

The Genetics of Cognitive Neuroscience

edited by Terry E. Goldberg and Daniel R. Weinberger

The MIT Press
Cambridge, Massachusetts
London, England

© 2009 Massachusetts Institute of Technology

All rights reserved. No part of this book may be reproduced in any form by any electronic or mechanical means (including photocopying, recording, or information storage and retrieval) without permission in writing from the publisher.

MIT Press books may be purchased at special quantity discounts for business or sales promotional use. For information, please email special_sales@mitpress.mit.edu or write to Special Sales Department, The MIT Press, 55 Hayward Street, Cambridge, MA 02142.

This book was set in Stone Sans and Stone Serif by SNP Best-set Typesetter Ltd., Hong Kong and was printed and bound in the United States of America.

Library of Congress Cataloging-in-Publication Data

The genetics of cognitive neuroscience / edited by Terry E. Goldberg and Daniel R. Weinberger.

p. cm. – (Issues in clinical and cognitive neuropsychology)

Includes bibliographical references and index.

ISBN 978-0-262-01307-9 (hardcover : alk. paper) 1. Neurogenetics. 2. Cognitive neuroscience.

I. Goldberg, Terry E. II. Weinberger, Daniel R.

QP356.22.G463 2009

612.8-dc22

2008044259

10 9 8 7 6 5 4 3 2 1

Index

- Aberdeen birth cohorts (ABC), 110
- Abnormal spindle-like microcephaly (ASPM), 110
- Active avoidance, 60
- Active rGE, 106
- Addiction, 70, 123, 147
- Addington, AM, 109
- Adenines, 14
- Adoption studies, xi
 - environmental factors and, 98–99
 - intelligence and, 98–100
 - socioeconomic status and, 98
- Affected sib pairs (ASP) method, 36, 46
- Affective disorders, 146
 - schizoaffective, 250–251
 - serotonin and, 148–153
- Affi, AK, 223
- Aggleton, JP, 80
- Agnosia, 228
- Akassoglou, K, 54
- Albinos, 43
- Alcoholism, 108–109, 112
- ALDH5A1, 108
- Aleman, A, 202
- Alleles, 80
 - Alzheimer's disease and, 221–235
 - animal models and, 51
 - anxiety and, 150–153
 - APOE and, 167–168
 - association of, 33
 - attention and, 129–130
 - candidate gene approach and, 109–112
 - dyslexia and, 184–186
 - environmental factors and, 43–46
 - Fisher's exact test and, 29
 - frequency of, 32–34
 - genetic component determination and, 30–32
 - genome-wide association (GWA) and, 27, 29, 39–43
 - haplotype analysis and, 33, 38
 - Hardy-Weinberg equilibrium (HWE) and, 32–33, 36
 - Hasemen-Elston regression and, 37
 - heterozygotes and, 32
 - homozygotes and, 32
 - identical by descent (IBD), 30, 36–37
 - interclass correlation coefficient (ICC) and, 30–31
 - linkage disequilibrium (LD) and, 33–34
 - markers and, 27–29, 32–43
 - pedigree structure and, 34–35
 - phase and, 38
 - pooled association and, 107–109
 - power calculation and, 46–47
 - sample size and, 46–47
 - schizophrenia and, 195–208, 245–255
 - statistical genetics and, 27–47
 - subpopulation data and, 41–43
 - 3-repeat, 129, 129–130
 - Valine, 129
- Allele-sharing values, 29
- Allen Brain Atlas* software, 22

- Almasy, L, 37
- Alpha-antichymotrypsin, 223
- Alzheimer's disease, 28, 74, 161–162, 168, 207
- age groups and, 228–229
- amyloid precursor protein and, 225–229
- animal models and, 222, 234–235
- antisocial behavior and, 226
- anxiety and, 226
- apathy and, 226
- apolipoprotein E (APOE) and, 231–234
- BDNF and, 223
- behavioral abnormalities and, 226
- beta-amyloid protein and, 223–224, 227–228, 232
- clinical practice implications and, 234
- dementia concept and, 8, 223–224
- depression and, 226
- Down's syndrome and, 223, 225, 227–228
- etiology of, 224
- familial, 224–226, 229–231, 234
- genetic basis for cognitive decline, 221–235
- Huntington's disease and, 223
- information processing and, 223–225
- insulin degrading enzyme (IDE) and, 233
- language deficits and, 223
- linkage analysis and, 225–226
- Mini-Mental State Examination (MMSE) and, 230
- motor deficits and, 223
- neurofibrillary tangles (NFTs) and, 223–225, 227
- paired helical filaments (PHFs) and, 223–224
- pathology of, 223–225
- presenilins and, 228–231
- protein products and, 221–223
- race and, 230–231
- Rett syndrome (RS) and, 222–223
- senile plaques and, 223–224, 227
- SORL1 and, 233–234
- sporadic, 224–226, 233
- Trails Making Test and, 230
- ubiquitin and, 233
- visuospatial deficits and, 223
- Wisconsin Card Sorting test and, 230
- young-onset, 229
- Ambrosius, WT, 46
- Amino acids
- functional variations and, 12–16
- transcription phase and, 13–14
- Amir, RE, 223
- Amygdala
- animal models and, 68–70, 74
- temperamental anxiety and, 150–152
- Amyloid precursor protein (APP), 52, 224–229
- Anagnostaras, SG, 59
- Andersen, RA, 125
- Andreasen, NC, 102
- Andrews, W, 182
- Angelman syndrome, 12
- Animal models
- advantages over pharmacological models, 51
- allele dose and, 51
- Alzheimer's disease and, 222, 234–235
- amygdala and, 68–70, 74
- attention and, 65–67, 135–136
- Barnes maze and, 60
- behavioral tests and, 58–68, 80
- brain-derived neurotrophic factor (BDNF)
- mice and, 75–76
- calcium/calmodulin-dependent protein kinase II and, 68–69
- candidate gene approach and, 109
- chimpanzees and, 10
- cognition and, 51–81, 160–161
- color and, 65
- conditioned punishment and, 67
- confounders and, 78–80
- corticotropin-releasing factor (CRF) system and, 69–70
- decision making and, 67
- declarative memory and, 58–61
- delayed matching to sample (DMTS) and, 64–65
- delayed nonmatching to sample (DNMTS) and, 64–65
- dog breeds and, 4

