

Index

Note: Italicized page numbers indicate a table or box on the designated page

- acetazolamide, in NPH treatment, 72, 145
- acquired factors in white matter disorders, 163, 163
- acute confusional state. *See* delirium
- acute disseminated encephalomyelitis, 58
- acute toxic leukoencephalopathy, 97
- ADC. *See* AIDS-dementia complex
- addiction disorders
 - inhalant abuse, 148
 - possible white matter derangement in, 38, 105
 - toxic leukoencephalopathy and, 148
- adolescent dementia, 37
- adrenoleukodystrophy, 51, 76, 77, 145–146
- age-associated memory impairment, 121
- agnosia
 - in AD, 29, 59, 175
 - amnesia in, 29
 - in BD, 48
 - intracortical myelin damage and, 109
 - in subcortical dementia, 30
 - tau and, 175
- AIDS (acquired immunodeficiency syndrome), 65. *See also* human immunodeficiency virus (HIV) infection
 - articulation deficits in, 105
 - dementia in, comparison with AD, 172
 - history, 144
 - white matter dysfunction in, 66
- AIDS-dementia complex (ADC), 65
- ART treatment, 67, 144
- memory retrieval deficit in, 103
- myoclonus in, 106
- neuropsychological deficits in, 66
- normal procedural memory in, 106
- relatively preserved language in, 66
- treatment, 65, 144
- visuospatial function and, 66
- white matter changes in, 65, 144
- AIDS encephalopathy, 65
- Akiguchi, I., 146
- Albert, Martin, 30, 96
- alexia without agraphia, 6
- Alzheimer, Alois, 2, 27, 28, 46
- Alzheimer's Disease (AD). *See also* neuritic plaques/neurofibrillary tangles
 - accepted neuropathology of, 1–2, 3
 - age range of onset, 37
 - aging risk factors, 172
 - amnesia in, 29, 59, 103
 - amyloid hypothesis of, 173–175, 178, 179, 180
 - BD comparison, 46, 47, 142
 - brain/cognitive reserve studies, 137–138
 - brain inflammation in, 121, 158
 - challenges for investigators, 172
 - cholinergic augmentation in, 154
 - cognitive deficit patterns in, 59
 - concussions and, 188
 - cortical damage in, 28, 29, 36, 177
 - corticocentric diagnostic bias, 46
 - corticospinal dysfunction and, 128
 - diffuse axonal injury in, 165
 - drug trials/failures, 174
 - early onset, 37, 181
 - early-onset autosomal dominant, 162
 - early-onset familial, 33, 178
 - epidemiological studies, 137, 162
 - exercise as preventive measure, 180
 - FTLD's comparison with, 29
 - genetic influence of myelin repair, 167
 - genetic mutations in, 33, 162
 - HD, distinctions from, 30–31
 - higher prevalence in women, 177–178
 - historical background of, 2, 27, 28
 - hypertension risk factors, 162, 164
 - language impairment in, 100, 102
 - late onset, 181
 - MCI as precursor to, 123–124
 - modifiable risk factors, 162
 - MRI studies, findings, 108
 - MS comparison, 100, 102, 105, 138, 167
 - MS comparison studies, 100
 - myelin alteration in, 22
 - myelin model of, 175–179, 180, 181, 191
 - NAWM abnormalities in, 119
 - NPH comparison, 101–102
 - PD, distinctions from, 30–31, 96
 - prevention/treatment implications, 179–181
 - procedural memory preservation in, 106
 - research on genetic basis of, 33
 - sleep/ β -amyloid clearance, 165
 - sporadic AD, 178
 - stem cell therapeutics potential, 168
 - symptoms/diagnostic criteria of, 28–29
 - SYST-EUR trial findings, 164
 - TBI association, 57, 176
 - transgenic mice trials, 174, 175
 - vascular disease with, 32, 176
 - white matter and, 172–181
 - WMD similarities, 172
 - WMH in, 177
- amantadine, in TBI, 143
- aminoacidurias, 74
- 4-aminopyridine, in MS treatment, 144
- amnesia
 - in AD, 29, 59, 103
 - in concussions, 186
 - in DAI, 56
 - forgetfulness vs., 31
 - intracortical myelin damage and, 109
 - in mixed dementias, 32
 - in subcortical dementias, 30
 - tau and, 175
 - in TBI, 54, 186
- amyloid hypothesis of Alzheimer's Disease (AD), 173–175, 178, 179, 180
- amyotrophic lateral sclerosis (ALS), 188
- anatomy of white matter, 17–20, 153–155
- ANI. *See* asymptomatic neurocognitive impairment

Index

- anisotropy/anisotropic (directional) diffusion, 11
 Ankney, C. D., 23
 antiretroviral therapy (ART), 65, 66–67, 144. *See also* zidovudine
 apathy
 in BD, 47, 48, 49
 in gliomatosis cerebri, 74
 in NPH, 70, 71, 123
 in radiation leukoencephalopathy, 52
 in subcortical dementia, 31
 in toxic leukoencephalopathy, 119
 aphasia
 in AD, 29
 in BD, 48
 Broca's/Wernicke's observations on, 156
 conduction aphasia, 6, 105
 in cortical dementia, 30
 intracortical myelin damage and, 109
 in mixed dementias, 32
 neoplasms and, 72–73
 primary progressive aphasia, 153
 tau and, 175
 apraxia
 in AD, 29, 59, 175
 in BD, 48
 in cortical dementias, 30
 intracortical myelin damage and, 109
 in NPH, 71
 tau and, 175
 Armstrong, C., 53
 arousal network, 156
 arterial spin labeling PWI, 13
 association tracts
 cognition/emotion role, 18
 conduction velocity, 20
 development of, 21
 DTI tractography reconstruction depiction, 12
 LA and, 45
 MS and, 110
 relevance to behavioral neurology, 18
 TBI and, 189
 WMD resultant from damage to, 36
 astrocytomas, 73
 asymptomatic neurocognitive impairment (ANI), 65
 athletes
 CTE in, 185, 188
 dementia pugilistica in, 187
 diffuse white matter injury in, 189–190
 attention deficit-hyperactivity disorder (ADHD)
 NAWM abnormalities in, 119
 possible white matter derangement in, 38
 sustained attentional disturbances in, 102
 autism
 NAWM abnormalities in, 119
 possible white matter derangement in, 38
 autoimmune dementia, 28, 32
 axonal peripheral neuropathy, 96
 axo-oligodendroglial synapses, 21, 139
 Babikian, V., 48
 Baló's concentric sclerosis, 58
 bapineuzumab, 174
 Bartzokis, G., 105
 basal forebrain, 154
 basal ganglia, 3
 ADC and, 65, 66, 106
 AD/FTLD and, 29
 arousal network, 156
 gliomatosis cerebri and, 74
 gray matter changes in, 66
 HD/PD and, 3
 HIV infection and, 66, 144
 movement disorders and, 106, 131
 procedural memory and, 107
 subcortical dementia and, 30
 T2 hypointensities in, 50
 white matter tracts in, 18, 19
 BD. *See* Binswanger's Disease
 behavioral interventions, in WMD and MCD, 147–148
 behavioral neurology. *See also* lesion method
 basic tenet of, 5
 of the cerebellum, 158
 description/focus, 1, 4, 30
 establishment of, 30
 Geschwind's contributions to, 6
 literature review/meta-analysis of, 39
 Behçet's disease, 62
 benign senescent forgetfulness, 120–121
 Bennett, D. A., 47
 bevacizumab, in recurrent glioblastoma multiforme treatment, 145
 Binswanger, Otto, 27, 46
 Binswanger's Disease (BD), 46–49
 abnormal NAWM in people with, 48
 AD comparison, 46, 47, 142
 articulation deficits in, 105
 autopsy studies, 142
 CADASIL's similarity to, 75
 cerebrovascular risk factors, 46–47
 characteristics of, 46
 clinical/imaging criteria for ante-mortem diagnosis, 46–47 47
 cognitive dysfunction in, 48–49
 corticospinal dysfunction in, 47
 depression in, 105
 diagnosis, 127
 executive dysfunction in, 101
 hypertension risk factors, 46–47
 leukoaraiosis, relationship to, 43
 medical treatment of, 142
 MRI studies, 46
 neuroradiology of, 48
 NPH comorbidity with, 70
 prognosis, 135, 136
 psychiatric dysfunction in, 47
 questions/controversy about, 46
 relatively preserved language in, 47, 49
 subcortical/frontal-subcortical pathology, 48–49
 sustained attentional disturbances in, 102
 bipolar disorder
 cognitive impairment in, 37
 NAWM abnormalities in, 119
 blast injuries, 54, 57, 185
 blood-brain barrier, 53, 65, 159
 Boone, K. B., 45
 Boston Process Approach, 130–131
 boxers/boxing. *See* dementia pugilistica
 bradyphrenia, 30
 brain. *See also* specific structures
 development and aging, 21–22
 neuron count, 20
 19th century view of, 2
 size/intelligence correlation, studies, 23–24
 white matter percentage data, 17
 brain-behavior relationships
 cortico-centric perspective expansion and, 195, 199
 distributed neural networks and, 155
 Geschwind's interests in, 197
 Gestalt thinking about, 30
 interpretation complications, 63
 leucocentrism and, 198–199
 limitations in understanding, 108
 neuroimaging's role in understanding, 5, 10, 15
 reconsideration of, 1–7
 SLE and, 120
 toluene leukoencephalopathy and, 97
 20th century ignoring of, 2
 white matter tracts implicated in, 18
 brain biopsy, 73, 109, 128, 131–132
 brain connectivity. *See also* brain disconnectivity; connectome

