Index

A β . See β -amyloid (A β); cerebral amyloid angiopathy (CAA) a-dystroglycan, 103, 106 $\alpha\beta$ -galactosidase deficiency, 293–294, See also Fabry's disease ABri precursor protein (ABriPP)related cerebral amyloid angiopathy, 86-88 acute small deep infarcts (ASDI), 129-132 acute stroke care, 323-325 anticoagulation, 228 antiplatelet therapy, 227-228, 325 blood pressure management, 227 intra-arterial stenting, 228-229 stroke unit care, 229 thrombolytic therapy, 226-227, 323-324 adhesion molecules, 193-194 age-related changes blood-brain barrier, 54 large artery aging related to white matter pathology, 93 Aicardi-Goutières syndrome (AGS), 69,86 albumin, blood-brain barrier evaluation, 54 Alzheimer's disease (AD), 29, See also dementia anti-Aβ immunotherapy, 73 cerebral amyloid angiopathy association, 8-13, 200, 205-206 cerebral blood flow studies, 184 cerebral microbleeds, 35-36, 237, 302 cognitive significance, 238 diagnosis, 298 familial (FAD), 205 mixed dementia, 299 small vessel-disease interaction, 300-302 challenges, 304-305 mechanisms, 304 vascular cognitive impairment relationship, 16 vascular dementia pathology relationship, 200, 302-304 white matter changes, 301-302

nonfocal white matter disease, 20 American Heart Association/ American Stroke Association (AHA/ASA) guidance, 349-350 amyloid disease, animal models, 45, See also β -amyloid (A β); cerebral amyloid angiopathy (CAA) amyloid precursor protein (APP), 70, See also β -amyloid (A β) APP metabolism biomarkers, 207 APP metabolism disturbance, 207 APP-related cerebral amyloid angiopathy, 86 mutations, 71, 86 amyloid-specific molecular imaging, 159-160 angiotensin II (ANGII), 95, 194 angiotensin receptor (AGTR) genes, 88 angiotensin-converting enzyme (ACE) gene polymorphisms, 88, 194 angiotensinogen gene (AGT), 195 M235T variant, 88 animal models, 42, 46-48 β-amyloid deposition, 71–72 blood-brain barrier, 54-56 COL4A1/COL4A2 mutations, 75 comorbidities, 45-46 advanced age, 45 amyloid disease, 45 diabetes mellitus, 45-46 embolic models, 43 hypertensive models, 44 primates, 44 stroke-prone spontaneously hypertensive rats (SHRSP), 44 hypoperfusion-based models, 43 acute global ischemic challenge, 43 chronic carotid stenosis, 43 chronic hypoperfusion, 43 focal hypoperfusion, 43 mouse unilateral common carotid occlusion (UCCAo), 43 intervention studies, 46 utility, 46-47 vessel damage-based models, 44-45

CADASIL-Notch3 transgenic mice, 44-45, 66 hyperhomocysteinemic rodents, 44 $M5R^{-/-}$ transgenic mice, 45 anterior cerebral artery (ACA), 220 anterior choroidal artery, 220 anterior inferior cerebellar artery, 220 anticoagulation, 228 atrial fibrillation and, 330 intracerebral hemorrhage association, 33 antioxidants, 195-196 antiplatelet therapy, 227-228, 324-325 secondary stroke prevention, 325-328 anxiety, 266-267 apathy, 263, 267-268 prevalence in brain disorders, 267 APOE ɛ2 allele, 32-33 APOE £4 allele, 32, 35, 206, 318 apoptosis, 60 arterial pulsatility, 60 arterial spin labeling (ASL), 174-176, 182 continuous (CASL), 174 pseudo-continuous (pCASL), 174 pulsed (PASL), 174 arterial stiffness, 315 arterial system. See also specific arteries heterogeneity, 92-93 large artery aging related to microvascular brain damage, 93 arteriolosclerosis, 56, 348 arteriosclerotic dementia, 16 aspirin, 36, 227-228, 325 secondary stroke prevention, 325, 328 astrocytes, 103-104 focal ischemia effects, 105, 107 astroglial reactivity, 202-203 asymmetric dimethylarginine (ADMA), 194 CADASIL patients, 197 ataxic hemiparesis, 221 atherosclerosis, 6-7, 348 common soil hypothesis, 93-95