- dopamine system and, 70–72
- dyslexia and, 182–183
- embryonic stem (ES) cells and, 54–58
- endocannabinoid system and, 72–73
- environmental factors and, 80
- extinction and, 66, 73
- fear conditioning and, 59, 69, 73–75, 78
- five-choice serial reaction time task (5-CSRT) and, 65–66
- flexibility and, 67
- fragile X knockout mice and, 73–74
- fruit flies and, 7
- galanin system and, 74–75
- genetically altered mice and, 51–58, 68–81, 234–235
- habituation-dishabituation paradigm and, 64
- heritability and, 4
- innovation in, 81
- instrumental learning and, 64–65
- intelligence and, 109
- maze-based shifting and, 67
- Morris water maze and, 58–60, 63, 69–70, 73–78
- neuregulin 1 and, 76–77
- new, 81
- nicotinic receptors and, 77–78
- NMDA receptor and, 76
- object recognition and, 63–64
- odor span task and, 63
- operant conditioning chamber and, 64
- opioid system and, 72
- oxytocin and, 77
- passive and active avoidance and, 60
- penetrance and, 51
- proline dehydrogenase and, 76
- radial maze and, 62–63, 71, 79
- rat studies and, 51, 68, 160
- reaction time and, 67
- recognition memory and, 63–68
- response latency and, 66
- reversal learning and, 66, 73
- schizophrenia 1 and, 76
- serotonin and, 150, 152–153
- sheep and, 5
- shifting and, 67
- shock and, 60–61, 66, 68
- social discrimination paradigm and, 64
- social recognition and, 63–64
- social transmission of food preference (STFP) and, 60–61
- species differences and, 78–79
- targeted gene knockout mice and, 54–58
- technical problems and, 79–80
- temporal characteristics and, 51
- T-maze and, 61–62, 67–68, 70–71, 76
- training time and, 80
- transgenic mice and, 51–54, 74, 80–81, 234–235
- vasopressin and, 77
- working memory and, 61–65
- Y-maze and, 60
- Ankyrin repeat and kinase domain containing 1 (ANKK1), 131
- Annett, LE, 59, 66
- Anokhin, AP, 135
- Ansorge, MS, 133
- Anterior cingulate cortex (ACC)
 - attention and, 125, 130–131, 134–137
 - genetic dissection of function of, 134–137
 - profiling candidates and, 135–137
 - Stroop task and, 125
- Anterior cingulate gyrus, 131
- Anthropometric Laboratory, 5
- Anxiety, 19, 123
 - alleles and, 150–153
 - Alzheimer's disease and, 226
 - association studies and, 146–147
 - HPA axis function and, 148
 - MAOA and, 151
 - serotonin and, 145–153
 - TPH2 and, 151–152
- Aphasia, 228
- Apolipoprotein E (APOE)
 - Alzheimer's disease and, 223, 231–234
 - cognitive aging and, 161–162, 167–168
 - intelligence and, 110

- Appels, MC, 201
- Apraxia, 228
- Apud, JA, 249
- Arnold, SE, 224
- Arriagada, PV, 225
- Association studies, xi–xii
- behavioral, 80, 146–149
 - candidate gene approaches and, 20, 29, 37–39
(*see also* Candidate gene approach)
 - emotion regulation and, 146–147
 - fine mapping and, 27
 - gene structure and, 8–10
 - genome-wide (GWA), 27, 29, 39–43 (*see also* Genome-wide association (GWA))
 - Hardy-Weinberg equilibrium (HWE) and, 32–33, 36–38
 - imprinting and, 29
 - limits of, 149
 - linkage, 19–21 (*see also* Linkage analysis)
 - McNemar test and, 29
 - pooled association and, 107–109
 - SNPs and, 21–23, 29
 - statistical, 8–10
 - structured, 42–43
 - threshold disorders and, 17, 19
 - two broad categories of, 29
- Attention
- animal models and, 135–136
 - ANKK1 gene and, 131
 - anterior cingulate cortex (ACC) and, 125, 130–131, 134–137
 - brain size and, 126
 - candidate gene approach and, 126–129
 - cell death and, 134
 - cholinergic system and, 129
 - complex phenotypes and, 17
 - COMT and, 127–132
 - Continuous Performance Task (CPT) and, 126
 - corpus callosum and, 126
 - cueing and, 125
 - DAT1 and, 130, 133
 - delayed response task and, 128
 - developmental constraints and, 132–133
 - dopamine system and, 127–133
 - DRD2 and, 131–132
 - DRD4 and, 130
 - ECEL1 and, 135–136
 - environmental factors and, 132–134
 - flexible switching and, 201–202
 - frontal cortex and, 126
 - gene expression constraints and, 130–132
 - heritability and, 125–126
 - HOXA1 and, 136–137
 - linkage disequilibrium and, 131–132
 - MAOA and, 128–130
 - MPTP and, 128
 - mRNA and, 136
 - neural networks and, 124–130
 - neuroimaging and, 129–130
 - nicotinic receptors and, 129
 - norepinephrine system and, 124
 - NPPC and, 135
 - NXP3 and, 135–136
 - orienting and, 125, 129
 - parietal lobe and, 125
 - prefrontal cortex and, 129
 - prepulse inhibition and, 132
 - raphe nuclei and, 130–131
 - reaction time and, 128
 - reliability and, 125–126
 - schizophrenia and, 123, 127, 135, 195–196, 200–202
 - SDK1 and, 137
 - selective, 126
 - sensorimotor gating and, 126
 - serotonin and, 129–130, 133–134
 - sFRP2 and, 135–136
 - smooth pursuit eye tracking and, 126
 - Span of Apprehension task and, 126
 - Spontaneous Selective Attention Task and, 126
 - Stroop task and, 125
 - superior temporal lobe and, 125
 - TAC1 and, 135–136
 - TaqIA polymorphism and, 131–132