- Broca/Wernicke, introduction of, 156
 cognition and, 4, 35, 196–197
 distributed neural networks, 30, 38, 153, 155–157, 156, 158, 197
 emotion and, 4
 foundational association/commis-
 sural tracts, 18
 in frontal lobes, 21
 functional neuroimaging studies,
 157, 195
 functional/structural, 14
 Geschwind on disconnectivity,
 6, 197
 gray matter microconnectivity,
 4, 107
 historical background, 197
 mapping of, 155, 199–200
 musical training benefits, 139
 role of myelination, 196
 study of Einstein's brain, 198
 white matter tracts macroconnec-
 tivity, 21, 107
 brain disconnectivity. *See also* brain
 connectivity
 disconnection syndrome, 5, 6
 DTI studies, 154
 frontal/temporal lobe damage
 and, 76
 Geschwind on, 6, 197
 leucocentrism and, 197–199
 PET studies, 74
 schizophrenia, lobotomy and, 146
 brain neoplasms, 5, 72, 72–74. *See also*
 focal white matter tumors;
 gliomas; gliomatosis cerebri;
 lymphomatosis cerebri
 CT evaluation of, 9
 focal white matter tumors, 72
 frontal and temporal lobe, 72
 gliomatosis cerebri, 73–74
 headaches and, 72–73, 122
 with increased intracranial
 pressure, 32
 motor dysfunction and, 73
 parenchymal, 72–73
 population-based study
 findings, 72
 primary, predilection for white
 matter, 122
 primary central nervous system
 lymphomas, 72
 radiation treatment for, 51
 seizures and, 72–73, 122
 treatment, 122, 145
 brain reserve. *See also* cognitive
 reserve
 concussions and, 191
 description, 107, 137–138
 onset of dementia and, 110
 Brief Repeatable Battery of
 Neuropsychological Tests for
 MS, 59
 Broca, Paul, 156, 197
 Broca's aphasia, 139
 Broca's area, 95, 106, 153
 Brodmann, Korbinian, 18, 19, 158
 Brodmann areas, cerebral cortex, 17
 bromocriptine, in TBI, 143
 Brooks, W. M., 64
 Brownell, B., 61
 CADASIL. *See* cerebral autosomal
 dominant arteriopathy with
 subcortical infarcts and
 leukoencephalopathy
Caenorhabditis elegans, connectome
 mapping in, 4
 Cajal, Santiago Ramon Y, 1
 California Verbal Learning Test
 (CVLT), 131
 callosal agenesis, 74
 cancer chemotherapy-induced
 leukoencephalopathy, 53–54
 BCNU (1,3-bis(2-chloroethyl)-
 1-nitrosourea), 53
 causative for leukoencephalopathy,
 53
 methotrexate, 53
 Caplan, L. R., 47
 carbonic anhydrase inhibitors, 145.
See also acetazolamide
 carbon monoxide intoxication,
 103, 104
 cardiorespiratory fitness in elders, 164
 cardiovascular disease
 BD risk factors, 48
 LA risk factors in, 44, 45
 caudate nucleus, involvement in
 HD, 30
 central pontine myelinolysis, 67, 136
 cerebellar-cognitive-affective
 syndrome (CCAS), 157
 cerebellum, 3, 17
 behavioral neurology of, 158
 distributed neural networks in, 155
 FXTAS and, 78
 MLD and, 77
 movement disorders and, 131
 MRI studies, findings, 157–158
 neurobehavioral importance of, 153
 role in cognition and emotion,
 157–158
 subcortical dementia and, 30
 toluene leukoencephalopathy and,
 50, 98
 white matter tract connections,
 18, 19
 cerebral amyloid angiopathy (CAA),
 43, 173
 cerebral autosomal dominant arterio-
 pathy with subcortical infarcts
 and leukoencephalopathy
 (CADASIL), 37, 75–76
 BD's similarity to, 75
 cholinergic projections'
 vulnerability in, 154
 diagnosis, 127
 diagnostic challenges, 75–76
 memory retrieval deficit in, 103
 MRI studies, findings, 76
 MS's similarity to, 75
 neurobehavioral manifestations
 of, 76
 neuroimaging studies of, 76
 relatively preserved language in, 75
 cerebral cortex
 AD and, 177
 Alzheimer's studies of, 2
 autopsy study findings, 50
 Brodmann areas, 17, 19
 cognition association, 2
 corticocentric bias and, 23
 distributed neural networks in, 156
 electroencephalographic studies, 3
 Gall's research on, 2
 gliomatosis cerebri and, 73, 74
 importance/functions, 28
 lesion method examination of, 5
 Luria's research on, 2
 mapping of, 18
 myelinated fascicles in, 154, 155
 myelination patterns, 19
 neuroimaging studies of, 3, 4, 14, 19
 neurotransmitters in, 154
 NPH and, 71
 Penfield's research on, 2
 plasticity in, 138
 radiation and, 52
 repetitive mTBI and, 191
 role of, 2
 special place in neuroscientific
 thinking, 1
 subcortical dementia and, 29, 31
 varied cellular architecture of, 158
 Vogt and Vogt, parcellating of, 19
 white matter fascicles in, 61
 white matter location relative to, 35
 white matter tracts, 18
 WMD and, 100
 cerebral disconnection syndrome, 5, 6
 cerebral ischemia, 158
 cerebrospinal fluid abnormalities, in
 mixed dementias, 32
 cerebrovascular disease. *See also*
 Binswanger's Disease;
 leukoaraiosis
 BD risk factors, 46–47
 as causative for cognitive
 dysfunction, 38

Index

- cerebrovascular disease (cont.)
 classification confusion, 42
 cognitive decline in, 128, 163
 dementia risk factors, 163
 diffusion weighting treatment value
 for, 11
 global prevalence of, 165
 homocysteine risk factor, 68
 morbidity/mortality in
 patients, 163
 white matter-behavior relation-
 ships in, 49
 young-onset dementia and, 37
 Charcot, Jean-Martin, 58, 95
 chemotherapy. *See also* cancer
 chemotherapy-induced
 leukoencephalopathy
 in brain neoplasia, 145
 “chemobrain” from, 122
 cognitive impairment from, 72, 122
 demyelination in, 53–54
 leukotoxic effects of, 72
 reduction of white matter disease
 burden, 145
 children
 ADHD study, 102
 dementia in, 37
 exercise benefits for, 164
 genetic white matter disorder
 treatment challenges, 145
 gliomatosis cerebri in, 73
 hydrocephalus in, 104
 learning disabilities in, 52
 MLD in, 76, 77
 MS cognitive decline in, 109
 radiation leukoencephalopathy
 and, 52
 traumatic brain injury in, 56
 cholinesterase inhibitors. *See also*
 donepezil; rivastigmine
 in TBI, 143
 in vascular cognitive
 impairment, 142
 in vascular dementia, 142
 chronic painters’ syndrome, 51. *See*
 also toluene
 leukoencephalopathy
 chronic traumatic encephalopathy
 (CTE), 163, 187–190
 in athletes, 185, 188
 clinical phenomenology of, 188
 cognitive reserve and, 189
 in combat veterans, 185, 188
 corticocentric bias and, 190
 dementia pugilistica similarity,
 187, 190
 frontotemporal dementia (FTD)
 similarity, 188
 incidence of, 188
 pathogenesis of, 191
 tau lesions in, 190
 TBI link with, 57, 165
 white matter changes and, 165, 189
 clinical evaluation
 HIV infection, 128
 metachromatic leukodystro-
 phy, 127
 mild cognitive dysfunction,
 127–129
 multiple sclerosis, 127
 toluene leukoencephalopathy, 127
 white matter dementia, 127–129
 Clock Drawing Test (CDT), 129
 cobalamin (vitamin B₁₂) deficiency,
 67–69
 corticospinal dysfunction in, 47
 mild cognitive impairment and, 145
 MRI studies, findings, 68
 myelination and, 68
 neurobehavioral manifestations
 of, 68
 neuropathological brain observa-
 tions in, 68
 reversibility of, 68–69
 treatment, 142, 145
 cognition
 association/commissural tracts
 and, 18
 brain connectivity and, 4, 35,
 196–197
 cerebral cortex and, 3
 early teachings on, xi, 2
 frontal lobe white matter losses
 and, 22
 gray matter’s importance for, 24,
 49, 109, 153
 myelinated systems role in, 17, 22
 neural networks mediation of, 1, 14
 subcortical gray matter and, xi
 and white matter, research
 perspectives, 153–159
 white matter lesions’ impact on, 5
 white matter’s role in, 5, 6, 17, 37
 cognitive behavioral therapy
 (CBT), 148
 cognitive impairment, 30, 32
 in Binswanger’s Disease, 48–49
 cancer chemotherapy and, 122
 in cerebrovascular disease, 38
 in cobalamin deficiency, 68
 concussions and, 188
 in depression, bipolar disorder,
 schizophrenia, 37
 in diffuse axonal injury in TBI, 57
 education’s impact on, 45
 HIV cognitive impairment and, 66
 inflammation in, 158
 in leukoaraiosis, 44, 45
 in mixed dementias, 32
 MRI’s role in understanding, 5
 in MS, 37, 58–62, 101, 121
 no dementia, 121
 normal aging and, 121
 in normal pressure hydrocephalus,
 70, 71, 122–123
 in NPH, 71
 radiation-related, 52
 in subcortical dementia, 30, 101
 in systemic lupus erythematosus, 64
 in toluene leukoencephalopathy,
 97–98
 vascular cognitive impairment, 122
 in white matter dementia, 100, 101
 white matter’s implication in
 pathogenesis, 4
 cognitive processing speed, 5, 100
 cognitive reserve. *See also* brain
 reserve
 concussions and, 191
 CTE and, 189
 description, 107, 137–138
 epidemiological studies of AD, 137
 onset of dementia and, 110
 role in LA mitigation, 45
 Colorado Medical Society Guidelines
 for the Management of
 Concussion in Sports, 186
 commissural tracts
 cognition/emotion role, 18
 conduction velocity, 20
 development of, 21
 DTI tractography reconstruction
 depiction, 13
 importance for higher functions, 20
 relevance to behavioral
 neurology, 18
 role in linking hemispheres, 18
 TBI and, 56
 vascular insults and, 176
 WMD and, 36
 computed tomography (CT), 9
 history of development, 9
 in HIV infection, 65
 inadequacy in white matter
 disorders, 129
 LA studies, 42
 MLD studies, findings, 77
 MRI comparison with, 9
 review of brain size/GMA
 studies, 23
 toluene leukoencephalopathy
 studies, 51, 98
 visuospatial function study,
 findings, 104
 concussions (mTBI)
 amnesia/confusion from, 54, 185
 in athletes, 186, 187
 blast injury similarity, 57
 Colorado Medical Society
 Guidelines for, 186

