

Index

- 11 C-PK11195, **199**
 2008 Nobel Prize in Physiology or Medicine, 26
- Academic Press journal, 33
 acetylcholine, 14, 43
 and heart rate, 44
 and pro-inflammatory actions, 171
 receptors, 14, 43
 acute CNS dysfunction, and peripheral inflammation, 165–7
 acute disseminated encephalomyelitis (ADEM), 83
 acute infection, 139
 acute stress, 66
 acute systemic inflammation, consequence of, 165
 adaptive immune activation, 324
 adaptive immune cells
 and neuroinflammation, 309
 circulating, 312–13
 adaptive immune system, 1, 2, 5, 9, 205, 292, 299
 activation of, 302
 and impairments in the, 300
 and Mhc, 9–10
 as T helper cells, 8
 B cells and, 10–12
 preclinical data and, 300–2
 response mechanisms, 197
 response of, 4
 T cells, 10–12
 Ader, Robert, 26, 30
 adrenalectomy, 171
 adrenocorticotrophic hormone (ACTH), 35, 52
 secretion, 259
 adult psychiatric illness, and childhood CNS infections, 77
 adult psychosis, and viral infections, 77
 affective disorders
 cellular immune pathways, 313–14
 circulating adaptive immune cells, 312–13
 circulating innate immune cells and, 7–8
 agoraphobias, inflammation and, 236
 AIDS, 26
 and behavioural changes in patients, 26
 and the field of immunology, 26
 alpha-synuclein, 198
 and neuroinflammation, 192
 ALSPAC
 birth cohort, **123**, 125, **140**
 birth cohort study and risk of depression shown, 139
 Mendelian randomization (MR) analyses of, 140
 alveolar macrophages (lungs), 4
 Alzheimer's disease (AD), 1, 53, 100, 164, 191, 213, **223**
 early form of, 215
 stress levels of caregivers of patients with, 35
 Th2 cells and, 216
 the etiology of, 190
 American Association of Immunologists, 34
 American Board of Hospital Medicine (ABHM), 29
 American Board of Medical Specialties, 28
 American Board of Physician Specialties, 29
 American College of Rheumatology, 88
 American Revolutionary War, 25
 amygdala morphology, 60
 amyloid (A β) protein, 214
 amyloid pathology, 172
 amyotrophic lateral sclerosis (ALS), 164
 low-grade inflammation, 2
 animal models, 53, 173, 176
 and autism, 277
 and autoimmune disorders, 300
 and birth cohorts, 77
 and causal mechanisms in research, 80
 and experimental medicine studies, 128
 and minocycline, 98, 281
 and prion disease, 170
 and responses to cytokines, 241
 and schizophrenia study, 78
 and systemic inflammation, 174
 IL-1 and TNF effects on, 175
 protective function of fractalkine on, 197
 antibiotic treatments, 266
 anti-B-lymphocyte stimulator (BLyS), 144
antibodies, 43–4
 caspr2, 88
 antibodies (B cells), 25
 antibody immunotherapy, 101
 antibody-mediated encephalitis, 13
 anti-brain antibodies, 27
 anti-brain autoantibodies, 297
 anti-cytokine antibodies
 antidepressant effect of, 144
 anti-cytokine drugs, **146**, 149, 150
 antidepressant effects of, 143–8, **145**
 anti-depressant interventions, new, 139
 antigen receptors, 10
 anti-inflammatory agents
 psychosis treatment, 96, **98**
 anti-inflammatory cholinergic pathway, 14
 anti-inflammatory cytokines, 16
 anti-inflammatory drugs, 151
 antidepressant effects of, 148–50
 trial of, **153**
 anti-inflammatory Th2 cytokines, 76

