Index

N-acetyl aspartate in ADHD 394 in obsessive-compulsive disorder 397-398, 399 in schizophrenia 380 predictive value 444 ADHD see attention-deficit hyperactivity disorder adolescence 70, 445-446, 447, 458 at-risk population studies 445-446, 447 brain development 70-75 myelination 71, 332 synapse elimination 70-71, 458, 462 cognitive development 69, 72-75, 82-83 executive functions 73-74 etiological factors 462-463 sequelae of preterm birth 94-96 affective disorders 390, 391 see also bipolar disorder; depression African-Caribbeans in the UK 234-235 unemployment 236 age of onset 274 possible origins of delayed onset 279-281 sex differences 331 alpha-linolenic acid 160 see also essential polyunsaturated fatty acids D-amino acid oxidase (DAOO) gene 24 amisulpiride 465 amphetamine psychosis 250-251 genetic determinants 254 sensitization 260-261, 273 amygdala 404-405 in bipolar disorder 112, 402, 404-405 in major depressive disorder 401-402 role in limbic lobe changes 298-299 fiber ingrowth into anterior cingulate cortex 302, 303-304 "mis-wired" circuit model 297, 304-305 sex differences 41 stress and emotional reactivity and 275, 276

amygdala-hippocampal complex (AHC) volume changes 359 in high-risk population 350-351 in unaffected relatives 358 see also amygdala; hippocampus Angelman syndrome 184 antecedents of schizophrenia see predictors of schizophrenia anterior cingulate 304 amygdalar fiber ingrowth 302, 303-304 dopamine input distribution 297-298 excitatory fiber changes 297, 298-299 in obsessive-compulsive disorder 396, 398, 404-405 anticipation, genetic 339 antidepressants 466 antioxidants 158-159 dietary supplementation 163-164, 165, 467 when and what to treat 166 antipsychotic drugs adverse effects 159 anti/pro-oxidant properties 164 efficacy 159 secondary prevention strategies 465 antisaccade task performance 53-55 apoL lipoprotein 219-220 apoptosis 162 neuropathological role 377-378, 382 synaptic 377-378 see also synaptic pruning arachidonic acid (AA) 160 in schizophrenia 160, 162 role in membrane signal transduction 161-162 role in neurodevelopment 160-161 see also essential polyunsaturated fatty acids arborization 39-40 arcuate fasciculus 38

Index

Cambridge University Press 0521823315 - Neurodevelopment and Schizophrenia Edited by Matcheri S. Keshavan, James L. Kennedy and Robin M. Murray Index More information

> at-risk populations see high-risk population studies attention-deficit hyperactivity disorder (ADHD) 40, 98, 390, 391-398 common neuropathology 391-398, 402-405 genetic basis 402-403 neuroimaging studies 57, 392-395 frontostriatal circuitry 393-395 total cerebral volume 392-393, 394 nutritional factors 166 role of basal ganglia 98 with velo-cardio-facial syndrome 124 attentional processes development 75 attentional set-shifting ability 74-75, 80-81 in schizophrenia 80-81 structural correlates 76-77 dysfunction as predictor of schizophrenia 423, 442-443 see also cognitive development; cognitive dysfunction attenuated psychotic symptoms 445, 457 see also prodromal phase automatic rerouting 100-101 Barrington's nucleus 276 basal ganglia in ADHD 98 in obsessive-compulsive disorder 399-400 in schizophrenia 141 sex differences 40-41 BDNF see brain-derived neurotrophic factor behavior conduct disorder 256-257 consequences of preterm birth 97 drug abuse and 255-257 in velo-cardio-facial syndrome 124-125 predictors of schizophrenia 425-426, 428, 437-438 archival-observational studies 428 high-risk studies 427 population-based studies 425-427 see also obsessive-compulsive disorder bipolar disorder (BPD) 390, 391-398 common neuropathology 112-113, 390, 391, 403, 404-405 genetic basis 403 neuroimaging studies 400-402 frontal cortex 401 medial temporal cortex 401-402 total brain volume 400-401

postmortem findings 295-298 dopamine system 297-298 GABA system 296-297 boxcar design 48-49 brain aging 332-333 sex differences 40-41, 331-333 structural abnormalities as potential endophenotypes 139 epigenetic model and 187 in ADHD 392-395 in obsessive-compulsive disorder 395-400 in schizophrenia 141-142, 174, 347-348, 350, 415 in unaffected relatives 143-148 in velo-cardio-facial syndrome 129-131 molecular genetics 148-149 predictive value 443-444 progressive structural changes 142, 379, 381, 459 state versus trait 142-143 see also premorbid structural abnormalities; specific abnormalities structural heritability 139-141 structure and function relationship 97-98 remapping following brain injury 100 see also plasticity total brain size 35-36, 40 in bipolar disorder 400-401 in high-risk population 351-352 in major depressive disorder 400-401 in obsessive-compulsive disorder 396 in unaffected relatives 145 in velo-cardio-facial syndrome 129 progressive decline 379-380 see also brain development; brain injury; central nervous system brain-derived neurotrophic factor (BDNF) 13, 15, 216, 258, 335 BDNF gene 17 brain morphometry and 149 changes in schizophrenia 16 expression 16 brain development 5-6, 39, 330, 332-335 aberrations 77-82, 142-143 animal models 278-279 childhood injury 78 developmental lesions 78-79 epigenetic model and 180–181 etiological factors 462-463