- TPH and, 133
twin studies and, 126
- Attentional set shifting, 67, 126
- Attention-deficit/hyperactivity disorder (ADHD), 109, 123, 127, 183–184
- Attention network test (ANT), 125–126, 129
- Attention Task, 74, 123
- Aubert, J, 40
- Auerbach, JG, 133
- Aultman, JM, 61
- Austin, MC, 131
- Australian studies, 108, 110, 168
- Autism, 109, 112
- Autosomes, 7
- Avishai-Eliner, S, 134
- Avoidance, 60, 77–78
- Axis II diagnostic scale, 17
- Baare, WF, 101
- Bach, ME, 69
- Bacterial artificial chromosome (BAC) clones, 52–53
- Baddeley, A, 197
- Baker, LA, 103
- Bakker, SC, 184
- Barnes, CA, 60
- Barnes maze, 60, 69
- Barnett, JH, 207
- Bartels, M, 98
- Bartlett, CW, 183
- Basolateral amygdala, 68
- Bateson, P, 79
- Batty, GD, 98
- Baunez, C, 65
- Bayesian models, 40, 42–43
- Beadle, GW, 9
- Bearden, CE, 132
- Beglopoulos, 136
- Behavior
addictive, 70, 123, 147
animal models and, 51–81 (*see also* Animal models)
anxiety and, 19, 123, 145–153, 226
association studies and, 146–149
attention and, 65–66
avoidance and, 60, 77–78
brain-derived neurotrophic factor (BDNF) and, 75–76
brain reaction diversity and, 10–11
calcium/calmodulin-dependent protein kinase II and, 68–69
change in habits, 66
conditioned punishment and, 60–61, 66–68
corticolimbic function and, 145–153
corticotropin-releasing factor (CRF) system and, 69–70
data interpretation and, 80
decision making and, 68
declarative memory and, 58–61
delayed comparison procedures and, 65
dopamine system and, 70–72, 147–148
dyslexia and, 177–186
emotion and, 3 (*see also* Emotion)
endocannabinoid system and, 72–73
environmental effects and, 3–4, 80, 98–101, 105–107
extinction and, 66, 73
extraversion and, 146–147
fear conditioning and, 59, 69, 73–75, 78
five-choice serial reaction time task (5-CSRT) and, 65–66
flexibility and, 67
galanin system and, 74–75
genetically altered mice and, 51–58, 68–81
genetic risk factors and, 3, 123
habituation-dishabituation paradigm and, 64
human diversity in, 3
imprinting and, 12
instrumental learning and, 64–65
knockout mice and, 52, 54–58, 73–74
Morris water maze and, 58–60, 69–70, 73–78
nature/nurture debate and, 3
NEOAC measure and, 17
NMDA and, 76
operant conditioning chamber and, 64
opioid system and, 72

- Behavior (cont.)
perseverative, 66
radial maze and, 62–63, 71, 79
reaction time and, 67–68
recognition memory and, 63–68
reversal learning and, 66, 73
schizophrenia and, 76, 195–208 (*see also* Schizophrenia)
serotonin and, 145–153
shifting tasks and, 67
shock and, 60–61, 66, 68
social discrimination paradigm and, 64
T-maze and, 61–62, 67–68, 70–71, 76
transgenic mice and, 51–54
working memory and, 61–65
- Bejar, R, 69
- Bellini, G, 182
- Bender, HU, 15
- Bendixen, MH, 169
- Benes, FM, 134
- Benmoyal-Segal, L, 70
- Bennett, DA, 168, 232
- Benyamin, B, 98
- Berchtold, NC, 171
- Beriman, L, 45
- Bertolino, A, 248–249
- Bertram, L, 233
- Beta-amyloid protein, 223–224, 227–228, 232
- Betz, UA, 52
- Bialystok, E, 159
- Bible, 5
- Bielsky, IF, 77
- Bigos, Kristin L., 145–157
- Bilder, RM, 71, 199, 201–203, 246–248
- Binet, Alfred, 16
- Binomial distribution, 34–35
- Biocomputing Platforms Ltd., 39
- Bioinformatics. *See also* Neuroimaging
Alzheimer's disease and, 226
data mining algorithms and, 45
DISC1 and, 8
picking genes for study, 19–24
random forest and, 45
serotonin and, 149–153
training set and, 45–46
- Bipolar disorder, 19
- Bird, TD, 231
- Birrel, JM, 67
- Black fly, 19
- Blackwood, DH, 196
- Blakely, RD, 14
- Blasi, G, 201
- Blier, P, 149
- Blindness, 19
- Block design test, 168
- Blood-oxygen-level-dependent (BOLD)
activation, 160, 170
- Body mass index, 207
- Boehnke, M, 46
- Bondi, MW, 168
- Bonney, GE, 31
- Bontekoe, CJ, 74
- Bookheimer, S, 232
- Boomsma, DI, 98
- Borkenau, P, 103
- Bosker, R, 31
- Bouchard, TJ, Jr, 98–99
- Braff, DL, 126, 197
- Brain. *See also* Cognition; Specific structure
aging and, 159–171
Alzheimer's disease and, 221–235
attention and, 65–66, 123–137
axospinous synapses and, 160
dendritic branching and, 160
developmental constraints and, 132–133
environmental factors and, 133–134 (*see also* Environmental factors)
gene expression constraints and, 130–132
pharmacogenetic approaches and, 245–255
plasticity and, 160
schizophrenia and, 195–208 (*see also* Schizophrenia)
- Brain-derived neurotrophic factor (BDNF)
Alzheimer's disease and, 223
animal models and, 75–76
bioinformatics and, 15