- global mTBI prevalence, 186
 in military personnel, 186, 187
 prognosis, 186
 subconcussive injuries, 186–187
 tauopathy and, 165
 tau's protective role in, 191
 TBI and, 185–187
- conduction aphasia, 6, 105
- confusion, 42
 in BD, 48
 cancer chemotherapy and, 53
 cobalamin deficiency and, 68
 in concussions, 185, 186
 in gliomatosis cerebri, 74
 in metabolic toxic encephalopathy, 165
 in mixed dementias, 32
 in radiation leukoencephalopathy, 52
 in TBI, 186
 in toluene leukoencephalopathy, 97
 in toxic leukoencephalopathy, 119
- connectivity. *See* brain connectivity
- connectome
 changes during sleep, 21
 defined, 4
 Human Connectome Project, 4, 195–196
 mapping in *Caenorhabditis elegans*, 4
 neuroimaging studies of, 4, 17
 white matter tracts and, 21
- continuous positive airway pressure (CPAP), 164–165
- corpus callosotomy, 54
- corpus callosum
 CADASIL and, 76
 creativity, association tracts, and, 198
 DAI and, 55, 55
 dementia pugilistica and, 187
 disconnection syndrome and, 5
 FXTAS and, 78
 gliomatosis cerebri and, 73
 HIV infection and, 65, 66
 leukodystrophies and, 76
 linking role of, 18
 memory retrieval and, 104
 MS and, 76, 136
 musical training impact on, 139
 neuroimaging studies, findings, 66, 71, 136, 144, 147–148, 164
 NPH and, 71
 role in attentional processing, 102
 TBI with DAI and, 189, 189
- cortical atrophy, 36
- cortical contusion, 55
- cortical dementia, 28–29. *See also* Alzheimer's Disease;
- frontotemporal lobar degeneration; Pick's Disease
 associated symptoms, 30
 cortical damage in, 36
 distinction from subcortical dementia, 3, 28, 30, 31, 95, 100, 107
 encoding deficit in, 62
 MS differentiation from, 62
 overlap with other dementias, 38
- cortical mantle, 1
- corticobasal degeneration, 28, 32
- corticocentric bias (view of brain-behavior relationships)
 AD diagnosis and, 46
 contemporary neuroscientists' belief in, 1, 3, 23, 108–109, 138
 CTE and, 190
 example of justification for, 96–97
 functional neuroimaging and, 14
 going beyond, 195–200
 Hughlings-Jackson's advancement of, 2
 MRI's role in counteracting, 97
 problems created by belief in, 35–36
- corticospinal dysfunction, 47, 50, 128
- corticosteroids
 in brain neoplasia treatment, 145
 in SLE treatment, 63, 142, 144
- cranial irradiation
 DTI studies, findings, 122
 self-limited confusional state from, 135
- C-reactive protein, 121, 158, 164
- Creutzfeldt-Jakob Disease, 28, 32
- Critchley, Macdonald, 188. *See also* chronic traumatic encephalopathy
- CT. *See* computed tomography
- CTE. *See* chronic traumatic encephalopathy
- Cummings, I. L., 48–49
- DAI. *See* diffuse axonal injury
- Darwin, Charles, 22, 38
- DBS. *See* deep brain stimulation
- declarative memory
 AIDS-dementia complex and, 66
 description, 103
 distributed network for, 157
 TBI and, 56
 white matter dementia and, 100
- deep brain stimulation (DBS), 149
- default mode network (DMN), 14
- degenerative dementia, 54. *See also* Alzheimer's Disease; chronic traumatic encephalopathy
- delirium
 abnormal NAWM in, 119
- critical illness/cognitive impairment and, 165
 white matter damage in, 163
- delusions
 in white matter lacunar dementia, 105
- dementia. *See also* Alzheimer's Disease; cortical dementia; mixed dementias; strategic infarct dementia; subcortical dementia; white matter dementia
 age-related onset data, 37
 causes of, 2, 27, 32, 36, 37
 circular reasoning on structural basis of, 3
 definition, 27
 early-onset, 37
 epidemiological studies, 38, 39, 162–163
 genetic-mediation/genetic mutations and, 162
 hypertension control and, 180
 modifiable risk factors, 162
 Netherlands study of risks in elders, 33
 neuritic plaques/neurofibrillary tangles in, 3
 neuroanatomic overview of, 27–33
 phenomenology/etiopathogenesis of, 2
 public health prevention approach, 163
 radiation-induced, 52
 traditional categories, specific diseases, 28
 white matter's neurorelevance in, 35
- dementia pugilistica, 185, 187, 190
- demyelination. *See also* demyelinating diseases; myelination; remyelination
 in ADC, 65, 67
 in BD, 70
 in brain tumors, 72
 in cancer chemotherapy, 53–54
 cobalamin and, 68
 CT observations of, 74
 dysmyelination distinction, 75
 fatal dementia from, 52
 gliomas and, 73
 in gliomatosis cerebri, 74
 in HIV infection, 67
 in LA, 44
 LA and, 44
 in MLD, 76–77
 in MS, 20, 44, 59–60, 61–62, 103, 104, 110, 120, 121, 166
 myelin repair and, 166–168