475 Index

impact of 77-79 in schizophrenia 72, 79-82, 174-175, 278 predictive value 443-444 sequelae of preterm birth 94-96 see also premorbid structural abnormalities brain function 45 electroencephalography studies 47 fMRI studies 47-55, 56-57 language development 56-57, 89-90 PET studies 47 cell adhesion 10-14 cognitive development relationships 75-77, 83 see also cognitive development corpus callosum 38 critical periods 90, 445-446 dopaminergic system 334 during adolescence 70-75 myelination 71, 332 synapse elimination 70-71, 458, 462 estrogen role 334-335 genetic basis 6-8 epigenetic factors 185 see also transcriptomes gray matter 39-40 MDN-DLPFC circuitry 311, 317-321 nutrition role 158 essential polyunsaturated fatty acids 160-161 schizophrenia as model 79-82 segmentation 8-10 serotonergic system 333-334 sex differences 332-333 aging 332-333 estrogen role 334-335 myelination 332 social factors 239 animal models 224-226 see also limbic lobe; neurodevelopmental model; plasticity brain injury childhood injury 78 following preterm birth 92 consequences of persisting abnormality 96-97 patterns of 93-94 prevalence 94 sequelae in adolescents 94-96 University College Hospital London Study 92-93 perinatal, drug abuse and 260 plasticity after 91-92, 99-101 at the connectivity level 100-101

at the neural network level 99-100 at the neuronal level 99 Kennard principle 91 limits of 101 remapping of functions 100 rerouting 100-101 see also obstetric complications breast-feeding 162 Brn-1 transcription factor 10 Brn-2 transcription factor 10 Broca, Paul 91 Broca's area 38 language function 56, 91 cadherins 10-12 cadherin motif 10-11 cadherin neuronal-related receptors (CNRs) 11-12 seven-pass transmembrane cadherins 11 Cajal-Retzius neurons 14 Cambridge Neuropsychological Test Automated Battery (CANTAB) 73 cannabis-induced psychosis 251-253, 257 sensitization 260-261 CATCH 22 (cardiac anomalies, abnormal facies, thymic hypoplasia, cleft palate, and hypocalcemia) 123 see also velo-cardio-facial syndrome catechol-O-methyltransferase 128 COMT gene 127, 128, 403 in bipolar disorder 403 methamphetamine abuse and 259 polymorphisms 128 caudate nuclei ADHD and 98, 395 in obsessive-compulsive disorder 399-400 cell adhesion 10-14 cell adhesion molecules (CAMs) 10-13 cadherin superfamily 10-12 immunoglobulin superfamily (IgSF) 10, 12-13 NCAM 12-13 cell differentiation 180 embryonic cells 181, 182 central nervous system (CNS) development 3 cell adhesion 10-14 genetic mechanisms 3, 6-8 neuronal survival 14-18 neurulation 5-8 segmentation 8-10 see also brain development

Index

Cambridge University Press 0521823315 - Neurodevelopment and Schizophrenia Edited by Matcheri S. Keshavan, James L. Kennedy and Robin M. Murray Index More information

> cerebellar cognitive-affective syndrome 98 cerebellum in ADHD 395 in velo-cardio-facial syndrome 129, 130 sequelae of preterm birth 95 consequences 98 cerebral atrophy, following preterm birth 94 cerebral blood flow (CBF), estrogen effect 336 cerebral cortex, asynchronous development 332 see also brain development cerebral volume 37 heritability 140 in ADHD 392-393, 394 in schizophrenia 141 in unaffected relatives 145-146 IQ relationship 36 sex differences 40 cerebrospinal fluid (CSF), sulcal spaces 145-146, 355 chandelier neurons 320-321 abnormalities in schizophrenia 323-324 childhood abuse 228-229, 239 childhood antecedents see predictors of schizophrenia childhood behavior see behavior childhood neuroimaging see pediatric neuroimaging chromosome 22q11.2 deletion 126-127 see also velo-cardio-facial syndrome ciliary neurotrophic factor (CNTF) 18 cingulate 404-405 see also anterior cingulate city of birth effect 191, 230 city of upbringing effect 230 civilization 157 clinical high-risk studies 438-439 see also high-risk population studies cloning studies 184 clozapine 467 cocaine-induced psychosis 259 sensitization 260 cognition 72 estrogen effect 335-336, 337, 338 social cognition 339 see also cognitive development; cognitive dysfunction cognitive behavioral therapy (CBT) 465, 466 cognitive development 46-47, 69-70, 82, 311 cerebral development relationships 75-77, 83

during adolescence 69, 72-75, 82-83 executive functions 73-74 early brain lesion effects 79 pediatric fMRI studies 47-55 schizophrenia as model 79-82 voluntary response suppression 51-55 working memory 49-51, 73 in schizophrenia 80-81 structural correlates 76 see also attentional processes; executive functions cognitive dysfunction 310 glutamate role 460-461 in velo-cardio-facial syndrome 123-124 predictive value 419-425, 442-443, 458 high-risk studies 423-425 population-based studies 419-423 premorbid phase 376, 455-457 progressive impairment 375-376, 381 social factors 238 see also working memory cohort studies 433-434 communal upbringing 227-228 communication deviance in parents 227 complexins 22 complexin I 22 complexin II 22 COMT see catechol-O-methyl transferase conduct disorder 256-257 conotruncal anomaly face syndrome 123 see also velo-cardio-facial syndrome coordination problems 417-418 Copenhagen High-Risk Project 350, 354, 361, 363 corpus callosum (CC) 36-38 development 38 function 38 in ADHD 395 in bipolar disorder 402 in depression 402 in obsessive-compulsive disorder 400 in unaffected relatives 147 sex differences 331-332 thinning following preterm birth 95 consequences 98 cortical dysgenesis 129 cortical volume reduction 111-112 animal model 279 corticotropin-releasing factor (CRF) 113-114, 115 stress response 275-276