- cognitive aging and, 161, 170
emotional reactivity and, 152
schizophrenia and, 203, 206
Brain Explorer software, 22
Brain size, 126
Brain volume, 101–103
Branchek, TA, 74
Bray, NJ, 251
Breast cancer, 28
Breeding, 4–5, 20, 51, 58, 79, 81
Bretsky, P, 168
Brito, GN, 61
Brito, LS, 61
Broad sense heritability, 30
Bronfenbrenner, U, 185
Brouwers, N, 226
Brown, RM, 128
Brown, VJ, 67
Browne, WJ, 31
Brozoski, TJ, 128
Brunkan, AL, 228–229
Brute-force algorithms, 23
Buchanan, RW, 250
Buckholtz, JW, 199–200
Buhle, J, 200
Bujard, H, 53
Bunsey, M, 61
Burdick, Katherine E.
 intelligence and, 111
 pharmacogenetics and, 245–255
 schizophrenia and, 199–200, 204, 207
Buresova, O, 63
Bush, G, 125, 135
Butcher, LM, 108, 112
Buxbaum, JD, 109
Buyske, S, 108

CA1 region, 63, 76, 160
CA3 region, 160
Caballero, IM, 223
Cadoret, RJ, 185
Calcium/calmodulin-dependent protein
 kinase II, 52, 68–69

California Verbal Learning Test, 202
Callicott, JH, 197, 199, 204
Callosal sulcus, 134–135
Caloric restriction, 161
Cambridge Examination for Mental Disorders
 of the Elderly, 228
Cambridge Neuropsychological Test, 199
Campion, D, 225, 228
Candidate gene approach
 animal models and, 109
 attention and, 126–129
 biological plausibility and, 109–110
 dyslexia and, 181–183
 efficiency of, 37
 intelligence and, 109–112
 migratory patterns and, 127
 neuroimaging and, 129–130
 pharmacogenetics and, 246–248
 schizophrenia and, 195–208
 statistical methods and, 20, 29, 37–39
Canli, T, 123, 133–134, 152
Cannabinoid receptors, 72–73
Cannon, TD, 126, 135, 196, 198, 201–204
Capecchi, MR, 54
Cardinal, RN, 68
Cardno, AG, 195, 198
Carey, G, 148
Carlson, CS, 107
Carroll, JB, 97
Carter, CS, 135, 197
Cases, O, 72
Caspi, A, 124, 129, 134, 150, 153, 185
Castner, SA, 197
Catechol-O-methyltransferase (COMT), 11,
 13, 15, 71
 attention and, 127–132
 cognitive aging and, 168–169
 intelligence and, 110–111
 personality and, 147
 schizophrenia and, 199, 201, 203, 206–207,
 248–249, 253–254
Cecchi, C, 229
Ceci, SJ, 185

- C. elegans*, 161
- Centimorgan (cM), 7
- Central nervous system (CNS)
- cognitive aging and, 161, 167, 171
 - history of genetics and, 4–24
 - nicotinic receptors and, 77–78
 - schizophrenia and, 206, 249, 251
- CERAD cognitive tests, 167–168
- Cerebral cortex, 69–70
- Cerebrospinal fluid, 69–70
- Champiaux, N, 77
- Change in habits, 66
- Changeux, JP, 77
- Chapman, J, 232
- Cheek swabs, 128
- Chen, Jingshan, 15, 51–94, 248
- Chen, Q, 252
- Chen, WJ, 201
- Chen, ZY, 75
- Cheverud, JMK, 126
- Children
- Down's syndrome and, 8, 223, 225, 227–228
 - dyslexia and, 177–186
 - environmental factors and, 98–99
 - Huntington's disease and, 223
 - intelligence and, 98–114
 - maltreatment effects and, 129
 - Rett syndrome (RS) and, 222–223
 - twin studies and, 98–101
- Childs, B, 15
- Chimpanzees, 7
- China, 21, 131
- Chi-square tests, 33, 37–38
- Cholinergic basal forebrain, 74
- Cholinergic muscarinic receptor 2 (CHRM2) gene, 111
- Cholinergic system, 129
- Christensen, K, 101
- Christiansen, L, 161
- Chromosomes, 6
- Alzheimer's disease and, 221–235
 - arm/band identity and, 7
 - attention networks and, 126–130
 - autosomes and, 7
 - bacterial artificial chromosome (BAC) clones and, 52–53
 - base pair mismatch and, 8
 - candidate gene association studies and, 20, 29, 37–39
 - copy number variations (CNVs) and, 11–12
 - crossover events and, 8
 - disorders from misrouting of, 8
 - dyslexia and, 181–183
 - family-based association test (FBAT) and, 39
 - fragile X knockout mice and, 73–74
 - gender and, 7
 - genome-wide association (GWA) and, 27, 29, 39–43
 - homologous, 7–8
 - imprinting and, 12
 - intelligence and, 108 (*see also* Intelligence)
 - linkage analysis and, 27–29, 34–37
 - marker statistics and, 27–29, 32–43
 - meiosis and, 7–8
 - neuroimaging and, 123
 - pair exchange and, 7–8
 - phase and, 38
 - random distribution and, 7
 - schizophrenia and, 195–208, 245–255
 - sequencing abnormalities and, 8
 - structure of, 7
 - transmission disequilibrium test (TDT) and, 29, 38–39
 - trend tests and, 38
- Chudasama, Y, 65, 80
- Chumakov, I, 252
- Churchill, JD, 133
- Cingulate cortex, 59
- Cirillo, MA, 202
- Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), 247
- Coccaro, EF, 147
- Coding
- Alzheimer's disease and, 222–223
 - dyslexia and, 179
 - enzymes and, 9