Index

atorvastatin, 328 atrial fibrillation, 330 atrophy, 351 diagnostic signficance, 299, 302-303 Axenfeld-Rieger anomaly, 85 axonal degeneration biomarkers, 207-209 β -amyloid (A β), 95 aggregation, 71 anti-A β immunotherapy, 73 blood-brain barrier dysfunction and, 206 clearance pathways, 206 diagnostic significance, 303 CSF levels, 206-207, 303 inflammatory response, 12-13 matrix metalloproteinase activation, 32 molecular in vivo imaging, 159-160 pathological effects, 72-73 synthesis and clearance, 71 transport across blood-brain barrier, 206 vascular deposition, 8-10, 71-72, 205, 304, See also cerebral amyloid angiopathy (CAA) cerebral microbleed association, 35 topographic distribution, 153 β -catenin, 102 balance disorders, 251 classification, 251-253 LADIS study, 253-254 management, 257-258 pathological mechanisms, 256-257 role in impaired mobility, 255 white matter lesion association, 255-256 basal ganglia, dilation of perivascular spaces, 8 basement membrane, 73 Benedikt's syndrome, 222 Binswanger's encephalopathy, 8, 117 cerebral blood flow study, 184 biomarkers, 201, See also cerebrospinal fluid (CSF) bipolar disorder, 265-266 bleeding globes, 5 microaneurysm rupture, 5 blood pressure. See also hypertension CADASIL interaction, 287 cerebral microbleed relationships, 318-319 management, 227, 343 secondary stroke prevention, 328-330

white matter pathology relationships, 315-316 blood-brain barrier (BBB), 53-59, 201 age-related changes, 54 animal models, 54-56 dysfunction, 201-202 β -amyloid as mediator, 206 matrix metalloproteinases as biomarkers, 204 human clinical data, 57-59 management implications, 59 human pathological data, 56-57 normal findings, 53-54 permeability imaging, 58-59 brain blood vessels. See also cerebral microvasculature; specific vessels anatomy, 347-348 pathology, 348-349 brainstem syndromes, 222-224 BRI2 gene mutations, 70, 86 CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarct and leukoencephalopathy), 33-34, 64-66, 82-84, 283-290 clinical manifestations, 64, 82, 284-287, 294 cognitive impairment, 286 ischemic events, 284 migraine, 284-286 psychiatric symptoms, 286 visual symptoms, 287 diagnosis, 289 pregenetic screening, 289 disease progression, 287-288 hemodynamic studies, 188-189 imaging findings, 284, 288-289 diffusion tensor imaging, 170-171 magnetic resonance spectroscopy (MRS), 172–173 mechanisms of disease, 65-66 brain lesions, 66 endothelial dysfunction, 197-198 molecular genetics, 65, 84 pathology, 64-65, 283-284 phenotypic variation, 192, 287 prevalence, 82, 283 transgenic mouse models, 44-45, 66 treatment, 84, 289 calcifications, 149 candidate gene studies, 88 capillary cerebral amyloid angiopathy (capCAA), 9-10 capsular infarct, 6

capsular warning syndrome, 226, 324 antiplatelet therapy, 228, 324 thrombolytic therapy, 227 CARASIL (cerebral autosomal recessive arteriopathy with subcortical ischemic strokes and leukoencephalopathy), 66-68, 84, 290 clinical manifestations, 290, 294 mechanisms of disease, 68 molecular genetics, 67, 290 neuroimaging, 290 neuropathology, 290 cardiac arrest, 23 encephalopathy, 23 carotid endarterectomy (CEA), 330 carotid stenosis, 330 cavernous malformations, 148-149 cerebral amyloid angiopathy (CAA), 8-13, 152-157, 200, See also β -amyloid (A β) Alzheimer's disease association, 8-13, 200, 205-206 anti-Aß immunotherapy, 73 capillary CAA (capCAA), 9-10 cerebral microbleed association, 11, 35-36, 153-154 diagnosis, 156-158 grading system, 10 hereditary CAA, 69-73, 86-88, 159 ABri precursor protein-related, 86-88 amyloid precursor protein (APP)-related, 86 cystatin C-related, 86 molecular genetics, 70 imaging findings, 152-157 arterial spin labeling (ASL), 176 molecular in vivo imaging, 159-160 intracerebral hemorrhage association, 10-11, 31-33, 153, 158, 317 anticoagulation and, 33 hypertension and, 32 thrombolysis and, 33 pathology, 9, 13, 69-70, 205 β-amyloid aggregation, 71 β -amyloid deposition, 8–10, 71-72 brain lesion mechanisms, 72-73 cerebral white matter damage, 12, 155 inflammatory changes, 12-13, 156-157 microinfarcts, 12 subarachnoid hemorrhage association, 33, 152, 155