- anti-microbial peptides (AMPS), 213, 217
- antimicrobial Peptides (AMPS), 218
- antinuclear antibodies, 88, 297
- antioxidants, 102
- antipsychotics, 10, 102
- anti-TNF antibody
adalimumab, 143
- anti-TNF treatments, 178
- anti-TNF- α antagonists
etanercept, 143
- anxiety disorders, 233
and alterations in the immune system, 243–4
and contribution of inflammation to, 239–42
and similarities with PTSD, 236
and the role of the immune system in, 233
health behaviours and inflammation in, 239
health behaviours that contribute to inflammation in, 239
- anxiety-provoking stimuli, 233
- apoptotic cell debris, clearance of, 4
- Aspirin, 100
- astrocytes, 215–16
- astrocytic end feet, 2
- Asya Rolls, 42
- autism. *See* autism spectrum disorder (ASD)
- autism spectrum disorder (ASD), 84, 258, 269–80
and maternal antibodies
brain-reactive antibodies, 13
prevalence of, 269
role of microbiota in, 271
- autoantibodies, 13, 83
and Parkinson's disease, 13
- autoimmune diseases, 164
depression and, 297
- autoimmune encephalitis, 12, 83–5, 88, 90
features of, 91
research in, 86
- autoimmune psychosis, 84
research in, 86
- autoimmunity, 2, 9, 83, 84, 88, 92
as a side effect, 150
as an aetiological factor, 325
- comorbid, 325
thyroid, 297
- autonomic nervous system (ANS), 51, 259
- Avon Longitudinal Study of Parents and Children (ALSPAC), 122
- azathioprine, 101
- B cells, 13, 34
and adaptive immunity, 10–12
- bacterial endotoxin, 169
- bacterial lipopolysaccharide (LPS), 6
- bacterial metabolites, 264
- Bacteroides*, 268
Bacteroides fragilis, 277
Bacteroides thetaiotaomicron, 263
- Baltimore Longitudinal study of Ageing, 224
- Barré-Sinoussi, Françoise, 26
- Barret, LF, 64
- baseline CRP levels, 148
- Baune, Bernhard, 299
- Bayesian active inference, 64
- Bayesian brain, 51
immune response and stress, 64, 65
stress and, 63, 65
connections, 65
- B-cells, 296
- Begemann, MJ, 103
- behavior, microbiota
manipulation and, 264–6
- behavioral immunology, 26
- behavioral research
experiments
sickness to depression, 37–8
- Ben-Eliyahu, Shamgar, 43
- Besedovsky, Hugo, 35, 36
- Beutler, Bruce, 40
- Bicknell Neal, Josephine, 87
- Bifidobacteria*, 268
Bifidobacterium, 268
Bifidobacterium infantis, 265
Bifidobacterium longum, 259, 262
- biomedical research, 28–9
- biomedical specialization, 28–9
- bipolar disorder (BD), 4, 7, 309
and cytokines, 318
and low grade neuroinflammation, 309
chemokines, 320–1
- complement system and, 315
- C-reactive protein (CRP)
and, 7
minocycline and, 151
- birth cohort studies, 74–5, 80
and infection, 75–6
inflammatory biomarkers and, 76
- birth cohort, and animal models, 77
- Blalock, Edwin J, 34
- blood, 177
markers, 217
- blood and the cerebrospinal fluid (CSF), 2
- blood biomarkers, 204
- blood monocytes, 4, 62
infiltrating, 4
- blood-brain barrier (BBB), 2, 25, 96, 301, 310
and immune privilege, 41
and monoclonal antibodies, 144
and the Blood CSF Barrier, 3
dysfunction, 90
formation, 267
integrity of, 114, 266
modified, 114
- blood-brain interface, 25
- blood-cerebrospinal fluid barriers (BCSFB), 2
- bodily integrity, 2, 110
and threats to, 1
- Brachman, RA, 59
- brain
and bidirectional link with the immune system, 309
and gut microbiota, 265
and the circuit remodelling process, 258
immune challenges and, 240
lymphatic drainage in the, 42–3
microbiota manipulation and, 264–6
systemic inflammation on the diseased, 166
the action of Th17 cells, 294
- brain derived neurotrophic factor (BDNF), 265
- brain development, 258, 281
and gut microbiota, 266–9
- brain functions
and preclinical data and the adaptive immune system, 300

- brain parenchyma, 4, 41–2
 brain plasticity, 309
 brain structure, 77, 114, 115, 266, 321
 changes in, 55
 stress-induced changes in, 60–1
 brain to immune system, efferent signals, 34
Brain, Behavior, and Immunity, 33
 brain-derived neurotrophic factor (BDNF), 5, 61, 127, 300
 Brown, AS, 78
 Bullmore, Ed, 155
- caesarean section, preclinical models of, 268
 cancer patients
 and depression in, 38
 breast, 43
 cytokine immunotherapy, 16
 Cannon, Walter, 39
 Capuron, Lucile, 38
 cardiovascular risk, 150
 Carson, Monica, 27
 caspr2 antibodies, 88
 Catakunimab, controlled trial of, 101
 catecholamine norepinephrine (NE), 14
 CCL, 2, 8
 CD45RA, 12
 CD45RO, 12
 Celecoxib, 100
 antidepressant effects, 16
 cell based assays, 84
 cell death, 26
 cellular damage, indicators of, 170
 cellular immune pathways
 overall and differing patterns, 313–14
 cellular immunity (T cells), 25
 cellular infiltration, 83
 cellular mechanisms, 114
 cellular signalling
 mediators, 310
 cellular transporters, 2
 central communication, 14–16
 central nervous system (CNS), 2, 25
 and the immune system, 1, 53
 autoantibodies, 13
 drainage, 13
 homeostasis, 60
 immune privilege and, 41
 inflammation and
 modulators of, 219–21
 inflammation and molecular mediators of, 217–19
 inflammation of, 177, 215, 221
 interplay with the immune system, 1
 lymphatic system of, 15
 non-resident cells of, 216–17
 resident cells, 213–16
 resident microglia effects and stress on, 57, 59
 cerebrospinal fluid (CSF), 176–7
 biomarkers, 204
 markers, 217
 chemokines, 8
 alterations and psychiatric disorders, 321
 and bipolar disorder, 320–1
 and major depressive disorder (MDD), 319
 and psychiatric disorders, 319
 and schizophrenia, 320
 Child Health and Development Study (CHDS), 74
 childhood central nervous system (CNS)
 and viral infections and adult psychosis, 77
 Childhood Epstein-Barr infection, 77
 childhood infection, 77
 childhood stress studies, 62
 childhood trauma, 241
 and inflammation-related depression, 148
 chimeric antigen receptor (CAR), 36
 cholinergic anti-inflammatory pathway, 43
 choroid plexus, 2, 3, 4, 40, 42, 54, 115, 169, 302
 chronic peripheral inflammatory conditions, 172
 chronic restraint stress, 60
 chronic restraint/immobilisation stress model, 55
 chronic stress, 66
 chronic stress exposure, 60
 chronic unpredictable/mild/variable stress model, 54–5
 Churchward, MA, 58
 circuit remodelling process, in the brain, 258
 circulating inflammatory markers, 65
 circumventricular organs (CVOs), 2
 Class III genes, 10
 classic lymphoid drainage system, 25
 classic neurohormonal stress pathways, 300
 cluster of differentiation (CD), 217
 CNS. *See* central nervous system (CNS)
 cognitive behavioural therapy (CBT), 141
 cognitive decline and peripheral inflammation, 164–5
 and systemic inflammation, 1
 dementia and chronic inflammatory conditions, 165
 Cohen, Sheldon, 32, 40, 58
 Collaborative Perinatal Project (CPP), 74
 communication
 central and peripheral, 14–16
 efferent to afferent, 34–9
 communication network, 52
 comorbid depression, 139
 and new anti-depressant interventions, 139
 and RCTs, 149
 comorbid systemic infection, 169
 complement Factor H (CFH) protein, 315
 complement system, 7–8
 and psychiatric disorders, 314–16
 dysfunctions, 316
 dysfunctions and psychiatric disorders, 316
 in BD, 315
 in MDD, 314–15
 in schizophrenia, 315
 controlled trials (RCTs), randomized, 124