477 Index

cortisol 116 in major depression 113, 116 in schizophrenia 115 critical periods of development 90, 445-446 for learning 90 cultural differences ethnic minority status 233-234 methodological issues 234 nutrition 157 schizophrenia outcome 157-158 DA see dopamine DAOO gene 24 deficit syndrome 375 deletion 22q11.2 see chromosome 22q11.2 deletion Delta gene 6-7 delta sleep 458 dementia praecox 373 depression common neuropathology 112-113 cortisol role 116 glucocorticoid-related neurotoxicity 113 hypothalamic-pituitary-adrenal axis abnormalities 113-114, 115-116 see also major depression deprivation 237 development CNS 3 critical periods 90, 445-446 epigenetic factors 179-187 see also brain development; neurodevelopmental model developmental compensation see plasticity developmental delays in velo-cardio-facial syndrome 123-124, 174 predictive value 418 diencephalon 6 diet see nutrition dietary supplementation see nutritional strategies diffusion tensor imaging (DTI) 36, 61-62 DiGeorge syndrome 123 see also velo-cardio-facial syndrome discrimination 235-236, 239 dissociative identity disorder 229 distributed neural systems 36 dizygotic (DZ) twin studies see twin studies Dlx1 gene 9 Dlx2 gene 9 DNA demethylase 175

DNA methylation 175-177 during embryogenesis 182-183 cloned embryos 184 knockout models 184 maintenance 180-181 see also epigenetics DNA microarray studies 210-212 cDNA microarrays 211-212 future directions 220 synthetic oligonucleotide probe arrays 212 transcriptome assessment 210 data analysis and interpretation 214-215 experimental design 212-213 gene expression changes in schizophrenia 215-220 DNA methyltransferases 175 docosahexaenoic acid 160 dietary supplementation 163-165 in schizophrenia 160, 162 role in membrane signal transduction 161-162 role in neurodevelopment 160-161 see also essential polyunsaturated fatty acids dopamine (DA) system 281-285 D₁ receptor 461-462 D₂ receptor (DRD2) gene 258 D₃ receptor (DRD3) gene 258 D₄ receptor (DRD4) gene 258-259 development 301, 304, 334 late maturation of dopamine projections 301-303 estrogen effect 336-337 in ADHD 395, 403 in schizophrenia 273, 281-285, 402-403 glutamatergic effects 460-462 sensitization 261, 273 phasic dopamine levels 283 postmortem findings 297-298 regulation 281-285, 460-462 sensitization 260-261 in schizophrenia 261, 273 stress response 277, 281 tonic dopamine levels 283 dorsolateral prefrontal cortex (DLPFC) see MDN-DLPFC circuitry; prefrontal cortex drug abuse as cause of psychosis 250-254 amphetamine-induced psychosis 250-251 cannabis-induced psychosis 251-253

478

Index

drug abuse (<i>cont.</i>)	epigenetics 175–177, 180, 181
individual differences in liability 254	misregulation 185–187
LSD-induced psychosis 253–254	relevance to schizophrenia 178–179, 185–187
phencyclidine-induced psychosis 253	role in development 179–187
association with psychosis 248-249	see also DNA methylation; histone modification
childhood development and personality	ES2 gene 127
factors 255–257	essential fatty acids (EFAs) 158-159
familial predisposition 257–258	essential polyunsaturated fatty acids (EPUFAs)
direction of association 249-250	159, 160
common factor hypothesis 249–250	dietary intake 162–163
self-medication 249	dietary supplementation
vulnerability hypothesis 250	benefits 163–164, 166
dopamine sensitization 260-261	dose and quality of EPUFA 165
molecular genetic studies 258–260	duration of treatment 165
dopamine D ₂ receptor gene 258	placebo control 165
dopamine D ₃ receptor gene 258	preferred combination 165
dopamine D ₄ receptor gene 258–259	type of EPUFA 164–165
perinatal brain damage, animal models 260	when and what to treat 166
dysbindin gene 24	in schizophrenia 160, 162
dysfunctional family environment 227	role in membrane signal transduction
dyslexia, neuroimaging studies 57–58	161–162
	role in neurodevelopment 160–161
early parental loss 228	oxidative breakdown 163–164
early rearing environment 200	antioxidant benefits 163–164
economic deprivation 237	estrogen 334-337, 340-341
Edinburgh High Risk Study (EHRS) 350-351	effect on cognitive function 335–336, 337, 338
EF motif see cadherin motif	effect on dopaminergic function 336-337
eicosapentaenoic acid (EPA) 160	effect on serotonergic system 336
dietary supplementation 163–165	role in brain development 334–335
see also essential polyunsaturated fatty	therapeutic use 340
acids	estrogen receptors 335
electroencephalography (EEG), developmental	ethnic minority status see minority groups
studies 47	ethyleicosopentaenoic acid 466
embryogenesis 182–183, 184–185	N-ethylmaleimide-sensitive factor (NSF) 216
pluripotent cell differentiation 181, 182	evoked response potentials 438, 443
emotional reactivity 275–277	executive functions 72
Emx1 gene 9	development 46, 72–74
<i>Emx2</i> gene 9	attentional set-shifting ability 74–75, 80–81
endophenotypes 138–139	frontal lobe development and 75-76
cerebral volume 145–146	implications for neural development 80–81
frontal lobe 147	in adolescence 73–74
subcortical structures 146	see also cognitive development
temporal lobe 146	see also working memory
ventricular enlargement 144–145	expressed emotion 228
enhanced high-risk strategies 439–440, 446	
environmental risk factors see risk factors	family factors see social factors
epigenesis 179	family history 353–360
epigenetic inheritance system 177	CT studies 354–355
epigenetic landscape 180, 181, 185, 186	structural MRI studies 355–356
epigenetic metastability 177, 178, 179	famine see malnutrition