Index

superficial siderosis association, 11, 34, 152, 155 cerebral arteries, 347 anterior cerebral artery (ACA), 220 microangioarchitectural changes, 7 middle cerebral artery (MCA) flow velocity measurement, 182 posterior cerebral artery (PCA), 220 cerebral autoregulation, 183 imaging studies in small vessel diseases, 188 cerebral blood flow (CBF), 180 arterial spin labeling studies, 174-176 autoregulation, 183 imaging studies, 188 CADASIL relationship, 188-189 in small vessel diseases, 183-187 large artery aging relationships, 93 local regulation, 105 measurement, 180-183 contrast CT perfusion, 182 magnetic resonance perfusion, 182 nuclear medicine methods, 180-182 transcranial Doppler ultrasound (TCD), 182 volume flow methods, 182 regional variation, 100 cerebral hemorrhage. See intracerebral hemorrhage (ICH) cerebral microbleeds (CMB), 11, 34-37, 300, 304, 317-319 Alzheimer's disease association, 35-36, 237-238, 302 as surrogate markers, 340-342 cerebral microangiopathy association, 342 clinical outcome correlation, 342 cerebral amyloid angiopathy association, 11, 35-36, 153-154 cognitive implications, 237-238 definition, 143-144 differential diagnosis, 147-150 calcifications, 149 causes other than cerebral small vessel disease, 149-150 cavernous malformations, 148-149 cerebral metastases from malignant melanoma, 149 vascular flow voids, 147-148 epidemiology, 34, 147 incidence, 342 imaging findings, 142-150 blooming effect, 143-145 echo time significance, 145

magnetic field strength role, 145 neuropathological correlates, 34-35 spatial resolution, 145 susceptibility-weighted imaging (SWI), 145-147 intracerebral hemorrhage relationships, 36 mimics, 143, 147 pathogenesis, 35-36 prognostic significance, 278-279 research definition, 351 risk factors, 318-319 topographical distribution, 35 vessel wall thickness relationship, 36 warfarin association, 33 cerebral microvasculature, 99-105 collateral system and protection, 100 - 101elements of, 101-104 astrocytes, 103 endothelium, 101-103 extracellular matrix (ECM), 103, 106 mast cells, 104 microglia, 104 pericytes, 103-104 focal ischemia effects, 105-107 clinically relevant microvessel effects, 107-109 edema, 107 focal no-reflow, 108-109 hemorrhagic transformation, 107-108 matrix adhesion, 106 microvessel-neuron relationships, 106-107 permeability barrier, 107 ultrastructural changes, 105-106 microvessel beds, 100 neuron relationships, 101, 106 focal ischemia effects, 106-107 vessel-neuron communication, 105 permeability barrier, 99, 104-105, 107 cerebral reactivity, 183 hypertension relationship, 175-176 imaging studies in small vessel diseases, 187-188 measurement, 183 white matter pathology association, 315 cerebral small vessel diseases (SVDs), 1,4 Alzheimer's disease interaction, 300-302, 304 challenges, 304-305 assessment, 23-26