- CORT, 66
 CORT exposure, 59
 cortex morphology, 60
 corticotrophin-releasing factor (CRF), 35, 259
 COX isoforms, 142
 COX-1 inhibitors, 150
 COX-2 inhibitor, 100
 C-reactive protein (CRP), 7
 CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology, 28
 Crohn's disease, 110, 111
 CRP concentrations, 241
 Cserr, H.F., 42
 CTNNA, 3, 79
 cytokine interferon, 25
 cytokine network, 8
 cytokines, 8–9, 25, 27
 and psychiatric disorders, 316
 and relationship to depression in cancer patients, 38
 anti-inflammatory, 16
 identification of, 40
 immunotherapy, 16
 in BD, 318
 in MDD, 316–17
 in schizophrenia, 317–18
 primary source of, 10
 pro-inflammatory, 139
 cytokines alterations
 and psychiatric disorders, 318–19
 Dalmau, Josep, 13, 85
 damage-associated molecular patterns (DAMPs), 6, 7, 41, 170, 214
 receptors, 310
 DAMPs. *See* damage-associated molecular patterns (DAMPs)
 degenerating brain
 and systematic inflammation, 169–70
 systemic inflammation effects, 175, 179
 dehydroepiandrosterone (DHEA), 66
 dendritic cells (DCs), 2, 4
 dendritic extension
 chronic stress, 60
 depressed patients, studies of, 121–2
 depression, 109
 and alterations in the adaptive immune system, 302
 and current treatments for, 141–2
 and immunity relationship between, 292, 298
 and psychotic experiences, 123
 as an autoimmune disease, 297
 comorbid, 139
 feature of, 118
 immune alterations on physical health, 298–9
 minocycline and, 151
 mood change and, 119–20
 risk of, 140
 symptoms of, 16
 treatment-resistant, 147
 with specific symptoms, 124–5
 depressive symptoms, and immunity, 297–8
 Derkits, EJ, 78
 Diagnostic and Statistical Manual of Mental Disorders (DSM-5), 321
 and anxiety disorders, 233
 diet
 and gut microbiota, 268, 277
 and omega-3 polyunsaturated fatty acids, 243
 Mediterranean, 149
 direct afferent neural route, 37
 discrete psychotic episode, 90
 disease, germ theory of, 25
 docosahexaenoic acid (DHA), 149
 dopamine receptors (DR), 14
 dopamine signalling, 14
 double stranded DNA (dsDNA), 88
 DSM-V defined categories, 326
E. coli infection, 173
 Early life stress (ELS) model, 55
 ecological studies, 80
 of prenatal infection and schizophrenia, 73–4
 efferent to afferent communication, 34–9
 eicosapentaenoic acid (EPA), 149
 Eisenberger, 119
 elderly people, and cognitive decline, 1
 emotional stress
 and immunological dysfunction, 29
 encephalitis, 83
 autoimmune, 88
 Leucine rich glioma-inactivated one (LGI1), 88
 N-Methyl D-aspartate receptor (NMDAR), 85–8
 encephalitis lethargica, 85
 encephalopathy, 84, 85, 88
 Hashimoto's, 87
 endothelial cells, 6
 English Longitudinal Study of Aging (ELSA), 122
Enterobacteriaceae, 263
 enzymatic activity of IDO, 17
 enzyme cyclooxygenase (COX), 142
 eosinophils cells, 4
 epidemiology
 studies, 205
 epigenetics, 79
 epigenomic regulatory factors, 324
 epinephrine acts
 and stress, 43
 Epstein-Barr virus, 35
 etanercept, anti-TNF- α antagonists, 143
 European Research Foundation, 30
 expected surprise
 and the brain, 63
 experimental approaches, 115–16
 experimental autoimmune encephalitis (EAE), 12
 expression of microRNAs (miRNAs), 235
 extracellular vesicles (EV), 167
 Farokhnia, 102
 Fate mapping studies, 4
 fatigue, 116–17
 Felten, David, 30, 42
 Felten, Suzanne, 42
 fever response, 2
 Finnish Prenatal Studies (FIPS), 74