479 Index

α-fetoprotein 334–335 first-episode studies 432 FMR1 gene 184, 339 fold changes 214 follow-back studies 434 forebrain development 5-6 see also brain development fragile X syndrome 184, 339-340 frontal lobes cognitive development and 72, 75-76 in bipolar disorder 401 in major depressive disorder 401 in schizophrenia 349 in unaffected relatives 147 in velo-cardio-facial syndrome 129-130 outcome of frontal lesions 78-79 see also brain; brain development functional magnetic resonance imaging (fMRI) 47, 48 abnormal populations 57-59 ADHD 57, 394-395 dyslexia 57-58 pediatric schizophrenia 58-59 block design 48-49 cognitive development studies 47-55 voluntary response suppression 51-55, 77 working memory 49-51 event-related designs 49 language development studies 56-57 pediatric studies 49, 57-59, 63 challenges 59-61 see also magnetic resonance imaging (MRI); pediatric neuroimaging G72 gene 24 GABA membrane transporter (GAT1) 320 GABA system abnormalities in schizophrenia 298, 299, 323-324 "mis-wired" circuit model 297, 304-305

development 299–301, 304 gene expression changes 216 postmortem findings 296–297 gamma-aminobutyric acid see GABA gametogenesis 182 Gbx2 9 gender differences see sex differences gene–environment interaction 237–238, 447 general population cohort studies 433–434 genetic anticipation 339 genetic factors ADHD 402-403 bipolar disorder 403 obsessive-compulsive disorder 403 velo-cardio-facial syndrome 126-129 see also genetics of schizophrenia genetic high-risk populations 435-437 preventive intervention strategies 464 see also high-risk population studies genetics of schizophrenia 138-139, 273-274, 447 brain structure 148-149 epigenetic theory 178-179, 185-187 family history 353-360 gene expression changes 215-220 see also DNA microarray studies heritability 138, 435 imaging specific gene effects 358-360 multifactorial susceptibility model 138 neurodevelopmental mechanisms 3, 4, 24 epigenetic factors 175, 179-185 susceptibility gene identification 138, 217-218 see also epigenetics; X chromosome germinal matrix haemorrhage 93 glial cell loss 112 glial-cell-derived neurotrophic factor (GDNF) 17 - 18gliosis 377 β -globin gene regulation 182 glucocorticoids corticotropin-releasing factor regulation 114 glucocorticoid receptor (GR) 114, 116 mineralocorticoid receptor (MR) 114 neurotoxicity 113, 116 stress response 280-281 see also cortisol glutamate cognitive role 460-461 developmental role 460 neurodegeneration and 461 transmission 273 gene expression changes 216 see also glutamatergic system glutamate receptor 2 (AMPA2) 216, 219 glutamatergic system 459-462 glutamatergic fiber changes 298-299 in obsessive-compulsive disorder 398, 399-400 therapeutic strategies 466, 467 see also glutamate

480	Index	
	aluterria arid daeash anglasa (CAD) 20(-207-200	ann differenn ann 41
	glutamic acid decarboxylase (GAD) 296–297, 300, 323	sex differences 41 stress effects on 279–281
	525 microarray studies 216, 219	volume abnormalities 111, 112, 277
	glycine 466	genetic basis 148–149
	glycogen synthase kinase 3 β 8 gray matter 39–40	in high-risk population 351–352 in major depressive disorder 401–402
	e ,	in unaffected relatives 146
	developmental changes 39–40	neurotrophin 3 gene relationship 360
	during adolescence 71, 332 in major depressive disorder 401	obstetric complications and 358, 362
	in schizophrenia 130, 131, 349, 379	see also amygdala–hippocampal complex
	1	
	progressive loss 379, 381	histone modification 176–177, 181–182
	in ultra-high-risk population 352	valproic acid effects 184–185
	in velo-cardio-facial syndrome 131	see also epigenetics
	GSCL (goosecoid-like) gene 127	homeobox (<i>Hox</i>) genes 9
		Hoxb1 9
	haloperidol 298	homeodomain 9
	Hensen's node 5	hormone replacement therapy (HRT) see estr
	heritability	hydrocephalus 94
	of brain structure 139–141	hyperactivity 20, 98
	of schizophrenia 138, 435	hypofrontality 380
	see also genetics of schizophrenia	hypothalamic-pituitary-adrenal (HPA) axis
	high-risk population studies 350–353, 432–436,	abnormalities in major depression 113–114
	437, 440, 446–448	115–116
	adolescents 445–446, 447	abnormalities in schizophrenia 115–116
	behavioral predictors 427, 437–438	amygdala influence 275
	clinical high-risk strategies 438–439	hypothalamus, corticotropin-releasing factor
	Copenhagen High Risk Project 350	(CRF)
	Edinburgh High Risk Study 350–351	hypersecretion 113–114
	enhanced high-risk strategies 439–440, 446	hypoxia see obstetric complications
	follow-back studies 434	
	general population cohort studies 433-434	immunoglobulin superfamily (IgSF) 10, 11, 1
	genetic high-risk studies 435–437	NCAM 12–13
	Melbourne High Risk Study 351–353	inequality 237
	methodological issues 440-441	infections, as risk factors
	generalizability to schizophrenia 441	neonatal and childhood 194
	reliability of parental diagnoses 440	prenatal 193–194, 362
	specificity to schizophrenia 440-441	influenza 192–194
	neurobehavioral high-risk strategies 437–438	influenza, prenatal, as risk factor 192–194
	neurointegrative predictors 418	inheritance see genetics of schizophrenia;
	neuropsychological predictors 423-425	heritability
	retrospective studies 434	injury see brain injury
	structural imaging 353	integrative neurochemical model 459–462
	family history 353–360	intellectual capacity as predictor 419–420
	working memory 58–59, 274–275	intelligence quotient see IQ
	hindbrain development 5–6	interleukin-1 β gene 149
	see also brain development	intervention strategies 463-467
	hippocampus	after disease onset 467
	possible origins of delayed disease onset	premorbid phase 463–464
	279–281	at-risk populations 464
	sequelae of preterm birth 95	universal interventions 463-464