balance disorder association, 255 - 256complexity, 218-219 lesion location, 219 stroke mechanism, 218-219 consequences, 273 definition, 1-2 new developments, 317 dementia relationship, 25-26 etiologic classification, 2 falls and, 256 future directions, 349-351 hemorrhagic, 29, 139, See also cerebral microbleeds (CMB); intracerebral hemorrhage (ICH) hereditary conditions, 64, See also specific conditions imaging findings, 117 computed tomography (CT), 118-121 magnetic resonance imaging (MRI), 118-125 ischemic consequences, 16-17 neurovascular unit and, 109-111 nosological issues, 1-2 pathogenic mechanisms, 52, 59, 349 apoptosis, 60 blood-brain barrier, 53-59 increased arterial pulsatility, 60 ischemia, 52-53 venous pathology, 59-60 prevalence, 29 research definitions, 351 subtypes, 2 cerebroretinal vasculopathy (CRV), 68, 85, 292 cerebrospinal fluid (CSF), 200-201 biomarkers, 201, 209 amyloid precursor protein metabolism, 207 axonal degeneration, 207-209 blood-brain barrier dysfunction, 201-202 glial involvement, 202-204 inflammation, 204-205 cerebrovascular disease (CVD)cognition relationships, 24 Charcôt-Bouchard aneurysm, 4 cholesterol. See also statin therapy cerebral microbleed relationship, 318 secondary stroke prevention, 328 white matter pathology relationships, 315-316 circle of Willis, 100 circulating progenitor cells (CPC) CADASIL patients, 197 Claude's syndrome, 222

355

Index

clopidogrel, 228, 325 secondary stroke prevention, 325, 328 cognitive function. See also dementia assessment, 239 attention, slowing and motor skills, 241-242 executive function, 240-241 global measures, 239-240 CADASIL patients, 286 magnetic resonance spectroscopy (MRS) studies, 173 microstructural brain tissue change impact, 342-343 small vessel disease impact, 236 cerebral microbleeds, 237-238 lacunes, 237, 339, 341 white matter changes, 236-237, 337, 340 COL4A1 mutations, 74, 85, 94, 290-292 clinical manifestations, 290-291, 294 genetics, 291-292 imaging findings, 291 modifiers of disease phenotype, 76 mouse models, 75 pathogenicity, 75-76 pathologic effects, 73-74, 85, 159 porencephalic phenotype, 291 COL4A2 mutations, 74 modifiers of disease phenotype, 76 mouse models, 75 pathogenicity, 75-76 pathologic effects, 73-74 collagen. See type IV collagen collateral system, 100-101 common soil hypothesis, 93-95 corpus striatum, 100 cortical microinfarcts, 20 C-reactive protein (CRP), 196 cystatin C-related cerebral amyloid angiopathy, 86

Dejerine's syndrome, 223–224 Dejerine–Roussy syndrome, 221 dementia, 25–26, *See also* Alzheimer's disease; cognitive function; vascular dementia (VaD) blood–brain barrier permeability relationship, 57–58 cerebral blood flow studies, 184 diabetes association, 239 lacune impact, 237 MRI role in assessment, 299–300 stroke association, 239 white matter pathology relationships, 236–237 depression, 263–265

356

post-stroke (PSD), 263 prevalence in the elderly, 263 vascular, 264-265 treatment implications, 264-265 diabetes animal models, 45-46 common soil hypothesis, 93-95 dementia association, 239 lacunar infarct risk factors, 312-313 white matter pathology risk factors, 315 diffusion tensor imaging (DTI), 168-172, 261, 342 diffusion-weighted imaging (DWI), 168 digital subtraction angiography (DSA) intracerebral hemorrhage, 142 dipyridamole, 228, 328 disability, 273 cerebral microbleed prognostic significance, 278-279 lacunar infarct prognostic significance, 277-278 white matter lesion prognostic significance, 273-277 dysarthria-clumsy hand syndrome, 222 edema, 107 embolic animal models, 43 endothelial dysfunction, 94-95, 193 hyperhomocysteine-induced, 195 in CADASIL, 197-198 in sporadic small vessel diseases, 193-195 inflammation relationship, 193 endothelial nitric oxide synthase (eNOS) gene variation, 195 endothelial progenitor cells (EPC), 194 CADASIL patients, 197 endothelium, 101-103, 192-193 epidermal growth factor receptor (EGFR), 65 Notch3 mutations, 65 European Centres of Excellence in Neurodegeneration guidance, 350-351 executive functions, 243 assessment, 240-241 impairment, 240, 243 exercise, gait disorder management, 257-258 extracellular matrix (ECM), 103 focal ischemia effects, 106 adhesion receptors, 106 matrix antigen loss, 106 matrix proteases, 106 Fabry's disease, 84-85, 292-294