- first episode psychosis
 serum anti-neuronal
 antibodies, 13
 First International Workshop on
 Neuroimmunomodulation,
 31, 31
 fish oil supplement
 antidepressant effect of, 149
 flow cytometry, 34
 fracktalkine, 197
 Frank-Starling law, 43
 French Revolution, 25
 frontotemporal dementia, 164

 GABA_AR negative allosteric
 modulator, 66
 GABAergic system, 261
 GAD, PD, and phobias with
 inflammatory signal, 236
 Galectin-3, 198
 Gallo, Robert, 26
 Garfield, James, 29
 GC receptor inhibition, 171
 GC-resistant monocyte
 pathway, 59
 gene expression of complement
 component, 7
 General Adaptation Syndrome,
 25, 39
 generalized anxiety disorders
 (GAD), 233
 inflammation and, 236
 genetic Mendelian
 randomization (MR)
 studies, 139
 genetic studies, 203–4
 causality from, 123–4
 Genome-Based Therapeutic
 Drugs for Depression
 (GENDEP) trial, 142
 genome-wide association
 studies (GWAS), 10, 79
 George III, 25
 germ free mice, 259, 263
 and antibiotics
 treatment, 266
 and preclinical work with,
 264–6
 studies on, 261
 germ theory of disease, 25
 GlaxoSmithKline, 144
 glucocorticoids, 38, 51, 126,
 149, 151, 171, 237
 glymphatic flow, 2
 glymphatic system, 13–14,
 15, 42

 good stress, 64
 Graus, F., 86
 gut bacteria, 264
 gut microbiota, and brain
 development, 266–9, 281
 gut-brain axis, 259, 260
 pathways of, 260

 Hans Selye, 39
 Haour, France, 40
 Harling-Berg, C. J., 42
 Hart, B.L., 37
 Hashimoto's
 encephalopathy, 87
 high-mobility group box 1
 (HMGB1), 41
 hippocampus morphology, 61
 hippocampus-dependent
 cognition, 5
 histocompatibility complex
 (MHC) locus, 78
 HIV. *See* human
 immunodeficiency
 virus (HIV)
 HIV patients
 and RCTs, 149
 Hoffmann, Jules, 41
 hormones, 259–61
 HPA axis, 259
 human immunodeficiency
 virus (HIV)
 macrophage-trophic strains
 of, 26
 discovery of, 26
 human interferon, 25
 human studies, 115
 humans, microglial priming
 and, 172–3
 Huntington's disease
 (HD), 164
 hypothalamic-pituitary-
 adrenal (HPA) axis, 51,
 111, 233, 310

 IDO, enzymatic activity of, 17
 immune activation, 109
 and the brain, 109
 immune ageing, 172
 immune alterations, 298–9
 and treatment, 299
 immune cell dysregulation,
 309–14
 immune cells
 and pattern recognition
 receptors (PRRs), 170
 developmental origins of, 11

 immune dysfunction
 and psychotic disorders, 96
 immune hyperactivation, 298
 immune mediated
 inflammatory disorders
 (IMIDs), 110
 immune response
 and stress, 53
 and the Bayesian brain,
 64, 65
 immune system, 262–3
 across psychiatric
 disorders, 322
 activation of, 109
 and association with
 psychiatric disorders, 292
 and central nervous
 system, 54
 and PTSD, 233–6
 and stress, 51, 53–4
 and the central nervous
 system (CNS), 53
 and the future outlook of
 psychiatric disorders, 321–6
 and use of cellular
 pathways, 114
 as a sixth sense, 34
 classification of, 1–2
 clinical studies of stress
 and, 62–3
 communicating the state of,
 112–15
 function of, 1
 non-immune functions of, 2
 overview of, 1–2
 role of in neurodegenerative
 and psychiatric
 disorders, 1
 stress and the, 35
 immune system signalling, 14
 immune-brain
 communication, 14, 29–30
 immune-mediated
 inflammatory
 pathways, 53
 immune-modulating
 agents, 104
 immune-privileged site
 and central nervous
 system, 1
 immune-to-brain
 communication
 pathways, 109
 immunity
 and relationship with
 depression, 298