- functional variations and, 12–16
- logistic regression and, 38
- phonological, 179
- proteins and, 9
- statistical association and, 8–10
- Cognition
 - aging and, 159–171
 - Alzheimer's disease and, 221–235
 - animal models and, 51–81
 - association studies and, xi–xiii (*see also* Association studies)
 - attention and, 65–66, 123–137
 - change in habits and, 66
 - complex phenotypes and, 16–19
 - Darwin's theory and, 5
 - decision making and, 68
 - declarative memory and, 58–61
 - delayed comparison procedures and, 65
 - developmental constraints and, 132–133
 - dyslexia and, 177–186
 - emotion and, 3 (*see also* Emotion)
 - extinction and, 66, 73
 - familial personality and, xi (*see also* Family studies)
 - fear conditioning and, 59, 69, 73–75, 78
 - flexibility and, 67
 - gene expression constraints and, 130–132
 - general cognition factor and, 97–98
 - genetically altered mice and, 51–58, 68–81
 - heritability and, 3–4 (*see also* Heritability)
 - history of genetics and, 4–24
 - imprinting and, 12, 29
 - instrumental learning and, 64–65
 - intelligence and, 97–114
 - knockout mice and, 52, 54–58, 73–74
 - Morris water maze and, 58–60, 69–70, 73–78
 - neuroimaging and, 123–130
 - operant conditioning chamber and, 64
 - pharmacogenetics and, 245–255
 - radial maze and, 62–63, 71, 79
 - reaction time and, 65–66, 68, 103–105, 128
 - recognition memory and, 63–68
 - reversal learning and, 66, 73
 - schizophrenia and, 195–208 (*see also* Schizophrenia)
 - shifting tasks and, 67
 - spatial networks and, 12
 - speed of information processing and, 103–105
 - T-maze and, 61–62, 67–68, 70–71, 76
 - transgenic mice and, 51–54
 - working memory and, 61–65
- Cognitive aging
 - animal models and, 160–161
 - APOE and, 161–162, 167–168
 - axospinous synapses and, 160
 - BDNF and, 161, 170–171
 - block design test and, 168
 - blood oxygen level and, 160, 170
 - central nervous system and, 161, 167, 171
 - COMT gene and, 168–169
 - conceptualizing effects of, 159–160
 - dementia and, 161
 - DISC1 gene and, 169
 - environmental factors and, 159, 161
 - fluency and, 168–169
 - Flynn effect and, 160
 - gender and, 169
 - longevity and, 160–171
 - serotonin and, 169–170
 - SIR2 and, 160
 - SLC64A and, 169–170
 - Tower test and, 168
 - twin studies and, 161, 167, 170
 - Werner's syndrome and, 161, 169
 - WRN gene and, 161
- Cohen, JD, 137
- Collaborative Study on the Genetics of Alcoholism (COGA), 108–109, 112
- Color, 4–6, 43, 65, 125, 179, 221
- Comings, DE, 111
- Comorbidity, 183–184
- Conditional knockout technology, 55–57
- Conditional stimulus (CS), 68

- Conditioning
animal models and, 59–61, 64, 66, 68, 72–74
contextual, 59
cued, 59
fear, 59, 69, 73–75, 78
punishment and, 68
shock and, 60–61, 66, 68
Skinner box and, 64
- Confidence interval (CI), 44–45
- Confounding
animal models and, 75, 78–80
pharmacogenetics and, 253–255
schizophrenia and, 205–206
statistical methods and, 41
- Conklin, HM, 198, 202–203
- Conover, JC, 55
- Contextual conditioning, 59
- Contingency tables, 43–44
- Continuous Performance Tasks (CPT), 126
molecular genetics and, 201–202
schizophrenia and, 200–202, 204–205
- Coon, H, 126
- Cope, NA, 182
- Copy number variations (CNVs), 11, 14
- Corbetta, M, 125
- Corder, EH, 231
- Cornblatt, BA, 126, 200
- Corpus callosum, 126
- Cortico-basal degeneration, 223
- Corticolimbic function
affective disorders and, 148
anxiety and, 145–153
association studies and, 146–147
depression and, 145–146
dopamine system and, 147–148
neuroimaging and, 145
personality and, 147–148
risk assessment and, 145–146, 153
serotonin and, 145, 147–153
- Corticotropin-releasing factor (CRF) system, 69–70
- Corvin, Aiden, 195–219
- Costa, PJ, 17
- Cotman, CW, 171, 249
- Coutureau, E, 68
- CpG islands, 23
- Craik, FIM, 159
- Craiu, R, 40
- Crawley, JN, 58–59, 64, 78
- Cre, 55–56
- Crome, L, 227
- Crossover events, 8
- Cross-trait cross-twin correlation, 102
- Crowell, SL, 127
- Cryptochidism, 12
- Crystal structures, 22
- CTCTAC, 251
- Cued conditioning, 59
- Cultural transmission, 106
- Cummings, Jeffrey L., 222–244
- Curtis, ME, 177
- Cystic fibrosis, 28
- Cytogenetics, 7
- D-amino acid oxidase activator (DAOA), 195, 199, 201, 204–208, 252
- Darwin, Charles, 5
- Databases, 10, 20, 22–23
- Data integration, xi
- Data mining algorithms, 45
- David, SP, 150, 153
- Davidson, MC, 129
- Davignon, J, 231
- Daw, EW, 233
- dbSNP, 10
- D-cycloserine, 250
- Deary, Ian J.
cognitive aging and, 162, 168–169
intelligence and, 97–121
- Decision making, 68
- Declarative memory, 58–61, 202–203
- DeFries, JC, 179, 182
- de Geus, Edo JC, 97–121
- Delay discounting, 68
- Delayed comparison procedures, 65