Fabry's disease, 84–85, 292–294 clinical manifestations, 293–294 heterozygous females, 293

imaging findings, 293 pathophysiology, 293-294 therapy, 294 falls. See also balance disorders impact in the elderly, 255 prevention, 257-258 white matter lesion association, 256 familial amyloidosis - Finnish type (FAF), 70 familial British dementia (FBD), 70, 86-88 familial chilblain lupus, 69 familial Danish dementia (FDD), 70, 86-88 familial transthyretin (TTR)-related amyloidosis, 70 fibrin deposition, 108-109 fibrinoid necrosis, 4, 56, 348 fibrohyalinosis, 5 folate, 315 Foville's syndrome, 223 fractional anisotropy (FA), 168 functional magnetic resonance imaging (fMRI), 159, 173-174 arterial spin labeling (ASL), 174-176 functional status, 273 global functioning assessment, 274 gait disorders, 251 classification, 251-253 LADIS study, 253-254 management, 257-258 pathological mechanisms, 256-257 small vessel disease association, 254 - 255generalized anxiety disorder (GAD), 266 genome-wide association studies (GWAS), 89 GLA gene mutation, 84 glia limitans, 99 glial fibrillary acidic protein (GFAP), 203 - 204gliosis, reactive, 202-203 global brain ischemia, 23 global functioning assessment, 274 granular osmiophilic (GOM) deposits, 44.66 hallucinations, 266 HANAC (hereditary angiopathy with nephropathy, aneurysms and cramps) syndrome, 74, 85, 291-292 head trauma, 149-150 health, 273 hematologic disorders, 150 hemiparesis ataxic, 221 pure motor, 220

Index

hemorrhagic transformation, 107-108 hemosiderin deposition, 150, See also superficial siderosis cerebral microbleeds, 34-35, 143 heparin, 228 hereditary cerebral hemorrhage with amyloidosis Dutch type (HCHWA-D), 70, 86, 159 Icelandic type (HCHWA-I), 70, 86 hereditary cerebral small vessel diseases (SVDs), 64, See also specific conditions monogenic conditions, 82-83 hereditary endotheliopathy with retinopathy, nephropathy, and stroke (HERNS), 68, 85, 292 clinical manifestations, 294 hereditary vascular retinopathy (HVR), 68, 85, 292 HINTS assessment, 223 hippocampal pathology atrophy, 242, 302-303 cardiac arrest, 23 homocysteine. See hyperhomocysteinemia HTRA1, 290 functions, 68 mutations, 67-68, 84 hyalinosis, 5 hyperhomocysteinemia, 195 CADASIL patients, 197 rodent model, 44 white matter pathology association, 315 hyperlipidemia, white matter pathology relationships, 315 hypertension, 57, 192, See also blood pressure animal models, 44 cerebral amyloid angiopathy relationship, 32 cerebral vasoreactivity relationship, 175-176 cognitive decline relationship, 238-239 intracerebral hemorrhage relationship, 317 lacunar infarct risk factors, 312 therapeutic induction, 227 vessel wall changes, 317 white matter pathology association, 314, 336 hypertensive vasculopathies, 4-8 arteriopathy, 31 microangiopathy, 157-159 imaging findings, 157-159 pathological findings, 13, 157-158

hypoxia, 201-203 inflammation, 196-197 cerebral amyloid angiopathy, 12-13, 156-157 cerebrospinal fluid biomarkers, 204-205 endothelial dyfunction relationship, 193 focal ischemia effects, 103, 105-106 integrins, 101, 103 focal ischemia effects, 106-107 interleukin-6 (IL-6), 196 internal carotid arteries, 220, 347 intra-arterial stenting, 228-229 intracerebral hemorrhage (ICH), 29-34, 316-317 acute, 139 anticoagulation association, 33 cerebral amyloid angiopathy association, 10-11, 31-33, 153, 158, 317 cerebral microbleed relationships, 36 chronic, 139 hemorrhagic transformation, 107 - 108hypertensive microangiopathy association, 158-159 imaging findings, 139-142 computed tomography (CT), 139-141 digital subtraction angiography (DSA), 142 ICH stages, 141, 143 magnetic resonance imaging (MRI), 141, 143 primary versus secondary bleeding causes, 141 neuropathology, 29-31 primary, 139 risk factors, 317 secondary, 139 spontaneous, 10 intracranial branch atheromatous disease, 7 intracranial hemorrhages, 29, See also cerebral microbleeds (CMB); intracerebral hemorrhage (ICH); subarachnoid hemorrhage Kunitz protease inhibitor (KPI), 32 lacunar infarcts, 7, 52-53, 129, 217,