- depressive symptoms and, 297–8
- immunological dysfunction and emotional stress, 29
- immunology
and mental illness, 1
early research in, 25, 27
- immunology laboratory, early (1970), 27–8
- immunophenotyping, 176
- immunopsychiatry, 1, 25, 26, 292
and CNS diseases, 176–7
and lupus, 92
and PNI, 44
history of, 34
main notion of, 34
- immuno-suppressants, 101–2
- immunotherapies, 13
adverse effects of, 150–1
patents and benefits from, 151–4
for depression, 154–5
- immunotherapy, antibody, 101
- in utero* development, 267
- infection
birth cohort studies of, 75–6
- infections
and changes in mood, 109
physiological response to, 16
- infectious encephalitis, 84
- infiltrating blood monocytes, 4
- inflamed depression, 139
- inflammasome, 6–7
- inflammation
and current treatments for depression, 141–2
and link to depression, 125, 127
in depression, 141
pathological studies and, 202–3
systemic, 26
teaching about, 26
- Inflammation and Psychiatry Research Group at the University of Cambridge, 155
- inflammation-related depression
and childhood trauma, 148
- inflammatory biomarkers, birth cohort studies of, 76
- inflammatory cytokines, 204
- inflammatory reflex, 14
- innate (natural) immune system, 1–2
- innate immune activation
in neurodegenerative processes, 175
- innate immune cells, 6, 309–10
circulating, 310–11
- innate immune system, 2–4
and linking adaptive immunity, 8–9
and NLRs, 6
and the complement system, 7–8
barriers and, 2
macrophages/microglia cells, 4–5
molecules and, 6–8
NK cells, 5–6
NLRs and inflammasome molecules, 6–7
toll-like receptors (TLR) molecules, 6
- innate lymphoid cells (ILCs), 4
- Institute of Experimental Medicine, 30
- Institute of Immunology (Zagreb), 27
- integrative medicine, summary of trends in, 30
- interferon
approval of, 38
- Interferon signature, 90
- interferons, 9
- interferon- α therapy
and major depression, 38
- interleukin, 1, 197
- interleukins, 40
- International Max Planck Research School for Translational Psychiatry (IMPRS-TP), 155
- International Society of Neuroimmunomodulation (ISNIM), 31
- intracellular adhesion molecule (ICAM), 56
- Irwin, Michael, 35, 37
- Jankovic, Branislav D., 27
- Janssen pharmaceuticals, 148
- Janssen Research & Development, 144
- Jenner, Edward, 25
- Journal of Immunology*, 36
- kainic acid, 100
- Kapozi, Moriz, 83
- Kappellmann, 144, 145, 146, 155
- Kappellmann, Nils, 155
- Kelly, 59
- Kemeny, Margaret, 30
- Khandaker, 101, 140
- Khandaker, Golam M., 155
- Kiecolt Glaser, Janice, 35
- killer cell cytotoxicity, anturial, 292
- Knopf, P. M., 42
- Kohler, 25
- Konsman, 34
- Korneva, 29, 31
- Krzystyniak, A, 66
- Kupffer cells (liver), 4
- kynurenine, 241
- Kynurenine pathway, 16, 17
- Lactobacillus reuteri*, 261, 262
- Lactobacillus rhamnosus*, 259, 261, 262
- Lactobacillus* species, 267
- Langerhans cells (skin), 4
- leptomeninges, 25
- Leucine rich glioma-inactivated one (LGI1) encephalitis, 88
- Leucine-rich repeat kinase 2 (LRRK2), 197
- Leukocytes, 42–3
- Lewy body dementia (LBD), 164, 190
and alpha-synuclein, 192
- Lipopolysaccharide (LPS), 216
- Lo, David, 27
- longitudinal cohort studies, causality from, 122–3
- Louis XVI, 25
- low emigration rate, Finland's, 74
- low-dose lipopolysaccharide (LPS), 115
- low-grade inflammation, 139, 142
and MDD, 139
and treatment-resistant depression, 147
- Lrrk2427, 197
- lupus, 83
and the brain, 83
systemic, 88–9
- lupus psychosis, 90
- lymphatic drainage
in the brain, 42–3

- lymphatic drainage system, 13
 lymphatic system, 13
 lymphocyte proliferation studies, 293–5
 lymphocyte subsets, 298
 lymphocytes, 9
- Macfarlane Burnet, Frank, 41
 macromolecules, 12
 macrophage T lymphocyte theory, 312
 macrophages/microglia, 4–5, 6, 32, 33
 and cytokines, 8
 major depressive disorder (MDD), 1, 309
 and chemokines, 319
 and cytokines, 316–17
 and diagnosis, 139
 and elevated cortisol-DHEA ratio, 66
 and inflammation, 292
 and interferon- α therapy, 38
 and low-grade inflammation, 139
 and monoaminergic antidepressant medication, 141
 and sickness behaviours, 109
 complement system and, 314–15
 new anti-depressant interventions, 139
 symptoms of, 139, 297
 major histocompatibility complex (MHC), 5
 major neurodegenerative processes, 164
 Marie Antoinette, 25
 mass cytometry, 176
 mast cells, 4
 and cytokines, 8
 maternal antibodies brain-reactive antibodies and autism, 13
 Maternal C-reactive protein (CRP), 76
 maternal cytomegalovirus infection (CMV), 79
 maternal exposure to infection and increased risk of schizophrenia, 80
 maternal infections and schizophrenia, 73, 76
maternal microbiome, 267
 maternal separation, 55
 maternal stress, 62
 Matheson Commission, 87
 Max Planck Institute of Psychiatry, 155
 McEwen, Bruce, 39
 McIntyre, RS, 147
 MCP-1 expression, statins and, 103
 MDD patients and reduced NK cell numbers, 5
 Medawar, Peter, 41
 Medical Research Council, 30
 Mediterranean diet, 149
 memory, 121
 memory cells, 12
 Mendelian randomization (MR), 123
 meningeal lymphatic vasculature lining, 13
 meningeal macrophages, 4
 mental illness and immunology, 1
 metabolic syndrome, 165
 methodological approaches and future progress, 178
 methotrexate, 101
 Mhc, 9–10
 MHCII complex, 205
 microbial antigens, 10
 microbial metabolites, 263–4
 microbiota and neurodevelopmental disorders, 269–81
 microbiota manipulation, 264–6
 microglia, 4, 5, 191, 213–15
 and neurodegenerative diseases, 170
 and neurodegenerative processes, 169
 anti-inflammatory effects on, 171
 CNS-resident, 57, 59
 in MPTP, 191
 primed for exaggerated responses, 172
 priming and humans, 172–3
 what primes, 170–2
 microglial activation, 8, 198, 201
 and psychiatric and neurodegenerative disorders, 5
 brain cancer treatment, 5
 microglial cytokine expression, 58
 mild cognitive impairment (aMCI), 215
 Miller, 38, 317
 Miller, Andrew
 research group of, 38
 Milstein, 25
 mind-body interactions, early research on, 29
 mini mental state examination (MMSE) scores, 201
 minocycline, 98, 148–9, 151
 molecular mediators of CNS inflammation, 217–19
 monoamine oxidase (MAO) inhibitors, 141
 monoaminergic antidepressant medication and treatment of MMD, 141
 monoclonal antibodies, 25
 monoclonal antibodies (mAbs), 143
 monocytes, 4
 monocytosis, in major depressive disorder, 324
 mononuclear cells, 216–17
 mononuclear phagocyte system (MPS), 321
 Montagnier, 26
 Montagnier, Luc, 26
 mood
 changes in and infections, 109
 mood change and depression, 119–20
 Morrissey, P.J., 36
 motivational change, 117–18
 mucosal epithelium, 2
 multiple sclerosis (MS), 1, 164
 N-acetylcysteine (NAC), 102
 Nance, Dwight, 37, 43
 Nasu-Hakola disease, 191
 National Institutes of Health, 26, 31
 National Science Foundation, 30
 natural immune system. *See* innate immune system
 natural killer (NK) cells, 4, 34, 43, 298
 necrosis, 26
 Nedergaard, Maiken, 13, 42
 nervous system (CNS), 191