Index 481 prodromal phase 464-467 locus coeruleus low-dose atypical antipsychotic drugs 465 corticotropin-releasing hormone effects 276 naturalistic treatment studies 465-466 stress response 275, 276 LSD psychosis 229 non-antipsychotic medications 466 psychotherapeutic treatments 466-467 intraventricular haemorrhage, preterm birth and magnetic resonance imaging (MRI) 35, 48 93 region of interest (ROI) approach 349 IO risk factor studies brain size relationship 35-36 family history 355-356 decline during adolescence 82 velo-cardio-facial syndrome 129-131 following preterm birth 96-97 voxel-based morphometry (VBM) 349 in velo-cardio-facial syndrome 123, 124 see also functional magnetic resonance predictive value 419-420 imaging isolation of rearing 225 magnetic resonance spectroscopy (MRS) 62 see also social factors phosphorus-31 62, 380 major depressive disorder (MDD) 391-398 Kennard principle 91 common neuropathology 112-113 exceptions to 91-92 hypothalamic-pituitary-adrenal axis Krox20 gene 8-9 abnormalities 113-114, 115-116 neuroimaging studies 400-402 labor complications see obstetric frontal cortex 401 complications medial temporal cortex 401-402 lamotrigene 467 total brain volume 400-401 language development 56-57, 89-90 see also depression critical periods 89-90 malate dehydrogenase (MAD1) 217 developmental compensation following brain malnutrition 156, 158 injury 100-101 prenatal, as risk factor 194-195 remapping 100 see also nutrition rerouting 100-101 Mash1 gene 6 in velo-cardio-facial syndrome 123, 124 MDN-DLPFC (mediodorsal nucleus-dorsolateral predictive value 421 prefrontal cortex) circuitry 310, 312 learning, critical periods 90 development 311, 317-321 learning disabilities dysfunction in schizophrenia 321-324 in velo-cardio-facial syndrome 124 function 310-311 psychiatric disorders and 125 future directions 324-325 see also language development organization 313-317 life events 236-237 see also mediodorsal nucleus; prefrontal cortex; limbic lobe 295, 296 thalamus amygdala role in changes 298-299 MECP2 mutations 184 "mis-wired" circuit model 304-305 mediodorsal nucleus (MDN) 310 postnatal maturation of circuitry 299-304 volume reduction in schizophrenia 321, 322 amygdalar fiber ingrowth into anterior see also MDN-DLPFC circuitry; thalamus cingulate cortex 303-304 Melbourne High Risk Study (MHRS) 351-353 GABA system 299-301 memantine 467 late maturation of dopamine projections membrane signal transduction 161-162 301-303 memory, estrogen effects 335-336 linolenic acid 160 see also working memory see also essential polyunsaturated fatty mental retardation acids in fragile X syndrome 339 lithium 466 in velo-cardio-facial syndrome 123, 124

<u>fore mormation</u>

482 Index

mental retardation (cont.) psychiatric disorders and 125 see also IQ mesencephalon development 5-6 meta-cognition 69 metabolic changes 216-217, 380 metencephalon 6 methamphetamine psychosis 250-251 familial predisposition to schizophrenia and 257-258 genetic studies 259 premorbid characteristics 255-257 sensitization 261 N-methyl-D-aspartate receptors see NMDA receptors methyl azoxymethanol acetate (MAM) 278-279 methylphenidate 394-395 microarray studies see DNA microarray studies midbrain development 5-6 see also brain development migration 233-234 see also minority groups mineralocorticoid receptor (MR) 114 minor physical anomalies as risk factors 195-196, 443 minority groups 233-234 African-Caribbeans in the UK 234-235 discrimination 235-236, 239 methodological issues 234 second generation 235 monozygotic (MZ) twin studies see twin studies mood disorders see bipolar disorder; depression mother-child relationship 226 motor coordination dysfunction 417-418 multifactorial susceptibility model 138 myelination 36, 47, 332 diffusion tensor imaging studies 61-62 during adolescence 71, 332 gene expression changes 219 rerouting plasticity and 101 sex differences 332 NAA (N-acetylaspartate) in ADHD 394 in obsessive-compulsive disorder 397-398, 399 in schizophrenia 380 predictive value 444 NCAM see neuronal cell adhesion molecule NCAM1 gene 12, 13

negative symptoms 445 progression 375, 457 neonatal risk factors 200 nerve growth factor (NGF) 15, 335 expression 16 neural ectoderm 5 neural plate 5 neural tube 5 neurobehavioral high-risk studies 437-438 see also high-risk population studies NeuroD 7 neurodegenerative disorders 374 neurodegenerative models 373, 382-383, 459 clinical psychopathology and cognition 374-376 integrative neurochemical model 459-462 neuroimaging studies 379-381 correlation between imaging data and outcome 380-381 functional and spectroscopic studies 380 structural studies 379-380 postmortem findings 376-378 potential mechanisms of neurodegeneration 381-382, 463 versus neurodevelopmental model 81-82, 111-112 neurodevelopmental model 3, 79-82, 111, 174-175, 373, 415 animal models 277-279 early developmental model 457-458 genetic mechanisms 3, 4, 24 epigenetic factors 175, 179-187 integrative neurochemical model 459-462 late developmental model 458-459 limitations of 373 pediatric fMRI studies 58-59 support for 121 unifying model 455 velo-cardio-facial syndrome as model for schizophrenia 122 versus atrophy/neurodegeneration 81-82, 111-112 see also brain development neurogenins 7 Ngn1 7 Ngn27 neuromeres 6 neuromotor dysfunction 417-418, 443 neuron 37 neuronal cell adhesion molecule (NCAM) 12-13 gene NCAM1 12, 13