- Delayed matching to sample (DMTS) tasks, 64–65
- Delayed nonmatching to sample (DNMTS) tasks, 64–65
- Deletions, 8, 11–12
- Delta measure, 33–34
- δ -opioid receptor, 72
- Dementia. *See* Alzheimer's disease
- Demonet, JF, 181
- Demonstrator mouse, 61
- de Montigny, C, 149
- Dempster, E, 170, 203
- Dendrites, 160
- Depression
- Alzheimer's disease and, 226
 - corticolimbic function and, 145–146
 - HPA axis function and, 148
 - major, 19
 - manic, 146
 - serotonin and, 145–153
- De Quervain, DJ, 204
- Descarries, L, 128, 130
- D'Esposito, M, 160
- Detera-Wadleigh, SD, 252
- Detterman, DK, 97
- Developmental neurobiology, 177–186
- Devlin, B, 33, 43
- Diabetes, 4, 19, 207
- Diagnostic and Statistical Manual of Mental Disorders*, 17, 223, 253
- Diamond, A, 71
- Dias, R, 66
- Diaz-Asper, CM, 161
- Diaz-Olavarrieta, C, 230
- Dick, DM, 108–109, 111
- Dickens, WT, 106
- Digging, 67
- Dinucleotide repeats, 11
- Dinwiddie, SH, 124
- Discourse comprehension, 178–181
- Disease. *See also* Specific type
- χ^2 -square tests and, 33, 37–38
 - corticolimbic function and, 145–153
 - family studies and, 29–31 (*see also* Family studies)
 - genome-wide association (GWA) and, 27, 29, 39–43
 - monogenic genes and, 28
 - multiplex families and, 28
 - neuroimaging and, 123–124
 - random-effect logistic models and, 31
- Disequilibrium (LD), 21
- Disrupted in schizophrenia 1 (DISC1)
- animal models and, 76, 79
 - cognitive aging and, 169
 - schizophrenia and, 8, 76, 79, 169, 195–196, 199, 204–206, 208, 253
- Dizygotic (DZ) twins. *See also* Twin studies
- attention and, 126
 - cognitive aging and, 161, 167, 169
 - intelligence and, 99, 102–106
 - schizophrenia and, 198, 203
 - statistical genetics and, 28, 30
- DNA (deoxyribonucleic acid), xii
- Alzheimer's disease and, 221
 - attention and, 126–130
 - base pair mismatch and, 8
 - chromosomes and, 7 (*see also* Chromosomes)
 - copy number variations (CNVs) and, 11–12
 - dinucleotide repeats and, 11
 - ease of sampling and, 245–246
 - epigenetic function control and, 12
 - exons and, 10
 - functional variation effects and, 12–16
 - human genome project and, 9–10
 - imprinting and, 12
 - inducer sites and, 9
 - inhibitor sites and, 9
 - knockout technology and, 52, 54–58, 73–74
 - linkage studies and, 19–21 (*see also* Linkage studies)
 - marker statistics and, 27–29, 32–43
 - mice and, 80
 - pooled association and, 107–109
 - sequencing abnormalities and, 8
 - splicing and, 10

- DNA (cont.)
 statistical association and, 8–10
 transcription phase and, 13–14
 variable number tandem repeats (VNTRs)
 and, 11
 variation principles of, 10–12
 whole genome approach to intelligence and,
 107–109
- Dobkin, C, 74
- Dodart, JC, 134
- Dogs, 4–5
- Dominant traits, 6, 43
- Donohoe, Gary, 195–219, 252–252
- Dopamine system, 11
 animal models and, 70–72
 attention and, 127–130, 133
 extraversion and, 146–147
 intelligence and, 111
 personality and, 147–148
 pharmacogenetics and, 248–249
 schizophrenia and, 127, 199, 248–249, 254–255
- Doran, M, 223
- Dorsolateral prefrontal cortex (DLPFC), 128
- Dorus, S, 109
- Down's syndrome, 8, 223, 225, 227–228
- DRD2 gene, 131–132
- DRD4 gene, 130
- Drosophila, 161
- Drug resistance, 56–57
- D-serine, 250, 252
- Dudbridge, F, 40
- Duncan, GE, 76
- Duplications, 8, 11–12
- Durston, S, 123, 130
- Dysbindin
 intelligence and, 111–112
 schizophrenia and, 195, 199, 201, 206, 208,
 250–252
- Dyslexia
 ADHD and, 183–184
 animal models and, 182–183
 candidate gene approach and, 181–183
 cognitive dissection of, 177–181
 comorbidity and, 183–184
 defining, 178
 discourse comprehension and, 178–181
 genetic loci and, 179–181
 G x E interactions and, 184–186
 G x G interactions and, 184–186
 language impairment (LI) and, 183
 linkage analysis and, 185–186
 listening comprehension and, 178–181
 LOD scores and, 183–184
 orthographic coding and, 179
 phonological awareness (PA) and, 179
 phonological coding and, 179
 rapid serial naming (RSN) and, 179, 184
 reading comprehension and, 177–181,
 185–186
 risk loci and, 183–184
 speech sound disorder (SSD) and, 183–186
 syntax and, 179
- Ebstein, R, 147
- Eckert, M, 181
- Edwards-Lee, T, 226
- Edwards syndrome, 8
- Effort-based decision-making, 68
- Efron, B, 40
- Egan, MF, 11, 15
 animal models and, 71
 attention and, 127, 129, 131
 cognitive aging and, 170
 intelligence and, 102, 170
 schizophrenia and, 197, 199, 201–204, 248,
 252
- Eggs, 7–8
- Eichenbaum, H, 59, 61
- Eley, TC, 185
- Elgersma, Y, 69
- El-ghundi, M, 70
- Elston, RC, 37
- Embryonic stem (ES) cells, 54–58
- Emotion, 3
 affective disorders and, 148–153
 anxiety and, 19, 123, 145–153, 226

- brain reaction diversity and, 10–11
- corticolimbic function and, 145–153
- depression and, 19, 145–146, 148, 226
- DISC1 and, 8
- dopamine system and, 147–148
- enzymes and, 151–152
- extraversion and, 146–147
- HPA axis function and, 148
- serotonin and, 145–153
- ENCyclopedia Of DNA Elements (ENCODE), 10
- Endocannabinoid system, 72–73
- Endothelin converting enzyme-like 1 (ECEL1), 135–136
- Enolase, 52
- Environmental factors, 9, 11
 - animal models and, 80
 - attention and, 132–134
 - cognitive aging and, 159, 161
 - dyslexia and, 184–186
 - epistasis and, 43–46
 - familial aggregation studies and, 28
 - gene-gene interaction and, 43–46
 - G x E interactions and, 105–107
 - intelligence and, 98–101, 105–107
 - rGE correlations and, 105–107
 - statistical genetics and, 27–47
 - training set and, 45–46
- Enzymes. *See also* Specific enzyme
 - Alzheimer's disease and, 228–229, 233
 - animal models and, 71–72
 - attention and, 127–128, 132, 135–136
 - emotion and, 151–152
 - functional variations and, 14–15
 - gene coding and, 9
 - reaction sites and, 15
 - schizophrenia and, 199, 248
- Epigenetic control, 12
- Epistasis
 - emotion and, 153
 - schizophrenia and, 206–207, 254
 - statistical genetics and, 43–46
- Equations
 - full model, 43
 - interclass correlation coefficient (ICC), 31
 - LD measure delta, 33
 - LOD score, 34
 - Pearson's chi-square test, 33
 - recombination likelihood, 34–35
 - reduced model, 43
- Erlenmeyer-Kimling, L, 196
- Ethical issues, 124
- Eukaryotic genes, 52
- Evans, PD, 109–110
- Evenden, JL, 66, 68
- Evocative rGE, 106
- Evolution, theory of, 5, 10, 80, 127
- Ewens, WJ, 38
- Exons, 9–10
- Extinction, 66, 73
- Extraversion, 146–147
- Eysenck, Hans, 17, 103
- Ezquerria, M, 231