- Netherlands Study of Depression and Anxiety (NESDA), 122
- neural, 262
- neural circuits, 4
- neurodegeneration, 2
- neurodegenerative and psychiatric disorders, 17
- neurodegenerative pathology, microglia primed by, 172
- neurodevelopmental disorders and microbiota, 269–81
- neuroendocrine pathways, 309
- neurogenesis, 126–7
- neuroimaging studies, 109, 116, 126, 152, 310
- neuroimaging techniques, 115, 175–6
- as investigative tools, 62
- Neuroimmunodulation*, 31
- Neuroimmunology of Mood Disorders and Alzheimer's disease (NIMA), 155
- neuroimmunomodulation, 26
- neuroinflammation, 191–2, 213
- and alpha-synuclein, 192
- imaging of, 201–2
- in AD, 213
- in Alzheimer's Disease (AD), 213
- innate and adaptive immune cells and, 309–10
- role for in LBDs, 206
- role of in psychiatric disorders, 309
- neuroinflammatory disorders, 9
- neuronal dysfunction, 201–2
- neurons, 42–3
- neuroplasticity, 61–2
- neuropsychiatric disorders, 62, 79, 154
- and natural killer (NK) cells, 311
- pathophysiology of, 309
- risk factors for, 267
- neuropsychiatric onset, of neurodevelopmental disorders, 270
- neuropsychiatric symptoms
- advances in diagnosis, 92
- in lupus, 83
- neuropsychiatric systemic lupus erythematosus (NPSLE), 88–9
- biomarkers, 89–90
- neuroscience and immunology research, 27
- neurotransmitter
- acetylcholine, 43
- neurotransmitter function, 309
- neurotransmitter metabolism, 309
- neurotransmitter
- noradrenaline (NA), 171
- neurotransmitters, 261–2
- Actions of pro-inflammatory cytokines on, 127
- New England Journal of Medicine*, 38
- nicotinic acetylcholine receptor, 43
- NIH conference, 32
- NK cells, 4, 5–6
- NK-T cells, 4
- NLRs, and inflammasome, 6–7
- NMDAR encephalitis, 83
- NMDAR positive allosteric modulator, 66
- N-Methyl D-aspartate receptor (NMDAR) encephalitis, 85–8
- Nobel Prize, 25
- Nobel Prize in Physiology or Medicine, 41
- non-immune functions of the immune system, 2
- non-steroidal anti-inflammatory agents (NSAIDs), 99–100
- non-steroidal anti-inflammatory drugs, antidepressant effects of, 142–3
- novel anti-IL-6 mAb, 148
- NPSLE and obstacles
- biomarkers and, 89–90
- NPSLE syndromes, 89
- NRF, 2, 197
- nucleotide polymorphisms (SNPs), 236
- nucleotide-binding oligomerization domain (NOD), 6
- nucleus tractus solitarius, 2, 114
- offspring
- neurodevelopment, 267
- omega-3 fatty acids, 149–50
- trial in schizophrenia, 102
- Osler, William, 83
- oxidative stress, 90
- PAMPs. *See* pathogen-associated molecular patterns (PAMPs)
- panic disorder (PD), 233
- Pantell, 29
- Parkinson's disease (PD), 14, 16, 164, 190, 191
- and autoantibodies, 13
- and inflammation, 190
- and minocycline, 98
- and overactivation of the complement system, 7
- inflammation and, 236
- Pasteur, Louis, 25, 40
- pathogen-associated molecular patterns (PAMPs), 6, 7, 41, 167, 214
- receptors, 310
- recognized by TLRs, 6
- pathological studies, and the role for inflammation, 202–3
- pattern recognition receptors (PRRs), 5, 6, 40, 41, 170, 192
- peptidoglycans, 216
- peripheral communication, 14–16
- peripheral cytokine alterations, 317
- peripheral immune activation and psychosis, 96
- peripheral immune cells
- stress effects on, 55–7
- peripheral immune system and communication with the CNS, 14
- peripheral inflammation and acute CNS dysfunction, 165–7
- and clinical consequences in neurodegenerative disease, 177
- and cognitive decline, 164–5
- perivascular antigen presenting cells (APCs), 2
- Peters, A., 63
- phagocytes cells, 2
- phobias, 233
- and the immune system, 243–4
- plasma tryptophan, 16, 266