Cambridge University Press 0521823315 - Neurodevelopment and Schizophrenia Edited by Matcheri S. Keshavan, James L. Kennedy and Robin M. Murray Index More information

Index

function 12-13 isoforms 12 role in schizophrenia 13 neuronal cell loss 377 neuronal survival 14-18 neuroregulin 1 gene 24 neurotransmission 18-23 neurotrophins (NT) 14-17, 335 NT-3 15, 335 A3 allele 360 expression 18 NT-4/5 15, 335 expression 16 NT-6 15 neurulation 5-8 genetic basis 6-8 primary 5 secondary 5 NMDA receptors 282, 460, 461-462 estrogen effect 335 phencyclidine effect 253 role in neurodegeneration 381-382 role in neurodevelopment 460 Notch genes 6-7 NOTCH47-8 NSF (N-ethylmaleimide-sensitive factor) 216 NT-3 gene 17 see also neurotrophins nutrition 156 role in brain and behavioral development 158 role in health 156 role in schizophrenia 156-157, 158-159 undernutrition 156, 158 prenatal malnutrition as risk factor 194-195 see also essential polyunsaturated fatty acids nutritional strategies dietary supplementation 159, 163-164 antioxidants 163-164 essential polyunsaturated fatty acids 163-165 preferred combination 165 issues 164-165 adjunctive medication 164 age and duration of illness 164 dose and quality of essential polyunsaturated fatty acids 165 duration of treatment 165 placebo control 165 type of essential polyunsaturated fatty acids 164 - 165when and what to treat 166

obsessive-compulsive disorder (OCD) 40-41, 390, 391-398 common neuropathology 391, 404-405 genetic basis 403 neurodevelopment 397, 398 neuroimaging studies 395-400 basal ganglia 399-400 prefrontal cortex 396 thalamus 399 total brain volume 396 with velo-cardio-facial syndrome 125 obstetric complications (OCs) 143, 175, 197-199, 200-202, 403 imaging abnormalities and 360-363 hippocampi 358, 362 ventricles 360-361 neurodevelopmental deficits and 419 OCD see obsessive-compulsive disorder oculomotor delayed response (ODR) task 58-59, 310-311 see also working memory odds ratio 417 olanzapine 465 onset of disease 274, 457 possible origins of delayed onset 279-281 sex differences 331 oogenesis 182 Otx2 gene 9 outcome measures 441-442, 444-445 p75^{NTR} receptor 15 pandevelopmental retardation 418 parent-of-origin effects 178-179 parents communication deviance 227 early parental loss 228 mother-child relationship 226 reliability of parental diagnoses 440 parietal lobe, in velo-cardio-facial syndrome 129, 130 parvalbumin 313, 314, 315 chandelier neurons 320 wide-arbor neurons 320-321 Pax6 10 pediatric neuroimaging 49, 57-59, 63 abnormal populations ADHD 57 dyslexia 57-58 schizophrenia 58-59

484

Index

-	iatric neuroimaging (<i>cont.</i>)
c	hallenges to pediatric neuroimaging 59–61
	differences in performance 60–61
	head movement 59–60
	respiratory and heart rate cycles 60
	stress 59
	structural differences between child and adu
	brain 60
fı	iture directions 61–63
	ee also specific types of imaging
peri	gigantocellularis region 276
peri	ventricular hemorrhage (PVH) 94
peri	ventricular hemorrhagic infarction (PHI) 93
peri	ventricular leukomalacia (PVL) 93
РЕТ	see positron emission tomography
phe	ncyclidine (PCP) psychosis 253
phe	notype 138, 147–148
b	ehavioral
	childhood developmental delays 123-124
	childhood velo-cardio-facial syndrome
	124–125
se	ee also endophenotypes
pho	sphodiesters (PDEs) 62, 380
pho	spholipid breakdown 380
pho	sphomonoesters (PMEs) 62, 380
PIK	4CA gene 127
plas	ticity 89–90
fc	ollowing brain injury 91–92, 99–101
	at the connectivity level 100-101
	at the neural network level 99–100
	at the neuronal level 99
	Kennard principle 91
	remapping of functions 100
	rerouting 100–101
fc	ollowing preterm birth 92, 96–97, 99–101
	mits of 101
se	ee also brain development
poly	rsialic acid (PSA) 12–13
posi	itive symptoms 375
a	ttenuated prodromal symptoms 457
posi	itron emission tomography (PET),
•	developmental studies 47
POU	U domain family 9–10
Prac	der–Willi syndrome 184
	lictors of schizophrenia 415–417, 428–429,
-	441–444, 447
b	ehavioral predictors 425–426, 428, 437–438
	archival–observational studies 428
	high-risk studies 427