Index

- demyelination (cont.)
 neurobehavioral consequences
 of, 20
 in NPH, 71
 in radiation leukoencephalopathy, 52
 in SLE, 64, 120
 in toluene leukoencephalopathy, 50, 98–99, 108, 110, 136
 in toxic leukoencephalopathies, 101, 143
 vascular dementia, 43
 in white matter lesions, 132, 136
 demyelinating diseases, 58, 58–62. *See also* multiple sclerosis
 acute disseminated encephalomyelitis, 58
 Baló's concentric sclerosis, 58
 infectious disease similarities, 64
 Marburg's disease, 58
 neuromyelitis optica, 58
 Schilder's disease, 58
 tumefactive multiple sclerosis, 58
 demyelinating peripheral neuropathy, 96
 depression
 AD risk factors, 162
 BD and, 47
 CADASIL and, 76
 cognitive impairment in, 37
 in CTE, 188
 deep brain stimulation for, 149
 inflammatory mechanisms in, 158
 in MS, 105
 neoplasms and, 72
The Descent of Man (Darwin), 22
 descriptive studies, value of, 38
 Deter, Auguste, 2, 37
 developmental dyslexia, 38
 diabetes mellitus
 AD risk factors, 162
 dementia risk factors, 163
 LA risk factors in, 44
 diffuse axonal injury (DAI), in TBI, 165, 176
 AD and, 165
 autopsied brain findings, 189, 189
 concussions and, 192
 CTE and, 165, 190–191, 192
 Glasgow Coma Scale assessment, 56
 medical therapy treatment, 143
 microscopic studies, findings, 55–56
 in mild/severe TBI, 55
 monkey studies, 108
 neurobehavioral impact of, 56–57, 136
 neuroimaging studies, findings, 56
 phosphorylated tau accumulation in, 190, 191, 192
 post-mortem study, 55
 prefrontal leucotomy and, 191
 prognosis, 136
 static encephalopathy and, 165
 tauopathy and, 190–192
 widespread damage caused by, 55–57, 166
 diffuse necrotizing leukoencephalopathy, 53
 diffusion kurtosis imaging (DKI), 9
 crossing fibers phenomenon and, 13
 enabling of quantification of non-Gaussian water diffusion, 13
 gliomatosis cerebri studies, findings, 74
 diffusion spectrum imaging (DSI), 9, 12
 diffusion susceptibility contrast PWI, 13
 diffusion tensor imaging (DTI), 6, 9
 CADASIL studies, findings, 76
 capturing of Gaussian diffusion by, 13
 of cardiorespiratory fitness in elders, 164
 children/ADHD studies, findings, 102
 cognitive processing observations, 101
 connectome mapping by, 17
 corpus callosum studies, findings, 66, 144, 147–148, 164
 crossing fibers phenomenon issues, 12
 delirium assessment, 165
 evaluation of strokes, 104
 FXTAS studies, findings, 123
 glioma/cranial irradiation, studies, findings, 122
 gliomatosis cerebri studies, findings, 74
 history of development, 11–12
 HIV studies, findings, 66
 leukoaraisosis studies findings, 45
 memory retrieval studies, 104
 MS studies, findings, 61
 NAWM investigations, 13, 48, 119
 NPH studies, findings, 71
 SLE studies, findings, 64
 studies of non-pharmacologic interventions, 148
 TBI studies, 56, 57, 189–190
 tract-based spatial statistics, 12
 tract identification challenges, 14
 of white matter tracts, 12, 57, 74
 diffusion weighting amplification, MRI, 11
 disconnection syndromes, 5, 6, 154
 disconnectivity. *See* brain disconnectivity
 distributed neural networks, 30, 38, 153, 155–157, 156, 158, 197
 DMN. *See* default mode network
 donepezil
 for Binswanger's Disease, 142
 in TBI, 143
 in vascular dementia, 142
 dysmyelination
 CT observations of, 74, 77
 demyelination distinction, 75
 MLD and, 76–77
 early-onset Alzheimer's Disease, 33, 178
 early-onset autosomal dominant Alzheimer's Disease, 37, 162
 early-onset dementia, 37
 early-onset familial Alzheimer's Disease, 33, 178
 Einstein, Albert, 39, 198
 electroconvulsive therapy, 148
 electroencephalography (EEG)
 epilepsy monitoring, 129
 for excluding white matter involvement, 129
 of toluene leukoencephalopathy, 98
 of white matter, 3
 emotion
 association/commissural tracts and, 18
 myelinated systems role in, 17, 22
 neural networks mediation of, 1
 white matter lesions' impact on, 5
 white matter's role in, 5, 6, 17
 encephalitis subcorticalis chronica progressiva, 46
 encephalomalacia, 48
 ependymoma, 73
 epidemiological studies
 of cognitive reserve in AD, 137
 of dementia, 38, 39, 162–163
 epidural hematoma, 55
 epilepsy, 2, 129
 executive function
 ADC and, 66
 Binswanger's Disease and, 49, 101
 cerebral white matter's role in, 5
 cognitive slowing and, 64
 cortical structure's role in, 97
 distributed network for, 157
 fragile X tremor ataxia syndrome and, 102
 leukoaraisosis and, 45
 metachromatic leukodystrophy and, 77, 102
 MS and, 62
 neoplasms and, 72
 NPH and, 71, 101–102, 123

Index

- radiation treatment and, 52
 SLE and, 64
 TBI and, 56
 toluene leukoencephalopathy and, 50–51
 toxic leukoencephalopathy and, 101
 vitamin B₁₂ deficiency and, 68
 white matter dementia and, 100, 101–102
- exercise
 AD prevention and, 180
 white matter benefits from, 139, 164
- Extended Disability Status Scale (EDSS), 59
- extrapyramidal function/dysfunction
 Binswanger's Disease and, 47
 forms of dysfunction, 106
 mixed dementia and, 32
 white matter dementia and, 106
- florbetapir (amyloid ligand), 174, 179
- fluid-attenuated inversion recovery (FLAIR) images, 59
- focal cerebral infarctions, 42
- focal cerebral lesions, 27
- focal damage, 6, 197
- focal neurobehavioral syndromes, 7
- focal white matter tumors, 72
- Folstein, Marshall, 30
- fractional anisotropy (FA), 12, 158
- fragile X tremor ataxia syndrome, 78
 executive dysfunction in, 102
 memory retrieval deficit in, 103
 MRI studies, findings, 78
 NAWM abnormalities in, 119
 neuroimaging studies, findings, 123
 relatively preserved language in, 78
 white matter hyperintensities and, 78
- Franklin, G. M., 59
- Freud, Sigmund, 2, 30, 197
- frontal aslant tract, 153
- Frontal Assessment Battery (FAB), 71, 129
- frontal lobe neoplasms, 72
- frontal lobotomy, 54
- frontally-predominant leukodystrophy, 77
- frontal systems dementia. *See* subcortical dementia
- fronto-subcortical dementia. *See* subcortical dementia
- frontotemporal dementia (FTD), 188
- frontotemporal lobar degeneration (FTLD), 28
 AD's comparison with, 29
 comparison with Alzheimer's disease, 29
 cortical damage in, 29, 36
 HD/PD, distinctions from, 30–31
 young-onset dementia and, 37
- FTLD. *See* frontotemporal lobar degeneration
- fulminant fatal leukoencephalopathy, 65
- functional magnetic resonance imaging (fMRI), 9, 14
 cerebellum, studies and findings, 157–158
 connectivity studies, 157
 neural network identification, 14
- functional neuroimaging methods, 14–15. *See also* functional magnetic resonance imaging; positron emission tomography; single photon emission computed tomography
- gray matter emphasis of, 14
- neural networks identification by, 14
- FXTAS. *See* fragile X tremor ataxia syndrome
- gait disorder
 4-aminopyridine treatment, 144
 in BD, 47
 in CTE, 188
 leukoaraiosis and, 45
 in MLD, 76
 MRI/DTI studies, findings, 128
 in NPH, 70, 71–72
 periventricular lesions in, 44
- galantamine
 in Binswanger's Disease, 142
 in vascular cognitive impairment, 142
- Gall, Franz Joseph, 2, 95, 156, 197
- general mental ability (GMA), 23
- gene therapy, 77, 146
- genetic diseases, 74, 74–78. *See also* specific genetic diseases
- Gennarelli, T. A., 108
- Geschwind, Norman, 154, 197. *See also* disconnection syndromes
 on brain disconnectivity, 6, 197
 founding of behavioral neurology, 6
 NPH and, 70
- Glasgow Coma Scale, 54, 56, 57
- glatiramer, in MS treatment, 143
- gliomas, 72, 104. *See also* astrocytomas; ependymoma; oligodendroglioma
- cranial irradiation studies.
 findings, 122
 description, 73
 gliomatosis cerebri comparison, 73
 NAWM abnormalities in, 119, 122
 radiation treatment study, 52
- gliomatosis cerebri, 72, 73–74
- characteristics, 73
 diagnostic challenges, 73
 mortality rate, 73
 neurobehavioral alterations from, 74
 neuroimaging studies, findings, 73–74
 predislection for cerebral white matter, 122
 prognosis, 135
- global brain atrophy, 36, 109
- glutamatergic transmission, 21, 147
- Golgi, Camillo, 1
- gradient echo (GRE) imaging, 56
- gray matter
 AD and, 100, 107–108
 ADC and, 66
 aging and trajectory of, 21
 association tract interconnectivity, 18
 changes in HIV infection, 66
 cognitive importance of, 24, 49, 109, 153
 conventional emphasis on, 1–4
 conventional synapses in, 21
 cortical/deep fascicles of white matter, 20, 95
 cortical infarcts and, 96
 extrapyramidal function and, 106
 formation/development, during gestation, 21
 gliomatosis cerebri involvement, 66
 HD/PD neuropathology and, 30, 96
 intelligence and, 1
 lesion method examination of, 5
 MCI and, 124, 124
 metabolic activity comparison, 17
 microconnectivity of, 4, 107
 MRI scan, distinction from white matter, 10
 MS and, 59, 61, 62, 100, 138
 myelinated tracts within, 36, 106
 normal brain perfusion comparison, 13
 in NPH, 71
 plasticity property of, 138, 139, 147
 PWI assessment of, 14
 retrieval deficits/procedural memory and, 107
 subcortical, 1–4
 white matter's parallel functions with, 4
 WMD and, 108
- Hachinski, V. C., 43
- HAD. *See* HIV-associated dementia
- hallucinations
 mixed dementias and, 32