- PNI. *See*
 psychoneuroimmunology
 (PNI)
- Pollak, T., 84, 86
- polymorphisms, 203
- polyunsaturated fatty acids
 (PUFAs), 102
 and anxiety symptoms, 243
- population attributable risk
 (PAR), 77
- positron emission tomography
 (PET), 97, 190
 ligands, 175
 tracers, 5
- postnatal neurodevelopment,
 268–9
- post-traumatic stress disorder
 (PTSD), 233
 and the immune system,
 233–6
 with inflammatory
 signals, 234
- potential Role for IL-6/IL-6 R
 Pathway, 140
- Potvin, S., 317
- preclinical data, 54, 242
 and the adaptive immune
 system, 300–2
- preclinical experiments, and
 immune afferent
 signals, 38–9
- pregnant population, and
 schizophrenia cases, 78
- prenatal immune and
 infectious factors
 and schizophrenia, 73
- prenatal inflammatory
 biomarkers, and
 schizophrenia, 76
- prenatal
 neurodevelopment, 267
- prion diseases, 86, 164, 169,
 170, 171
- pro-inflammatory cytokines, 1,
 139, 164
- pro-inflammatory cytokines
 interleukin-8 (IL-8), 76
- psychiatric and
 neurodegenerative
 disorders
 and microglial
 activation, 5
- psychiatric disorders
 and chemokines, 319
 and chmokines, 321
 and cytokines, 316, 318–19
- and peripheral monocyte/
 macrophage numbers, 4
- and Th subsets, 10
- association with the immune
 system, 292
- complement system, 314–16
- complement systems
 and, 316
- immune cell dysregulation
 across, 309–14
- immune system and
 treatment, 309
- role of neuroinflammation
 in, 309
- psychiatric pathology,
 neuroplasticity and, 61–2
- psychiatric phenomena, and
 auto-immune
 disorders, 83
- dysregulated dopaminergic
 neurotransmission, 142
- psychological stress
 and reduced NK cell
 activity, 6
- psychomotor retardation,
 118–19
- psychoneuroimmunology
 (PNI), 25, 26, 39
 advances in, 39–44
 research, 29
- Psychoneuroimmunology
 Research Society
 (PNIRS), 32
 first members receipt, 32
- psychosis
 and treatment with anti-
 inflammatory agents,
 96, 98
 use of anti-inflammatory
 agents in, 103
- psychosocial
 neuroimmunology, 26
- PubMed, 190
- rabies vaccine, 25
- Rabin, Bruce, 32
- Raison, CL, 38, 147, 151
- randomised placebo controlled
 trials (RCTs), 224
 and Mendelian
 Randomization Analysis
 comparison, 141
- randomized controlled trials
 (RCTs), 140
 evidence from, 124
- RANTES levels, 204
- Rapaport, M. H., 100
- Reign of Terror, 25
- repeated social defeat
 triggers, 59
- Research Perspectives in
 PNI, 32
- resilience, 66
- adaptive immune system, 14
- Rheumatoid Arthritis, 110, 111
- Rubella Birth Defects
 Evaluation Project
 (RBDEP), 75
- Salmonella typhimurium*, 172
- Sampson, Wallace, 27
- Sanders, Virginia, 43
- Sapolsky, Robert, 35, 36
- Schedlowski, Manfred, 43
- schizophrenia, 1, 16, 73, 78,
 258, 280–1, 309
 and abnormal NK cell
 activity, 6
 and antioxidants, 102
 and Celecoxib
 treatment, 100
 and chemokines, 320
 and cytokines, 317–18
 and low grade
 neuroinflammation, 309
 and MHC genes, 10
 and prenatal exposure to
 infections, 73
 cellular immune pathways
 and, 313–14
 circulating adaptive immune
 cells, 312–13
 circulating innate immune
 cells and, 310–11
 complement system and, 315
 C-reactive protein (CRP)
 and, 7
 development in offspring, 79
 future investigations into the
 infectious causes of, 77–9
 minocycline and, 151
 novel therapeutic options in
 treating, 103–4
 role of microbiota in, 278
 Th17 cells and, 10
 trials of Omega-3 in, 102
- scholarly societies
 creation of, 30–3
- Schwartz, Michal, 300
- Science* magazine, 35
- scientific meetings, 30–3
- Sekar, A, 7, 8, 78