- Fallgatter, A, 200
- False discover rate (FDR), 40
- Familial aggregation, 27–28, 30
- Familial relative risk, 31
- Family-based association test (FBAT), 39
- Family studies
 - Alzheimer's disease and, 224–226
 - association studies and, 29 (*see also* Association studies)
 - component determination and, 30–32
 - environmental factors and, 105–107
 - Fisher's exact test and, 29
 - heritability and, 98–101 (*see also* Heritability)
 - imprinting and, 12, 29
 - intelligence and, 98–114
 - interclass correlation coefficient (ICC) and, 30–31
 - linkage analysis and, 34–37
 - LOD score and, 34–36
 - McNemar test and, 29
 - Pearson test and, 29
 - schizophrenia and, 192, 196, 198, 200–205, 246, 248–249

- Family studies (cont.)
 SES analysis and, 105
 transmission disequilibrium test (TDT) and, 29
 twin studies and, 202–203 (*see also* Twin studies)
- Fan, Jin, 123–144, 199, 248
- Fanselow, MS, 59
- Faraone, SV, 201, 203
- Farlow, M, 226
- Fat mass and obesity (FTO) gene, 207
- Fear conditioning, 59, 69, 73–75, 78
- Fenton, WS, 123
- Fernandez, G, 202
- Fine mapping, 27
- Finkel, D, 99, 167
- Finnish twin register, 198
- Fisher, PM, 150
- Fisher, R, 17
- Fisher, SE, 179, 182
- Fisher's exact test, 29, 33
- Five-choice serial reaction time task (5-CSRT), 65–66
- 5' end site, 9
- Floresco, SB, 63, 67
- Flory, JD, 168
- Fluency, 168–169
- Flynn, JR, 106
- Flynn effect, 160
- FMRP, 73–74
- Food
 animal models and, 60–63, 66, 74, 79–80
 caloric restriction and, 161
 social transmission of food preference (STFP) and, 60–61
- Footshock, 60–61
- Forbes, Erika E., 145–157
- Forrest, D, 55
- Fors-Petter, S, 52
- Fossella, John, 123–144
- Fox, HC, 229–230
- Fradley, RL, 76
- Fragile X protein, 73–74, 133
- Francks, C, 182
- Frangou, S, 195
- Franke, P, 201
- Frankland, PW, 69
- Frayling, TM, 207
- Freedman, R, 197
- Freimer, N, 148–149
- Frick, KM, 78
- Frontal cortex, 126, 199
- Fruit flies, 7
- Fry, AF, 103
- Full model, 43–44
- Functional magnetic resonance imaging (fMRI)
 anxiety and, 150–152
 attention and, 124–125, 129
 bioinformatics and, 23
 emotion and, 145
- Gabrieli, JDE, 160
- Galaburda, AM, 182
- Galanin (GAL), 52, 74–75
- Gallagher, M, 160
- Galton, CJ, 223
- Galton, Francis, 3, 5, 103
- Gamboa, R, 231
- Gametes, 8
- Gan, L, 71
- Garner, JP, 67
- Garpenstrand, H, 150
- Gasperoni, T, 198
- Gauderman, WJ, 46
- Gaussian distribution, 16–17
- Gayán, J, 179, 183
- Gender
 Alzheimer's disease and, 230, 232
 cognitive aging and, 169
 intelligence and, 102
- "Gene Atlas of the Mouse and Human Protein-Encoding Transcriptomes, A" (Su), 136
- Gene Expression Omnibus (GEO), 136
- Gene-gene interactions, 43–46
- General cognition factor, 97–98

- Genes
coding studies of, 8–10
defining, 6
enzymes and, 9
epigenetic control and, 12
eukaryotic, 52
exons and, 9
function of, 8–10, 12–16
introns and, 9
neuropsychological studies and, 19–24
proteins and, 9
statistical association and, 8–10
structure of, 8–10
transgene and, 51–54
- Genetic amplification, 98
- Genetic distance, 7
- Genetics
adoption studies and, xi, 98–100
Alzheimer's disease and, 221–235
animal models and, 51–81
brief history of, 4–24
chromosomes and, 6–8 (*see also* Chromosomes)
cognitive aging and, 159–171
copy number variations (CNVs) and, 11–12
corticolimbic function and, 145–153
Darwin on, 5
databases for, 10
defined, 3
dinucleotide repeats and, 11
dominant/recessive traits and, 6, 43 (*see also* Traits)
dyslexia and, 177–186
embryonic stem (ES) cells and, 54–58
environmental factors and, 9 (*see also* Environmental factors)
epigenetic function control and, 12
ethics and, 125
familial personality and, xi (*see also* Family studies)
Galton on, 5–6
genetically altered mice and, 51–58, 68–81
height and, 4
high-throughput genotyping platforms and, 39
human genome project and, 9–10
hybrids and, 5–6
intelligence and, 97–114
International HAPMAP Project and, 21
linkage studies and, 19–21 (*see also* Linkage studies)
longevity and, 160–171
meiosis and, 6–8
Mendel and, 5–6
migratory patterns and, 127
neuroimaging and, 23, 102–103, 123–124
pharmacogenetics and, 245–255
principles of variation and, 10–16
privacy and, 125
Punnet square and, 6
schizophrenia and, 195–208, 245–255
selective breeding and, 4–5
splicing and, 10
statistical methods in, 27–47
transcription phase and, 13–14
variable number tandem repeats (VNTRs) and, 11
- Gene trapped knockout mouse technology, 56
- Geng, Y, 57
- Genome-wide association (GWA), 27, 29, 37
Australian study and, 108
case-control, 39
confounding and, 41
Dutch study and, 108
false discovery rate (FDR) and, 40
family-based, 39
genomic control and, 42–43
haplotypes and, 39
high-throughput platforms and, 39
imputation and, 39
intelligence and, 107–109
linkage disequilibrium and, 39–40
multiple testing and, 39–41
permutation procedures and, 40
pooled association and, 107–109
population stratification and, 41, 43
p values and, 40