Index

- hallucinations (cont.)
 neoplasms and, 72
 white matter lacunar dementia and, 105
- HAND. *See* HIV-associated neurocognitive disorder
- HD. *See* Huntington's Disease
- Head, Henry, 197
- headaches
 mixed dementias and, 32
 neoplasms and, 72–73, 122
- Heaton, R. K., 58
- hematopoietic stem cell transplantation (HSCT), 145–146
- hemiparesis, neoplasms and, 72–73
- Higher Cortical Functions in Man* (Luria), 2
- histograms, whole brain, 11
- Hitler, Adolf, 22–23
- HIV-associated dementia (HAD), 47, 65, 67
- HIV-associated mild neurocognitive disorder (MND), 65, 67
- HIV-associated neurocognitive disorder (HAND), 65, 67
- Hughes, J. T., 61
- Hughlings-Jackson, John, 2
- Huisa, B. N., 47
- Human Connectome Project (U.S.), 4, 195–196
- De Humani Corporis Fabrica* (Vesalius), 95
- human immunodeficiency virus (HIV) infection, 65–67. *See also* AIDS (acquired immunodeficiency syndrome)
 antiretroviral therapy treatment, 65, 66–67, 144
 associated terminology, 65
 brain/cognitive reserve studies, 137, 138
 brain cortex studies, findings, 65, 66
 as causative for dementia, 37
 clinical evaluation, 128
 cognitive profile of brain infection in, 66
 DTI studies, findings, 66
 fulminant fatal leukoencephalopathy in, 65
 gray matter changes in, 66
 NAWM abnormalities in, 66, 119, 122
 prognosis, 136
 treatment, 142, 144
- Huntington's Disease (HD), 3, 28
 caudate nucleus involvement in, 30
 genetic mutations in, 162
 impaired procedural memory in, 106–107
 memory disturbances in, 102
- MS comparison studies, 100
 stem cell therapeutics potential, 168
 subcortical dementia symptoms in, 30
- hydrocephalus, 69. *See also* normal pressure hydrocephalus
- hydrocephalus ex vacuo, 69
- hyperlipidemia, 163
- hypertension
 AD risk factors, 162, 164
 BD risk factors, 46–48
 dementia risk factors, 163
 LA risk factors in, 44
 SYST-EUR study, 164, 180
 WHIs and, 164
- hypoxic-ischemic encephalopathy, 28, 32, 55
- immunomodulatory drugs, in MS
 treatment, 143–144
- immunosuppressive drugs
 in MS treatment, 143
 in SLE treatment, 144
- infectious diseases of white matter, 64, 64–67. *See also* specific diseases
- inflammation
 in Alzheimer's Disease, 121
 C-reactive protein and, 121
 in MS, 60, 61, 158
 radiation leukoencephalopathy and, 53
 in SLE, 63, 120, 121, 158
 white matter and, 158–159
- inflammatory white matter diseases, 64, 62–64. *See also* acute disseminated encephalomyelitis; Baló's concentric sclerosis; Marburg's disease; multiple sclerosis; neuromyelitis optica; Schilder's disease; tumefactive multiple sclerosis
- integrative review process, 38–39
- interferon β -1-a, in MS, 143
- interferon β -1-b, in MS, 143
- intracerebral hemorrhage, 55
- intracortical myelin, 20, 21–22, 109–110, 149, 155
- IQ, white matter integrity and, 104
- ischemic vascular dementia, 103
- ischemic white matter hyperintensities, 109
- Kaplan, Edith, 130. *See also* Boston Process Approach
- knowledge synthesis, 39
- Krabbe's Disease, 145
- LA. *See* leukoaraiosis
- Lafosse, J., 107
- language. *See also* relatively preserved language
 articulation deficits, 105
 cortical structure's role in, 97, 106
 frontotemporal lobar degeneration and, 29
 gray matter contributions, 4
 impairment in AD, 100, 102
 networks, neuroimaging identification, 14
 radiation treatment and, 52
 subcortical dementia and, 30
 white matter's role in, 5, 32, 106
- Lashley, Karl, 197
- left inferior frontal cortical injury, 5
- lesion method, in examining white matter, 5, 14, 27–28
- leucocentrism, disconnection and, 197–199
- leukoaraiosis (LA)
 abnormal NAWM in people with, 45
 arteriosclerotic changes in, 44
 Binswanger's Disease's relationship to, 43
 cardiovascular disease risks, 44, 45
 as causative for cognitive dysfunction, 38
 cholinergic projections' vulnerability in, 154
 DTI studies findings, 45
 education's impact on, 45
 executive function and, 45
 gait disorder and, 45
 genetic influences, 44
 historical background, 43–44
 incomplete infarction of, 122
 MRI studies, 42, 43, 43, 44, 45
 NAWM abnormalities in, 119
 neurobehavioral significance of, 44–45
 neurologic morbidity, mortality and, 45
 pathogenesis of, 44
 stroke risk factors, 44, 45
 treatment, 46
 white matter hyperintensities and, 43, 44
- leukodystrophies, 37
- Lewy bodies, 32
- Lewy body dementia, 28, 32
- limbic system, 18, 18, 157
- Luria, Alexander, 2
- lymphomatosis cerebri, 122, 145
- magnetic resonance imaging (MRI), 5, 9, 9–11
 AD studies, findings, 108
 advantage in WMD studies, 36, 38, 97, 129–130, 136

Index

- BD studies, 46
 CADASIL studies, findings, 76
 cobalamin deficiency studies, findings, 68
 cognitive processing observations, 101
 community-based brain scan studies, 195
 CT comparison with, 9
 detection of UBOs, 10
 detection of WMH, 10–11
 diffusion weighting amplification of, 11
 FXTAS studies, findings, 78
 gliomatosis cerebri studies, findings, 74
 history of development, 9, 36
 leukoaraiosis studies, 42, 43, 45
 macrostructural disruption evaluation, 6
 memory retrieval studies, 103–104
 MLD studies, findings, 77
 MS studies, findings, 5, 10, 15, 58, 59, 60–61
 neuropsychological testing combination, 130
 NPH studies, findings, 70
 post-mortem human neocortex studies, 20
 as preferred white matter assessment modality, 10–11
 radiation leukoencephalopathy studies, 53
 review of brain size/GMA studies, 23
 role in detecting/understanding diseases, 5–6
 role in toxic drug discoveries, 49
 role in understanding MS, 5, 10, 15
 SLE studies, findings, 64, 119–120
 tau studies, 191
 TBI assessment, 56
 toluene leukoencephalopathy studies, findings, 50–51, 98
 vascular dementia studies, 49
 white matter fascicles' studies, 155
 WMD studies, findings, 119
 WMH recognized by, 10–11, 43, 43, 51, 98
 magnetic resonance spectroscopy (MRS), 6, 9
 early abnormalities detected with, 11
 FXTAS studies, findings, 123
 gliomatosis cerebri studies, findings, 74
 NAWM investigations, 13, 119
 SLE studies, findings, 64, 120
 vascular dementia studies, findings, 48
 magnetization transfer imaging (MTI)
 advanced neuroimaging capabilities, 6, 9
 description/usefulness, 11
 NAWM investigations, 13, 119
 vascular dementia studies, 48
 magnetization transfer ratio (MTR), 11
 Marburg's disease, 58
 Markowitsch, H. J., 103
 MCD. *See* mild cognitive dysfunction
 McHugh, Paul, 30
 medulloblastoma, 53
 memory retrieval deficit, 102–104
 Mendez, M. F., 108
 meningismus, mixed dementias and, 32
 metabolic disorders of white matter, 67, 67–69. *See also* specific disorders
 metabolic-toxic encephalopathy. *See* delirium
 metachromatic leukodystrophy (MLD), 76–78
 adult-onset, 105
 in children, 76, 77
 clinical evaluation, 127
 diagnosis, 77, 127
 executive dysfunction in, 102
 HSCT treatment, 145–146
 NAWM abnormalities in, 119
 neuroimaging studies, findings, 77
 neuropathology of, 76–77
 neuropsychological testing, findings, 77
 relatively preserved language in, 77
 treatment, 77–78, 142
 methylphenidate, in TBI, 143
 mild cognitive dysfunction (MCD), 118–124
 ADC and, 65
 background research, 118–120
 characteristics, 120
 definition, 120
 diagnosis, 100, 127–132, 128
 brain biopsy, 131–132
 clinical evaluation, 127–129
 laboratory testing, 129
 neuroimaging, 129–130
 neuropsychology, 130–131
 increasing legitimacy of, 195–196
 inflammatory processes, 121
 leucocentrism and, 198
 mild cognitive impairment comparison, 123–124, 124
 MND similarities, 120, 122
 in MS, 120
 neurobiological advantage of, 123
 as precursor syndrome, 38
 preventive measures, potential, 154
 prognosis
 brain/cognitive reserve, 137–138
 influential factors, 135
 natural history, 135–137
 plasticity, 138–139
 in SLE, 64, 120
 treatment, 142, 142–149
 behavioral, 147, 147–148
 cholinergic augmentation, 154
 medical, 142–146
 psychiatric, 148–149
 rehabilitative, 147–148
 surgical, 146–147
 vitamin B₁₂ and, 69
 white matter tracts and, 124
 mild cognitive impairment (MCI)
 MCD comparison, 123–124, 124
 as pre-dementia state, 118, 178, 180
 vitamin B₁₂ supplementation and, 145
 WMH in, 177
 mild neurocognitive disorder (MND)
 in HIV infection, 65, 67
 MCD similarities, 120, 122
 mild traumatic brain injury (mTBI). *See* concussions
 military personnel
 blast injuries in, 54, 57, 185
 chronic traumatic encephalopathy in, 185
 concussions in, 186
 Luria's study of Russian soldiers, 2
 tauopathy in, 190
 VA TBI assessment, 186, 186
 mindfulness meditation, DTI study, 148
 Minimal Assessment of Cognitive Function in MS (MACFIMS), 59
 Mini-Mental State Examination (MMSE), 128–129
 mixed dementias, 28, 32–33. *See also* autoimmune dementia; corticobasal degeneration; Creutzfeldt-Jakob Disease; hypoxic-ischemic encephalopathy; Lewy body dementia; multi-infarct dementia; neurosyphilis; subdural hematoma
 MLD. *See* metachromatic leukodystrophy
 MND. *See* mild neurocognitive disorder
 Montreal Cognitive Assessment (MoCA), 129
 morbidity/mortality, 147
 APP knockout mice studies, 176
 cerebrovascular disease and, 163
 inflammation and, 158