- selective norepinephrine reuptake inhibitors (SNRIs), 141
- Selye's General Adaptation Syndrome, 25, 39
- sensory circumventricular organs, 114
- serotonergic system, 261
- serotonin reuptake inhibitors (SSRIs), 141
- serum anti-neuronal antibodies
and first episode psychosis, 13
- serum autoantibodies, 84
- Seth, AK, 64
- Shiozawa, S, 90
- short chain fatty acids (SCFA), 263
- sickness
and depression symptoms, 127–8
fatigue as a feature of, 116–17
social disconnection or withdrawal as a feature of, 119
- sickness and depression
comparison of symptoms, 112
similarities between, 111–12
- sickness behaviour, 16, 25, 36, 37, 109, 110–11, 139, 171, 217, 316
- and depression, 115
- and infections, 221
- and response to infection, 109
- and routes to the brain, 167–9
- fever response and, 8
- MDD, 326
- virus-induced, 41
- signalling path-ways, 113
- peripheral inflammation, 223
- Simmons, WK, 64
- SINAPPS2 trial, 87
- single nucleotide polymorphism (SNP), 215
- skin, the, 4
as a barrier, 2
- sleep/sleep disturbance, 120–1
- smallpox vaccine, 25
- social behaviours, 119
- social communication
dysregulation of, 277
- social communication, deficits in, 269
- social defeat (RSD) model, 53
- social disconnection or withdrawal, 119
- social stress, 53
- Solomon, George F., 26, 29
- Sommer, I.E., 100
- Souza, Errol de, 40
- statins, 103, 148
- Stein, A.H., 34
- Stephan, KE, 65
- sterile systemic inflammation, 165
- Stern, Felix, 87
- stress
acute, 66
and changes in the brain structure, 60–1
and immune system, 53, 54
and relationship between the immune system and the brain, 66
and the Bayesian brain, 63, 65
and the immune system, 35, 40, 51
and the immune system
clinical studies, 62–3
as uncertainty, 63–4
body's defence against, 66
chronic, 66
chronic restraint/
immobilisation model, 55
chronic unpredictable/mild/
variable model, 54–5
controlling response to, 51, 52
early life stress (ELS)
model, 55
effects of, 43
effects of on peripheral immune cells, 55–7
effects on CNS-resident microglia, 57, 59
forms of, 64
models of, 53
priming effects of, 58–60
repeated social defeat (RSD)
model of, 53
social, 53
what it is, 51
- stress-induced depression, 55
- stress-induced microglia
activation, 59
- subdiaphragmatic vagotomy, 37
- Swedish birth cohort, 75
- sympathetic nervous system (SNS), 51
activation of, 238
- sympathetic neuron-associated macrophages (SAMs), 33
- synaptic antigens, 85
- systemic inflammation, 26, 168, 221–2. *See also* inflammation
AD and PD pathology, 174
and acute and long-term impairments, 173–5
and anxiety disorders, 237–8
as a signal to healthy brain, 169
consequences of in neurodegenerative disease, 167
- systemic inflammation on the diseased brain, 166
- systemic lupus erythematosus (SLE), 88, 89
psychiatric symptoms in, 90
- systemic lupus erythematosus, Neuropsychiatric (NPSLE), 88–9
- T cell cytokines, 325
- T cell receptor (TCR)
complex, 9
- T cells, 10–12
role for, 312
- T helper cells, 8
- T regulatory cells (Treg), 9
- tai chi, 35
- T-cell cytokines, 295–6
- T-cell population, 32
- T-cell subsets and T-cell cytokines, 295–6
- Texas Southwestern Medical Center, 41
- Thelper cells, 34, 312
and caregivers, 35
- therapeutic antibodies, and access to the brain, 2
- therapeutic strategies, 222–5
- tissue-resident macrophage populations (microglia), 4
- TNF-alpha, 197
- tolerable stress, 64
- toll-like receptors (TLRs), 6, 26, 41, 192
- toxic stress, 64
- Toxoplasma gondii*, 74, 75, 280
- Tracey, Kevin, 43, 65

- transforming growth factor (TGF), 5
- translocator protein (TSPO), 5, 97, 201
- ligands, 215
- PET, 115
- treatment, and immune alterations, 299
- treatment-resistant depression, 147
- TREGs, 9, 10, 12, 14, 216, 313, 314, 325
- TREM, 2, 191, 216
- tryptophan dioxygenase (TDO), 16
- Tsuppressor, 34
- tumour necrosis factor (TNF), 5, 8, 37, 76, 109, 141, 214, 316
- UK Whitehall II cohort, 122
- Unified Parkinson's Disease Rating Scale (UPDRS), 201
- unipolar depression, 148
- vagal neurotransmission, 121
- vagotomy, 37, 114, 261, 262
- vascular cell adhesion molecule (VCAM) expression, 56
- ventral mPFC (vmPFC), activation of, 240
- Veterans Administration Hospital, 26
- Vincenzi, B., 103
- Virchow-Robin spaces, 2
- viscerosensory cortex (VSC), 64
- Wang, AK, 317
- Wang, J., 66
- Wellcome Trust, 30, 155
- Whale, Richard, 112
- Wittenberg, G., 144, **146**
- Wohleb, ES, 58
- Yirmiya, Raz, 37, 111
- Yokota, O., 100
- α -synuclein and microglia, **193**