electrophysiological measures 443 minor physical anomalies 443 negative predictive value 417 neuroimaging measures 443-444 neurointegrative predictors 416, 417-419, 443 archival-observational studies 419 high-risk studies 418 population-based studies 417-418 neuropsychological predictors 419-425 cognitive deficits 442-443, 458 high-risk studies 423-424, 425 population-based studies 419-422, 423 positive predictive value 417 prodromal symptoms 438-439 sensitivity 417, 421-423 specificity 417, 421-423 see also high-risk population studies; premorbid phase; risk factors prefrontal cortex dorsolateral (DLPFC) 310, 314, 319 structural abnormalities in schizophrenia 321-323 see also MDN-DLPFC circuitry in ADHD 57, 393-395 in bipolar disorder 401 in major depressive disorder 401 in obsessive-compulsive disorder 396 in schizophrenia 55, 274-275 metabolic changes 216-217, 380 possible origins of delayed onset 280-281 maturation 46 microarray studies 215-220 role in voluntary response suppression 52-53 role in working memory 49-51, 310-311 stress and emotional reactivity relationships 275 - 277premorbid phase 415, 456, 457-458, 460 cognitive impairments 455-457 progressive impairment 376 etiological factors 462 premorbid adjustment 363-364 premorbid personality and drug abuse 255-257 primary prevention strategies 463-464 see also high-risk population studies; predictors of schizophrenia premorbid structural abnormalities 347, 364-365 high-risk population studies 350-353 Edinburgh High Risk Study 350-351 Melbourne High Risk Study 351-353 premorbid adjustment and 363-364

wore information

485

Index

structural imaging and risk factors 353
family history 353–360
see also premorbid phase
prenatal infections 193-194, 362
influenza 192–194
prenatal risk factors see risk factors
preterm birth 92, 93
consequences of persisting brain abnormality 96–97
behavior 97
neurology 96
neuropsychology 96–97
limits of brain plasticity 101
perinatal brain injuries 93–94
link between brain structure and function
97–98
prevalence 94
sequelae in adolescent brains 94–96
possible plasticity mechanisms 99–101
at the connectivity level 100–101
at the neural network level 99–100
at the neuronal level 99
remapping of functions 100
rerouting 100–101
University College Hospital London study
92–93
follow-up 93
prevention see intervention strategies
prion protein (PRNP) gene 149
probes see DNA microarray studies
prodromal phase 432, 438–439, 456, 457
clinical high-risk strategies 438–439
intervention strategies 464–467
low-dose atypical antipsychotic drugs 465
naturalistic treatment studies 465–466
non-antipsychotic medications 466
psychotherapeutic treatments 466–467
progressive cognitive impairment 375–376
subthreshold symptoms 445, 457
proline dehydrogenase (PDH) 127
proneural genes 6–7
prosencephalon development 5–6
prostaglandins 162
proteolipid protein 1 (PLP1) 219
pruning see synaptic pruning
psychosis
drug-induced 250–254
early functional decline 457
neurotoxicity of untreated psychosis 380–381,
459

onset 457 see also schizophrenia psychotherapeutic treatments 466-467 PSYN group genes 215-216, 218, 219 puberty 70 racial discrimination 235-236, 239 Reelin 13-14 RELN gene 14 polymorphisms 14 role in schizophrenia 14 regulator of G-protein signaling 4 (RGS4) 217-218 remapping plasticity 100 rerouting plasticity 100-101 response suppression 51-55 developmental studies 51-55, 77 prefrontal cortex role 52-53 retrospective studies 434 Rett syndrome 184 rhesus incompatibility as risk factor 195 rhombencephalon development 5-6 risk factors 191, 353 family history 353-360 CT studies 354-355 structural MRI studies 355-356 neonatal risk factors 200 neonatal and early childhood infections 194 obstetric complications 143, 175, 197-199, 200-202, 403 imaging abnormalities and 360-363 prenatal risk factors 191-197, 201, 274 malnutrition 194-195 minor physical anomalies 195-196 prenatal infection 192-194, 362 rhesus incompatibility 195 stress exposure 196-197 time and place of birth 191-192, 362 schizotypal personality disorder 358 see also drug abuse; high-risk population studies; predictors of schizophrenia; social factors; urban effect risperidone 465 rubella, prenatal, as risk factor 193 schizophrenia 79-82 brain structure 141-142, 174, 347-348, 350 molecular genetics 148-149

> prefrontal cortex 55 state versus trait 142–143

Cambridge University Press 0521823315 - Neurodevelopment and Schizophrenia Edited by Matcheri S. Keshavan, James L. Kennedy and Robin M. Murray Index More information

Index

Index	
schizophrenia (cont.)	
chemical changes	
BDNF 16	
NCAM 13	
SNAP-25 20	
common neuropathology 112–113, 390–392,	
402–403, 404–405	
early course of disease 456, 457	
see also neurodegenerative models;	
premorbid phase; prodromal phase	
onset of disease 274, 457	
possible origins of delayed onset	
279–281	
sex differences 331	
outcome variability 157–158	
postmortem findings 295-298, 376-378	
dopamine system 297–298	
GABA system 296–297	
see also genetics of schizophrenia;	
neurodegenerative models;	
neurodevelopmental model	
schizophrenia spectrum of psychopathology	
444-445	
schizotypal personality disorder 358	
schizotypy 255, 445	
drug abuse association 255–256	
school change in adolescence 232	
season of birth, as risk factor 191–192,	
362	
segmentation 8–10	
self-medication 249	
sensitive periods see critical periods	
separation anxiety disorder 125	
serotonergic system	
development 333–334	
estrogen effect 336	
serotonin 333	
seven-pass transmembrane cadherins 11	
sex chromosomes 330	
see also X chromosome	
sex differences	
brain development 332–333	
aging 332–333	
estrogen role 334–335	
myelination 332	
brain structure 40–41, 331–332	
amygdala 41	
basal ganglia 40–41	
cerebral volume 40	
hippocampus 41	