311-314

hypoperfusion, 23

models. See animal models

hypotensive stroke, 18, 23

cerebral blood flow studies, 184 cognitive decline association, 239 epidemiology, 217-218 demographics and risk factors, 217 ethnicity, 217-218 percentage of acute strokes, 217 hypertensive microangiopathy, 158 prognostic significance, 277-278 risk factors, 312-314 community studies, 313 stroke studies, 312-313 silent lacunar infarcts, 132-136 differentiation from other cavities, 135-136 terminology, 136 lacunar stroke, 277, 323 acute care, 228-229, 323-325 antiplatelet therapy, 227-228, 325 blood pressure management, 227 thrombolytic therapy, 226-227, 323-324 acute imaging, 229-230 atrial fibrillation and, 330 carotid stenosis and, 330 cerebral blood flow studies, 184 recurrence, 323 secondary prevention, 325-330 antiplatelet agents, 325-328 blood pressure reduction, 328-330 lipid lowering therapy, 328 trials, 326 syndromes, 220-222 lacunar syndrome, 129, 136 lacunes, 17-19, 129, 311, 348, See also lacunar infarcts as surrogate markers, 339-340 cerebral microangiopathy relationship, 339 clinical outcome correlation, 339, 341 sample size calculation for trials, 339 cognitive impact, 237, 339, 341 incidence, 339, 341 research definition, 351 LADIS (Leukoaraiosis And DISability) study, 304 gait disorders, 253-254 white matter lesion prognostic significance, 274-276 language impairment, 242 lateral lenticulostriate arteries, 219 leptomeninges, basal ganglia, 8 leukoaraiosis. See white matter pathology

357

Index

Levels of Inflammatory Markers in the Treatment of Stroke (LIMITS) study, 197 lipid lowering therapy. See also statin therapy secondary stroke prevention, 328 lipohyalinosis, 6, 56-57, 348 long perforating artery occlusion, 129 $M5R^{-/-}$ transgenic mouse model, 45 magnetization transfer imaging (MTI), 342 mania, 265-266 Marie-Foix syndrome, 222 mast cells, 104 matrix metalloproteinases (MMPs), 32, 95, 196-197 as cerebrospinal fluid biomarkers, 204-205 focal ischemia effects, 106 medial lenticulostriate arteries, 220 medullary syndromes, 223-224 memory impairment, 242 metastases from malignant melanoma, 149 methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism, 195 microaneurysms, 4-5, 348 rupture, 5 microatheroma, 6, 57, 348 microglia, 104 microinfarcts, 12, 303-304 cortical 20 microstructural changes in brain tissue as surrogate markers, 342-343 cerebral microangiopathy relationship, 342 rate of progression, 342 microvasculature. See cerebral microvasculature midbrain syndromes, 222 medial midbrain syndrome, 222 midbrain tegmentum syndrome, 222 middle cerebral artery (MCA) branches, 219 flow velocity measurement, 182 migraine, 284 CADASIL patients, 284-286 mild cognitive impairment (MCI), 236, 238, 242, 298 Millard-Gubler syndrome, 223 Mini Mental State Examination (MMSE), 239 mixed dementia, 200, 299 Montreal Cognitive Assessment scale (MoCA), 240

