRs), 175–176 Translocation, 404–406 Treatment, 419–422 Treatment response biomarker, 8–9 Trkb gene, 75 Tryptophan hydroxylase 2 (Tph2) gene, 75 Tumor necrosis factor alpha (TNF-α), 412–413 U Unipolar depression vs. bipolar disorder, 85–87 Unsupervised learning, 121 V Valproic acid (VPA), 490–491 Vasopressin (AVP), 314, 318–319 Ventral prefrontal cortex (VPFC), 257–258 Vulnerability marker, 255–256 W Whole-genome analyses, 270–276, 281 Wisconsin Card Sorting Test, 257–258
Tail suspension test, 76 Tandem mass tag (TMT), 472–473 Targeted proteomics, 461	Y Young Mania Rating Scale (YMRS), 240–241