Index

- morbidity/mortality (cont.)
 leukoaraiosis and, 45
 TBI and, 163
- movement disorders. *See also* gait disorder; Parkinson's Disease
 causes of, 106
 in dementia in BD, 48
 extrapyramidal dysfunction and, 106
 in MS, 106
 myoclonus in ADC, 106
 uncommon in white matter disorders, 128
- MRI. *See* magnetic resonance imaging
- MRS. *See* magnetic resonance spectroscopy
- MTI. *See* magnetization transfer imaging
- MTR. *See* magnetization transfer ratio
- mucopolysaccharidoses, 74
- multi-infarct dementia, 28, 32
- multiple sclerosis (MS)
 AD comparison, 100, 102, 105, 138, 167
 assessment screening tools, 59
 brain atrophy in, 60, 61
 brain/cognitive reserve and, 137, 138
 brain inflammation in, 60, 61, 121
 CADASIL's similarity to, 75
 Charcot's initial insights about, 58
 clinical evaluation, 127
 cognitive impairment in, 37, 58–62, 101, 121
 cortical demyelination in, 20, 59–60, 61–62, 103, 104, 110, 120, 121
 corticospinal dysfunction in, 47
 depression in, 105
 differentiation from cortical dementias, 62
 DTI studies, findings, 61
 FLAIR studies, 59
 gray matter lesions in, 62
 HD comparison studies, 100
 inflammation in, 60, 61, 158
 intracortical myelin in, 109–110
 MCD in, 120
 memory retrieval deficit in, 103, 104
 MRI studies, 5, 10, 15, 58, 59, 60–61
 MRS studies, 11
 NAWM findings in, 58, 61, 119, 121
 neuropathology of, 59–60, 61
 neuropsychological deficits in, 61–62
 normal procedural memory in, 106
 prognosis, 135
 relatively preserved language in, 59, 62
- remyelination process in, 166–167, 168
 sustained attentional disturbances in, 102
 treatment, 142, 143–144
- Multiple Sclerosis Functional Composite (MSFC), 59
- muscular dystrophy, 74
- myelin. *See also* demyelination; demyelinating diseases; dysmyelination; myelination; remyelination; white matter tracts
 altered formation of, 22
 BD and, 48
 cancer chemotherapy and, 53–54
 cobalamin and, 67
 cognitive processing speed and, 100
 core neurophysiological function, 101
 DAI and, 55, 165
 intracortical myelin, 20, 21–22, 109–110, 149, 155
 language processing and, 106
 movement disorders and, 106
 MRI studies, 119
 MTI imaging, 11
 NAA as injury marker, 11
 repair of, 166–168
 role in white matter, 21
 role in white matter disorders, 36
 SLE and, 136, 144
 white matter anatomy and, 17, 19–20, 153–155
 white matter neuropathology and, 135
- myelination. *See also* demyelination
 in adolescents, young adults, 105
 of cerebral axons, 23, 36
 connectivity role, 196
 connectome role, 21
 evolution in the brain, 21, 22, 24
 MLD and, 76, 77
 plasticity of, 21, 139, 147
 psychiatric disturbance and, 105
 retardation in schizophrenia, 149
 role in cognition/emotion, 17, 22
 role in electrical conduction, 20
 schizophrenia treatment and, 149
 thyroid hormones and, 129
 treatments for enhancement of, 167
 Vogts' studies, findings, 19, 155
- myelin model of Alzheimer's Disease (AD), 175–179, 180, 181, 191
- myoclonus, 32, 106
- N-acetyl aspartate (NAA), 11, 120, 136, 146
- natalizumab, in MS treatment, 143
- Naville, F., 30
- NAWM. *See* normal-appearing white matter
- neoplasms. *See* brain neoplasms
- neuritic plaques/neurofibrillary tangles, in Alzheimer's Disease, 2, 3
 Alzheimer's discovery of, 28
 autopsy study findings, 173
 as cortical hallmarks in AD, 29, 172
 counteractive mechanisms, 108
 sequence in neuropathological appearance, 173
 white matter changes and, 33
- neuroanatomic overview of dementia, 27–33
 cortical dementia, 28–29
 mixed dementia, 32–33
 subcortical dementia, 29–32
 traditional categories, diseases, 28
 neurobehavioral domains, 5
 neurobiology of white matter, 17–24
 anatomy, 17–20
 brain development and aging, 21–22
 physiology, 20–21
- neuroimaging technologies. *See also* specific technologies
 in AD research, 174
 essential contributions of, 9, 9–15
 functional neuroimaging, 14–15, 17, 103
 growing advantages of, 5
 historical background, 5, 35, 100
 neuroanatomy combination, 18, 153–154
 role in observing white matter, 4, 5, 42
 structural neuroimaging, 11–14, 17, 23
 of tau, in the brain, 191
- neuromyelitis optica, 58
- neuron doctrine, 1, 36
- neuropsychiatric syndromes, 7, 63
- neuropsychological testing, 30
 of attention, 102
 in BD, 47
 Boston Process Approach, 130–131
 cognitive slowing and, 101
 forms of, 130–131
 MRI combination, 130
 of procedural memory, 106
 role in WMD/MCD diagnosis, 130–131
- neurosyphilis, 28, 32, 46
- neurotransmitter systems in white matter, 154
- Nevin, S., 55
- Niemann-Pick Disease, 77
- nitrendipine, 164
- non-fluent aphasia, 5

- non-paraneoplastic autoimmune dementia, 32
- normal-appearing white matter (NAWM)
 abnormal appearance of, 119, 119
 appearance in non-demented patients, 122
 BD studies, 48
 CADASIL studies, findings, 76
 cognition and, 123
 C-reactive protein and, 121
 HIV findings, 66, 119, 122
 LA studies, 45
 microstructural changes in, 111
 MS studies, 58, 61, 119, 121
 neuroimaging studies, findings, 13, 48, 58, 66, 110, 119, 120
 NPH studies, 70
 radiation therapy and, 122
 TBI studies, 56
 white matter inflammation and, 119
- normal pressure hydrocephalus (NPH), 37, 69, 69–72
 AD comparison, 101–102
 BD comorbidity with, 70
 clinical presentation, 70
 cognitive impairment in, 70, 71, 122–123
 CT evaluation, 9
 diagnosis of, 70
 DTI studies, findings, 71
 executive dysfunction in, 71, 101–102, 123
 Frontal Assessment Battery in, 71
 gait disorder in, 71–72
 gray matter in, 71
 MRI studies, findings, 70
 NAWM abnormalities in, 119
 neurobehavioral profile of, 71
 pathophysiology of, 70–71
 prognosis, 136
 treatment of, 142
 pharmacologic, 72, 145
 surgical, 69, 71, 146
 white matter hyperintensities and, 72
- NPH. *See* normal pressure hydrocephalus
- obesity, 44, 162, 180, 181
- obstructive sleep apnea (OSA), 164–165
- oligodendroglioma, 73
- Olszewski, J., 46
- Osimani, A., 68
- Paced Auditory Serial Addition Test (PASAT), 101, 131
- painted brain syndrome, 97. *See also* toluene leukoencephalopathy
- panic attacks, 72
- papilledema, 32
- paraneoplastic autoimmune dementia, 32
- parenchymal brain neoplasms, 72–73
- parkinsonism
 from carbon monoxide poisoning, 106
 in CTE, 188
 in dementia pugilistica, 187
 lower body (cerebrovascular gait disorder), 128
 mixed dementias and, 32
 postencephalitic, 30
- Parkinson's Disease (PD), 3, 28
 AD distinctions from, 30–31, 96
 brain reserve and, 137
 concussions and, 188
 dementia in, 30
 stem cell therapeutics potential, 168
 substantia nigra involvement, 30
- Penfield, Wilder, 2
- perfusion-weighted imaging (PWI), 9, 13–14. *See also* arterial spin labeling PWI; diffusion susceptibility contrast PWI
- periventricular lesions, 44, 145
- Peyser, J. M., 58
- phakomatoses, 74
- physiology of white matter, 20–21
- Pick, Arnold, 27, 29
- Pick bodies, 32
- Pick's Disease, 28, 29. *See also* fronto-temporal lobar degeneration
- plasticity
 benefits for WMD/MCD, 70, 139, 147
 bilingualism benefits, 139
 in the cerebral cortex, 138
 definition, 138
 of gray matter, 138, 139, 147
 musical training benefits, 138–139
 therapeutics for, 148
 white matter tracts and, 139
- polyarteritis nodosa, 62
- positron emission tomography (PET), 9
 amyloid studies, 174
 cerebral cortex studies, 3, 74
 connectivity studies, 157
 gliomatosis cerebri studies, findings, 74
 mechanics of, 14
 subcortical dementia study, findings, 109
 tau studies, 191
- post-concussion syndrome, 186
- postencephalitic parkinsonism, 30
- post-traumatic stress disorder, 185
- prefrontal leucotomy, 191
- primary angiitis of the central nervous system, 62
- primary progressive aphasia, 153
- procedural memory
 AIDS-dementia complex and, 66
 description, 103
 preservation in AD, 106
 TBI and, 56
 white matter dementia and, 100, 106–107
- progressive multifocal leukoencephalopathy, 37
- progressive supranuclear palsy, 28
- projection tracts, 17, 156
- psychosis, in adult-onset MLD, 105
- PWI. *See* perfusion-weighted imaging
- radiation, 51–53
 causative for dementia, 37, 52
 children's learning disabilities and, 52
 cognitive impairment from, 52, 72
 executive dysfunction from, 51–52
 leukotoxic effects of, 52, 72
 MRI studies, findings, 53
 neurotoxic effects of, 51–52
- radiation leukoencephalopathy
 cancer chemotherapy comparison, 53
 clinical sequelae of, 52
 cranial irradiation and, 52
 dosages causing, 52
 focal vs. whole brain, 52
 hypothesized causes of, 53
 memory retrieval deficit in, 103
 neuropathological abnormalities in, 52
- Rao, S. M., 58
- recognition memory, 103, 108, 131
- relatively preserved language
 in ADC, 66
 in Binswanger's Disease, 47, 49
 in CADASIL, 75
 in FXTAS, 78
 in MLD, 77
 in MS, 59, 62
 in SLE, 64
 in TBI, 57
 in vitamin B₁₂ deficiency, 68
 in WMD, 105–106
- remyelination
 in MLD, 77
 in MS, 166–167, 168
 in normal aging, 166
- repetitive transcranial magnetic stimulation (rTMS), 148
- reticular theory, Golgi's defense of, 1