mouse unilateral common carotid occlusion (UCCAo) model, 43 multi-infarct dementia (MID), 16 multimodal imaging, 177 multiple sclerosis (MS), 122, 124 myelin basic protein (MBP), 203 myeloperoxidase (MPO), 105 N-acetylaspartate (NAA), 172 neopterin, 197 neurofilament (NF), 207-208 CSF levels as biomarkers, 208-209 neuroimaging standards, 350-351 neuropsychological assessment, 239-243 attention, slowing and motor skills, 241-242 executive dysfunction, 240-241 global cognitive measures, 239-240 language impairment, 242 memory impairment, 242 visuoconstructional impairment, 242-243 neurovascular unit, 101, 105, See also blood-brain barrier (BBB); cerebral microvasculature focal ischemia effects, 106-107 small vessel disease and, 109-111 vessel-neuron communication, 105, 107 nitric oxide (NO), 183 non-focal lesions, 20 no-reflow phenomenon, 108-109 normal pressure hydrocephalus (NPH), 59-60 Notch3, 65 NOTCH3 mutations, 44, 65, 84, 88 animal models, 44-45 pathogenicity, 65-66 obsessive compulsive disorder (OCD), 267 oxidative stress, 193, 195-196 palipsychism, 225 paraoxonase, 196 pericytes, 103-104 perivascular spaces, 135, 351 dilated, 8, 158 differentiation from lacunar infarcts, 135-136 plasminogen activator inhibitor type 1 (PAI-1), 194 PMN leukocytes, 105 microvessel obstruction, 108 pontine syndromes, 222-223 inferior medial, 223 lateral, 222

ventral, 223 warning syndrome, 226 positron emission tomography (PET), 180-181 posterior cerebral artery (PCA), 220 posterior choroidal artery, 220 posterior inferior cerebellar artery, 220 post-stroke depression (PSD), 263 presenilin (PSEN) genes, 70 mutations, 71 prion-related cerebral amyloidosis, 70 protein C, 193 pseudoaneurysms, 5 psychiatric symptoms, 261, See also specific psychiatric disorders CADASIL patients, 286 small vessel disease association, 262-263 psychosis, 266 pure motor hemiparesis, 220 pure sensory stroke, 221 Raymond's syndrome, 223 reactive gliosis, 202-203 reactive oxygen species (ROS), 193, 195-196 recent small subcortical infarcts (rSSI), 351 recurrent artery of Heubner, 220 retinal vasculopathy with cerebral leukodystrophy (RVCL), 68-69, 85-86, 292 mechanisms of disease, 69 molecular genetics, 68, 292 reversible cerebral vasoconstriction syndrome (RCVS), 152 schizophrenia, 266 Secondary Prevention of Small Subcortical Strokes (SPS3) study, 217, 325-331 segmental arterial disorganization, 7 selectins, 193-194 sensorimotor stroke, 221 Short Physical Performance Battery (SPPB), 253 siderosis. See superficial siderosis silent infarcts, 133, See also lacunar infarcts single photon emission computed tomography (SPECT), 181 small vessel diseases. See cerebral small vessel diseases (SVDs) small vessels, 1, 347, See also cerebral microvasculature spontaneously hypertensive stroke prone rats (SHRSP), 44

Index

spontaneously hypertensive stroke resistant rats (SHRSR), 54-55 spot sign, 140-141 star-weighted angiography (SWAN), 147 statin therapy, 343 cerebral microbleed association, 318 intracerebral hemorrhage risk and, 317 secondary stroke prevention, 328 steal phenomena, 175 stenting, 228-229 STRIVE (Standards for ReportIng Vascular changes on nEuroimaging), 2 stroke, 200, See also acute stroke care; lacunar stroke; specific stroke syndromes cognitive impairment association, 239 hypotensive, 18, 23 pure sensory, 221 sensorimotor, 221 Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial, 328 stroke unit care, 229 subarachnoid hemorrhage (SAH) cerebral amyloid angiopathy association, 33, 155 focal (fSAH), 150 differential diagnosis, 152 mimics, 152 imaging findings, 150 subcortical arteriosclerotic encephalopathy. See Binswanger's encephalopathy subcortical hemorrhage, risk factors, 317, See also intracerebral hemorrhage (ICH) subcortical vascular dementia. See vascular dementia (VaD) sulfatide, 203-204 superficial siderosis, 11, 34, See also hemosiderin deposition cerebral amyloid angiopathy association, 11, 34, 155 differential diagnosis, 152 mimics, 152 supratentorial, 150 imaging findings, 150 pathophysiology, 152 superior cerebellar artery, 220 supratentorial superficial siderosis. See superficial siderosis surrogate markers, 336 lacunes, 339-340 microbleeds, 340-342