schizophrenia 331 clinical features 331 epidemiology 331 sex steroids 330 see also estrogen smooth pursuit eye movements (SPEM) 438, 443 SNAP-25 18, 19-20 changes in schizophrenia 20 SNARE proteins 18-19 see also SNAP-25; syntaxins social cognition 339 social drift 230-231 social factors 224, 225, 239-240 animal research on brain development 224-226 family factors 226-229 childhood abuse 228-229, 239 communal upbringing 227-228 dysfunctional family environment 227 early parental loss 228 expressed emotion 228 family communication deviance 227 mother-child relationship 226 unwantedness 226-227 interaction with other factors 237-238 cognitive processing 238 gene-environment interaction 237-238 life events 236-237 social causation versus social selection 238-239 social isolation 232-236 African-Caribbeans in the UK 234-235 at time of onset 233 discrimination 235-236, 239 during childhood 232 in young adult life 232-233 methodological issues 234 migration and ethnic minority status 233-234 moving schools in adolescence 232 second generation 235 unemployment 236 socioeconomic factors 237 impact on outcome 157-158 see also urban effect social maladjustment as predictor 425, 427 see also behavior social residue theory 231 sodium valproate, teratogenic effects 184-185 Sonic hedgehog (Shh) gene 7 speech difficulties as predictor 421 see also language development spermatogenesis 182

487 Index

strategic rerouting 101 stress 277, 281, 285 as risk factor 236-237 prenatal exposure 196-197 hippocampal damage 279-281 pediatric neuroimaging and 59 possible origins of delayed disease onset 279-281 prefrontal cortex and 275-277 role in neurodegeneration 382 structural magnetic resonance imaging (sMRI) see magnetic resonance imaging substance abuse see drug abuse subthreshold symptoms 445, 457 susceptibility genes identification of 138, 217-218 multifactorial susceptibility model 138 see also endophenotypes Suzuki method 90 synapsins 20-22 synapsin I 21 synapsin II 21-22, 216 synapsin III 21, 22 synaptic apoptosis 377-378 see also synaptic pruning synaptic marker reduction 377 synaptic pruning 39-40, 47, 130, 218, 458-459, 461 DLPFC 318-319 during adolescence 70-71, 458, 462 magnetic resonance spectroscopy studies 62 plasticity following brain injury 99 synaptic transmission 18-23 impaired synaptic function 218 synaptobrevins 18 syntaxins 18, 22

TBX1 gene 127–128 telencephalon 6 temporal lobe in unaffected relatives 146 in velo-cardio-facial syndrome 129–130 teratogenic effects on epigenetic regulation 184–185 testosterone role in brain development 334 thalamocortical projections *see* MDN–DLPFC circuitry thalamus axon development 318 volume changes in high-risk population 350, 357

in obsessive-compulsive disorder 399 in schizophrenia 146, 321, 349 see also mediodorsal nucleus topiramate 467 total brain size see brain Tourette's syndrome 40 transcription factors 10, 176 see also specific factors transcriptomes 210 assessment methods 210-212 experimental design in microarray studies 212-213 future directions 220 gene expression changes in schizophrenia 215 - 220microarray data analysis and interpretation 214-215 trinucleotide repeats 339-340 Trk (tyrosine kinase) receptors 15-16 TrkA 15, 16 TrkB 13, 15 TrkC 15, 16 tumor necrosis factor receptor II (TNF-RII) gene 149 Turner syndrome 338-339 twin studies 435 brain structure 139-141, 143, 355-356 cerebral volume 145 corpus callosum 147 frontal lobe 147 discordance in monozygotic twins 179 obstetric complications 360-361 tyrosine kinase receptors see Trk receptors UFDIL gene 127 ultra-high-risk population study 351-353 see also high-risk population studies undernutrition 156, 158 see also nutrition unemployment 236 universal intervention 463-464 University College Hospital London preterm birth study 92-93 see also preterm birth unwantedness 196, 226-227 urban effect 230-232

city of birth 191, 230 city of upbringing 230 possible explanations 231–232 social drift and social residue theories 230–231

Index 488 valproic acid, teratogenic effects 184-185 voluntary response suppression 51-55 developmental studies 51-55, 77 velo-cardio-facial syndrome (VCFS) 122 prefrontal cortex role 52-53 as neurodevelopmental model for schizophrenia 122 voxel-based morphometry (VBM) 349 childhood behavioral phenotype 124-125 childhood developmental delays 123-124 Wernicke's area 38 genetics of 126-129 white matter 36-38 medical aspects 122-123 changes during adolescence 71, 332 neuroimaging 129-131 changes in major depressive disorder 401 psychiatric presentation in adulthood sequelae of preterm birth 95 125 wide-arbor neurons 320-321 schizophrenia risk and 122, 125, Wnt signaling pathway 7 128-129 abnormalities 8 ventricular dilatation 111 working memory following obstetric complications development 49-51, 73 360-361 in schizophrenia 80-81 following preterm birth 94 structural correlates 76 sequelae in adolescent brains 95 DLPFC role 310-311 genetic marker association 360 dysfunction in schizophrenia 310-311 in high-risk population 350 see also cognitive dysfunction family history 354-355 in high-risk group 58-59, 274-275 in schizophrenia 141, 349 oculomotor delayed response task 58-59 common neuropathology 112 pediatric studies 50-51 progressive change 379-380, 381 prefrontal cortex role 49-51 in unaffected relatives 144-145, thalamic mediolateral nucleus role 310-311 356-357 ventricular volume, heritability 139-140 X chromosome 338-341 vesicle-SNAREs (v-SNAREs) 18 trinucleotide repeats 339-340 vesicular ATPase 216 Xash3 gene 6 vitamin C supplementation 165 vitamin D hypothesis 159 Yemenite Jews 235 vitamin E supplementation 163, Zucker Hillside Recognition and Prevention (RAP) 165 vitamin requirements 158-159 program, New York 465-466