Index

- rivastigmine, in TBI, 143
 Roberts, A. H., 187
 rodent studies, 2–3
 Román, G. C., 48
 Ropper, A. H., 48
 Rosenberg, N. L., 47
 rTMS. *See* repetitive transcranial magnetic stimulation
 Rushton, J. P., 23
- sarcoidosis, 62
 Schilder's disease, 58
 schizophrenia
 brain reserve and, 137
 cognitive impairment in, 37
 medication treatment, 146, 149
 myelination and, 37, 105
 NAWM abnormalities in, 119
 surgical treatment, 146, 191
 tau and, 191
 scleroderma, 62
 seizures
 gliomatosis cerebri and, 73
 in mixed dementias, 32
 neoplasms and, 72–73, 122
 uncommon in white matter disorders, 128
 shaken baby syndrome, 54
 Sheline, G. E., 52
 single photon emission computed tomography (SPECT), 9, 14
 Sjögren's syndrome, 62
 SLE. *See* systemic lupus erythematosus
 sleep medicine, 164–165
 smoking
 AD risk factors, 162
 LA risk factors in, 44
 solanezumab, 174
 somatic therapies, 148
 somnolence syndrome, 52
 spatial attention network, 157
 Spurzheim, Johann Kaspar, 2, 95, 156
 static encephalopathy, 54, 57, 165
 stem cell therapeutics, 77, 146, 168–169
 strategic infarct dementia, 27
 strokes
 BD and, 49
 brain inflammation in, 121
 CT evaluation of, 9
 DTI evaluation of, 104
 focal cerebral lesions from, 27
 LA risk factors in, 44, 45
 mixed dementias and, 32
 rehabilitation treatment, 147
 structural neuroimaging methods. *See* diffusion kurtosis imaging; diffusion spectrum imaging; diffusion tensor imaging; magnetic resonance imaging; magnetic resonance spectroscopy; magnetization transfer imaging; perfusion-weighted imaging
 Stuss, D. T., 48–49
 subacute HIV encephalitis, 65
 subcortical arteriosclerotic encephalopathy, 46
 subcortical dementia, 3, 28, 29–32. *See also* Huntington's Disease; Parkinson's Disease; progressive supranuclear palsy; white matter disorders; Wilson's Disease
 ADC characterization as, 66
 alternate descriptors, 30
 BD classification as, 48
 cobalamin deficiency and, 68
 cognitive impairment in, 30, 101
 contributions of concept of, 32
 cortical dementia distinction from, 3, 28, 30, 31, 95, 100, 107
 defense of concept of, 31
 historical background, 30, 35, 96
 MS qualification as, 62
 NPH's features of, 71
 opposition to concept of, 31
 overlap with other dementias, 38
 in SLE patients, 64
 toluene abuse and, 50
 WMD distinction from, 100
 subcortical ischemic vascular dementia (SIVD), 43, 46
 subcortical lesions, 44, 75, 167
 subdural hematoma, 28, 32, 55
 substantia nigra, in PD, 30
 supranuclear palsy, 30
 susceptibility-weighted images (SWI), 56
 Symonds, Sir Charles, 70, 137
 systemic lupus erythematosus (SLE), 63–64
 cognitive slowing in, 64
 immune-related myelinopathy in, 120
 inflammation in, 63, 120, 121, 158
 MCD in, 64, 120
 MMSE assessment, 144
 MRI studies, findings, 119–120
 MRS studies, findings, 64, 120
 NAWM abnormalities in, 119
 neuroimaging studies, 64
 neuropsychological study of cognitive dysfunction, 63–64
 pathogenesis of neuropsychiatric dysfunction, 63
 pathology of, 63
 prognosis, 136
 relatively preserved language in, 64
 treatment, 63, 142, 144
 white matter hyperintensities and, 64
 Systolic Hypertension in Europe (SYST-EUR) study, 164, 180
 Takeuchi, H., 147
 TAR DNA-binding protein 43 (TDP-43), 29
 tau
 as hallmark CTE lesion, 190
 mechanisms of spreading in the brain, 192
 neuroimaging of, 191
 protective role in concussions, 191
 vulnerability to injury, 190
 tauopathy
 in athletes, military personnel, 190
 CTE and, 165, 188
 diffuse axonal injury and, 190–192
 prefrontal leucotomy study, 191
 tau-positive (FTLD-TAU) protein, 29
 Tay-Sachs Disease, 77
 tCDS. *See* transcranial direct current stimulation
 temporal arteritis, 62
 temporal lobe neoplasms, 72
 thalamus, 3
 AD/FTLD and, 29
 arousal network, 156
 gliomatosis cerebri and, 74
 gray matter changes in, 66
 isolated vascular lesions of, 27
 subcortical dementia and, 30
 T2 hypointensities in, 50
 white matter tracts in, 18, 19
 therapeutic innovations in treatment, 162–169
 damage prevention, 162–165
 hypertension control, 164
 lifestyle modifications, 164
 myelin repair, 166–168
 sleep medicine, 164–165
 stem cell therapeutics, 168–169
 TBI control, 165
 toluene-induced cardiac arrhythmia, 98
 toluene leukoencephalopathy, 49–51
 alternate names for, 51, 97
 articulation deficits in, 105
 autopsy findings, 50, 97
 brain-behavior relationships and, 97
 causes of, 97, 98–99
 clinical evaluation, 127
 cognitive impairment in, 97–98
 corticospinal dysfunction in, 50
 CT studies/findings, 51, 98
 MRI studies/findings, 50–51, 98