microstructural changes in brain tissue, 342-343 white matter pathology, 336-339 susceptibility-weighted imaging (SWI), 262 cerebral microbleeds, 145-147 T2-star-weighted angiography (SWAN), 147 tau, 208 CSF levels as biomarker, 208-209 thalamic syndromes, 224-226 anterior territory infarction, 224-225 inferolateral territory infarction, 225 - 226paramedian territory infarction, 225 posterior territory infarction, 226 thalamogeniculate artery, 220 thalamoperforator artery, 220 thrombolytic therapy, 226-227, 323-324 intracerebral hemorrhage association, 33 thrombomodulin, 193 thrombosis endothelium anti-thrombotic function, 103 small penetrating arteries, 226 tight junction (TJ) complexes, 101-102 focal ischemia effects, 107 tissue factor, 193-194 tissue factor pathway inhibitor (TFPI), 194 tissue inhibitors of matrix metalloproteinases (TIMP), 205 tissue plasminogen activator (tPA), 194 acute stroke care, 323-324 transcranial Doppler ultrasound (TCD), 182 TREX1 functions, 68-69 mutations, 68, 86 pathological effects, 69 two-vessel gradual occlusion (2-VGO) animal model, 43 type IV collagen, 73 functions, 75 mutations, 74, 94, See also COL4A1 mutations; COL4A2 mutations modifiers of disease phenotype, 76 mouse models, 75 pathogenicity, 75-76 pathology, 73-74, 85 synthesis and structure, 74

ultra-high field MRI, 160

VADAS-cog battery, 240 vascular cognitive impairment (VCI), 16-17, 298-299 Alzheimer's disease relationship, 16 vascular dementia (VaD), 16, See also dementia Alzheimer pathology relationship, 200, 302-304 cerebral blood flow studies, 184 diagnosis, 298-299 mixed dementia, 299 vascular depression, 264-265 vascular endothelial cadherin (VE-cadherin), 102 vasculitis, 19 vasoreactivity. See cerebral reactivity venous pathology, 59-60 vertebral arteries, 347 vertebrobasilar system, 220 Virchow-Robin spaces. See perivascular spaces visuoconstructional impairment, 242-243 vitamin B, 343 vitamin B12, 315 vitamin C, 196 vitamin E, 196 von Willebrand factor, 193 CADASIL patients, 197 Wallenberg's syndrome, 223 warfarin, 33 Weber's syndrome, 222 white matter hyperintensities (WMHs), 29, 118, 172, 261, 299-300 Alzheimer's disease and, 184, 301-302 blood-brain barrier relationships, 57 - 58cerebral blood flow relationship, 174-175, 184-187 research definition, 351 white matter pathology, 314-316, 349, See also white matter hyperintensities (WMHs) as surrogate marker, 336-339, 343 cerebral microangiopathy relationship, 336-337 clinical outcome correlation, 337, 340 sample size calculation for trials, 337-339, 341 assessment, 17 balance disorder association, 255-256 blood-brain barrier permeability relationship, 57-59 cerebral amyloid angiopathy (CAA), 12, 155

359

Index

white matter pathology (cont.) cerebrospinal fluid biomarkers, 202–204 cognitive implications, 236–237, 337, 340 dementia relationships, 236–237 falls and, 256 gait disorder association, 256–257 heritability, 88 candidate gene studies, 88 genome-wide association studies, 89 hypertension association, 336 imaging findings, 117, 126
computed tomography (CT), 118–121
magnetic resonance imaging (MRI), 118–125, 336–339
multiple sclerosis separation, 122, 124
quantitation of burden, 125–126
increased arterial pulsatility relationship, 60
ischemic origin, 53
large artery aging relationships, 93 mechanisms, 314 non-focal lesions, 20 prevalence, 236 prognostic signficance, 273–277 rate of progression, 337–338 risk factors, 314–315 for progression, 315–316 venous dysfunction, 59–60

xenon, 181-182

zonula occludens (ZO), 101