Index

- neurobehavioral sequelae of toluene abuse, 51
 neuropathological investigations, 51
 nonverbal ability impairment in, 104
 pathogenesis of dementia in, 50–51
 prognosis, 135, 136
 white matter dementia and, 96–99
 toxic leukoencephalopathy, 49, 50
 drug abuse and, 148
 executive dysfunction in, 101
 MRI studies, 53, 143
 stages of severity, 119, 119
 treatment of, 143, 148–149
 Tozzi, V., 144
 tracts. *See* white matter tracts
 Trail Making Test, Form A, 146
 transcranial direct current stimulation (tCDS), 148
 traumatic axonal injury (TAI). *See* diffuse axonal injury
 traumatic brain injury (TBI), 54–58.
 See also diffuse axonal injury (DAI), in TBI
 AD association, 57
 from blast injuries, in military conflicts, 54, 57, 185
 brain/cognitive reserve studies, 137, 138
 clinical presentation, 54–55
 concussion and, 185–187 (*See also* concussions)
 CTE link, with, 57
 CT evaluation of, 9
 diagnostic challenges, 55
 diffuse axonal injury in, 55–57, 165
 disinhibition/impaired impulse behavior in, 57
 DTI studies, 56, 57, 189–190
 executive function impacted by, 56
 Glasgow Coma Scale assessment, 54, 56, 57
 global prevalence of, 165
 lesions produced by, 55
 long-term outcomes, 57–58
 monkey research, 108
 morbidity/mortality of patients, 163
 mortality rate, U.S., 54
 MRI assessment, 56
 NAWM abnormalities in, 119
 NAWM studies in, 56
 neurobehavioral sequelae, 55
 neuropathology of, 57
 Nevin's research on, 55
 phosphorylated tau accumulation in, 190, 191
 prognosis, 135, 136
 recovery potential, 57
 relatively preserved language in, 57
 severity classification, 186, 186
 static encephalopathy and, 54, 57, 165
 tauopathy and, 188
 terminology related to, 54
 therapeutic innovations, 165
 treatment
 challenges, 57
 medical therapy, 143
 rehabilitation, 147
 therapeutic innovations, 165
 WAIS scores, 57
 in young adulthood, 54
 young-onset dementia and, 37
 treatment of WMD and MCD, 142, 142–149. *See also* under specific disorders
 medical, 142–146
 psychiatric, 148–149
 rehabilitative, 147, 147–148
 surgical, 146–147
 therapeutic innovations, 162–169
 tumefactive multiple sclerosis, 58
 unidentified bright objects (UBOs), 10
 unspecified leukoencephalopathy, 37
 urinary incontinence
 in frontal white matter dysfunction, 128
 in NPH, 70
 van Bogaert, L., 75. *See also* cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
 vascular cognitive impairment (VCI), 122, 142
 vascular cognitive impairment (VCI), no dementia (VCI-no dementia), 122
 vascular dementia. *See also*
 Binswanger's Disease; cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
 AD combination, 32
 BD as causative for, 42–43
 hypertension control and, 180
 ischemic vascular dementia, 103
 medical treatment of, 142
 MRS studies, findings, 48
 MTI studies, findings, 48
 reversibility of, 122
 rTMS treatment for, 148
 strokes and, 42
 subcortical, 109
 subcortical ischemic vascular dementia, 43, 46
 subcortical vascular dementia, 109
 SYST-EUR treatment study, 164
 vascular diseases of white matter, 42–49, 43
 Binswanger's Disease, 46–49 (*See also* Binswanger's Disease)
 cerebral amyloid angiopathy, 43, 173
 leukoaraiosis, 43–46 (*See also* leukoaraiosis)
 migraine, 43, 75
 MRI studies, 42, 43, 44, 45, 49
 MTI studies, 48
 subcortical ischemic vascular dementia, 43, 46
 ventricular enlargement, 36
 Vesalius, Andreas, 95
 visual recognition network, 157
 visuospatial function/dysfunction
 AIDS-dementia complex and, 66
 BD and, 47, 49
 cerebral white matter's role in, 5
 cortical structure's role in, 97
 CT study of, 104
 metachromatic leukodystrophy and, 77
 radiation treatment and, 52
 SLE and, 63
 vitamin B₁₂ deficiency and, 68
 white matter dementia and, 104
 visuospatial network, 157
 vitamin B₁₂ deficiency, 68. *See also* cobalamin (vitamin B₁₂) deficiency
 Vogt, Cecile and Oskar, 18, 19, 155
 WAIS. *See* Wechsler Adult Intelligence Scale
 Wechsler Adult Intelligence Scale (WAIS), 57
 Wegener's granulomatosis, 62
 Wernicke, Karl, 95, 156
 white matter
 Alzheimer's Disease and, 172–181
 anatomy, normal, of, 153–155
 anisotropic (directional) diffusion in, 11
 axo-oligodendroglial synapses in, 21, 139
 behavioral neurology of, 5–7
 cognition and reflections on the study of, 199–200
 research perspectives, 153–159
 CTE and, 165
 defined, 155
 in distributed neural networks, 155–157, 156
 electroencephalographic studies, 3
 enhanced electrical conduction by, 20–21

Index

- white matter (cont.)
 evolution of, 4, 22–24
 formation/development, at
 birth, 21
 frontal lobes, losses in late life, 22
 gray matter's parallel functions
 with, 4
 historical background, 95–96
 inflammation and, 158–159
 lesion method examination of, 5
 myelin's special role in, 21
 neurobiology of, 17–24
 anatomy, 17–20
 physiology, 20–21
 neurorelevance in dementia
 pathogenesis, 35
 neurotransmitter systems
 within, 154
 pathology spectrum, 121–123
 percentage in non-human
 animals, 2
 role in language, 5, 32, 106
 role in lifespan, 5
 significance of, 4–5
 white matter dementia (WMD),
 95–111
 AD similarities, 172
 categories, 118
 clinical profile, 99
 cognitive slowing, 100, 101
 executive dysfunction, 101–102
 memory retrieval deficit, 102–104
 normal extrapyramidal func-
 tion, 106
 normal procedural memory, 100,
 106–107
 psychiatric disturbance, 105
 relatively preserved language,
 105–106
 sustained attention deficit, 102
 visuospatial impairment, 104
 cortical/subcortical dementia
 distinctions, 99–101, 100
 definition, 99, 118
 diagnosis, 100, 127–132, 128
 brain biopsy, 131–132
 clinical evaluation, 127–129
 laboratory testing, 129
 neuroimaging, 129–130
 neuropsychology, 130–131
 historical background, 95–96
 increasing legitimacy of, 195–196
 integrative review process in
 studying, 38–39
 introduction of, xi
 leucocentrism and, 198
 neuroimaging studies, findings,
 118–119
 overlapping dementia disorders,
 36, 38
 preventive measures, potential, 154
 Pub Med search citations for, 195
 subcortical dementia as
 precursor, 32
 toluene leukoencephalopathy
 turning point, 96–99
 treatment, 142, 142–149
 behavioral, 147, 147–148
 cholinergic augmentation, 154
 medical, 142–146
 psychiatric, 148–149
 rehabilitative, 147–148
 surgical, 146–147
 unresolved issues, 107–111
 co-existent gray matter
 neuropathology, 108
 corticocentric bias, 108–109
 intracortical myelin pathology,
 109–110
 lack of suitable animal
 models, 108
 threshold effect, 110
 WMH/absence of cognitive
 correlates, 107–108
 white matter disease of immaturity, 43
 white matter disorders, 3–4, 42–78.
 See also specific disorders
 acquired factors, 163, 163
 in adolescence, young adulthood, 37
 cancer chemotherapy-induced leu-
 koencephalopathy, 53–54
 cognitive slowing in, 101
 declarative memory impairment
 in, 103
 demyelinative diseases, 58, 58–62
 executive dysfunction in, 101
 genetic diseases, 74, 74–78
 hydrocephalus, 69, 69–72
 infectious diseases, 64, 64–67
 inflammatory diseases, 62, 62–64
 integrative review of, 39
 memory retrieval deficit in, 104
 metabolic disorders, 67, 67–69
 methods of studying, 6, 10, 15
 MRI's advantages in, 97
 neoplasms, 72–74
 neuropathology of, 6
 pathophysiology of, 21
 prognosis, 135–139
 brain/cognitive reserve, 137–138
 influential factors, 135
 natural history, 135–137
 plasticity, 138–139
 radiation, 51–53
 relatively preserved language in,
 105–106
 sustained attentional disturbances
 in, 102
 symptoms, 128
 therapeutic innovations, 162–169
 damage prevention, 162–165
 hypertension control, 164
 myelin repair, 166–168
 sleep medicine, 164–165
 stem cell therapeutics, 168–169
 vascular diseases of white matter,
 42–49, 43
 Binswanger's Disease, 46–49
 cerebral amyloid angiopathy,
 43, 173
 leukoaraiosis, 43–46
 migraine, 43, 75
 subcortical ischemic vascular
 dementia, 43, 46
 white matter disease of imma-
 turity, 43
 white matter hyperintensities (WMH)
 absence of cognitive correlates, 49,
 107–108
 age-related, 10
 in Alzheimer's Disease, 177
 FXTAS and, 78
 gray matter disease and, 49
 hypertension and, 164
 leukoaraiosis and, 43, 44
 in MCI, 177
 MRI recognition of, 10–11, 43, 43,
 51, 98
 MS white matter lesions and, 59–60
 NPH and, 72
 perceptual/constructional deficits
 with, 104
 SLE and, 64
 solvent exposure and, 51
 vitamin B₁₂ deficiency and, 68
 white matter lacunar dementia, 105
 white matter lesions. *See also* white
 matter hyperintensities
 assumptions made about, 4
 cognition-related neurochemical
 systems and, 154
 in the frontal lobes, 4
 impact on cognition, emotion, 5
 investigational challenges, 10, 36
 ischemic and global brain
 atrophy, 36
 neuroimaging studies of, 3, 6, 11, 36
 syndromes occurring with, 7
 in traumatic brain injury, 55
 white matter toxins, 50
 white matter tracts. *See also* associa-
 tion tracts; commissural tracts
 connecting peduncles of, 19
 connectome and, 21
 DKI visualization of, 13
 DTI studies, 12, 57, 74, 101
 frontal aslant tract, 153
 language-related, 106
 macroconnectivity of, 21
 MCD and, 124

Index

- MRI observations, 101
- musical training impact on, 139
- neural networks in, 14
- neurobehavioral impairment and, 35–36
- neuroimaging visualization of, 9, 9
- physiology of, 20
- plasticity and, 139
- projection tracts, 17, 156
- relevance to behavioral neurology, 18
- restoration of, 147
- rTMS and, 148
- size variances, 17
- subcortical dementia and, 30
- tracts relevant to behavioral neurology, 18
- unanswered questions about, 153
- Wallerian degeneration in DAI, 55
- Williams, M. A., 71
- Wilson, R. K., 71
- Wilson’s Disease, 28
- Wisconsin Card Sorting Test, 144
- WMH. *See* white matter hyperintensities
- young-onset dementia, 37
- zidovudine (AZT), 67, 144