- Genome-wide association (cont.)
q values and, 40
replication and, 40
schizophrenia and, 253–254
structured association and, 42–43
subpopulation data and, 41–43
training set and, 45–46
- Genomic control, 42–43
- Gerlai, R, 77
- Germany, 231
- Gerstein, MB, 9–10, 23
- Geschwind, N, 230
- Geyer, MA, 126
- Giese, KP, 69
- Gilbert, SL, 109
- Giovagnoli, AR, 231
- Glahn, DC, 198, 245–255
- Glatt, CE, 148–149
- Glickstein, SB, 70
- Gliososis, 134
- Glutamate, 201, 249–253
- Glycine, 250
- Goate, A, 225, 228–229
- Goghari, VM, 135
- Gogos, JA, 71, 132
- Goldberg, Terry E.
animal models and, 71
attention and, 123
cognitive aging and, 159–174
pharmacogenetics and, 247
schizophrenia genetics and, 195–219, 252
- Goldman-Rakic, PS, 128, 197, 249
- Gomez-Isla, T, 224–225
- Gong, S, 52
- Gong, Y, 224
- Gonzalez-Alegre, P, 223
- Good, KP, 196
- Gordon, JW, 52
- Gossen, M, 53
- Gosso, MF, 111
- Gottesman, II, 146, 195–198
- Gottfredson, LS, 97
- Gough, PB, 178
- Gould, TD, 197
- Gourovitch, ML, 202–203
- Greely, HT, 234
- Green, MF, 61, 196, 246
- Greenwood, TA, 129, 168
- Gu, H, 55
- Guarente, L, 161
- Gureje, O, 231
- Guttman, R, 101
- G x E interactions, 105–107, 184–186
- G x G interactions, 184–186
- Habituation-dishabituation paradigm, 64
- Hagberg, B, 222
- Hahn, MK, 14
- Haile, CN, 70
- Hale, S, 103
- Hall, J, 200
- Hallmayer, JF, 201, 203, 251
- Hamilton, RL, 224
- Handler, M, 229
- Hannula-Jouppi, K, 182
- Haplotypes
attention and, 131–132
bioinformatics and, 21
dyslexia and, 182
genome-wide association (GWA) and, 39
schizophrenia and, 200, 204–205, 250–252
statistical genetics and, 33, 36, 38–39
- HAPMAP sites, 21, 23, 131–132
- Hardy-Weinberg equilibrium (HWE), 32–33, 36–38
- Harhangi, BS, 232
- Hariri, Ahmad R., 131, 133, 145–157, 170, 203
- Harm, MW, 179
- Harris, SE, 111, 170
- Harrison, PJ, 123
- Harvey, PD, 247
- Harwood, DG, 231
- Haseman, JK, 37
- Haseman-Elston regression, 37
- Hatakeyama, S, 184
- Hauber, W, 68

- Hay, DA, 100
- Hayashi, K, 137
- Hedden, T, 160
- Hedgehog signaling, 137
- Height, 16
- Heinrichs, RW, 69, 201
- Heinz, A, 134
- Hemideletion, 11
- Hen, R, 148
- Hendrich, B, 223
- Hennah, W, 204, 207
- Heresco-Levy, U, 250
- Heritability, 3
- adoption studies and, 98–100
 - animals and, 4
 - attention networks and, 125–126
 - brain volume and, 101–103
 - broad sense, 27, 30
 - cognitive aging and, 161–162, 167
 - component determination and, 30
 - Darwin's theory and, 5
 - dominant/recessive traits and, 6, 43 (*see also* Traits)
 - family-based association test (FBAT) and, 39 (*see also* Family studies)
 - genome-wide association (GWA) and, 27, 29, 39–43
 - hybrids and, 5–6
 - intelligence and, 97–105, 111–112
 - longevity and, 171
 - marker statistics and, 32–34
 - Mendel and, 5–6
 - narrow sense, 27, 30, 32
 - plants and, 4
 - Punnet square and, 6
 - schizophrenia and, 192, 198, 201–205
 - selective breeding and, 5
 - statistical genetics and, 27–47
 - twin studies and, 98–101 (*see also* Twin studies)
 - variance component and, 27
- Herringa, RJ, 69
- Heterozygotic twins, 32, 38, 69, 71, 75, 77, 111
- Heyser, CJ, 72
- Higgins, GA, 65
- Hiltunen, M, 233
- Hippocampus, 23
- calanin system and, 74
 - conditioning and, 59
 - DISC1 and, 8
 - food and, 61
 - galanin system and, 74–75
 - learning and, 69
 - Morris water maze and, 63
 - recognition memory and, 64
 - serotonin and, 153
 - transgenic mice and, 52–53
 - working memory and, 63
- Ho, HZ, 103
- Holland, F, 228
- Holmes, A, 150, 153
- Holmes, C, 70
- Holsboer, F, 75
- Holter, SM, 73
- Holtzman, DM, 232
- Homozygotic twins
- animal models and, 51, 75, 77, 79
 - attention and, 136
 - cognitive aging and, 169–171
 - intelligence and, 111
 - schizophrenia and, 204, 248–249
 - statistical genetics and, 32
- Hoover, DM, 178, 183
- Hori, Y, 226
- HOXA1, 136–137
- Hsiung, GY, 184
- Hulshoff Pol, 101–103
- Human Gene Nomenclature Committee, 182
- Human genome, 9
- brain reaction diversity and, 10–11
 - complex phenotypes and, 16–19
 - estimated number of genes in, 16
 - intelligence and, 107–109, 112–114
 - mice and, 54, 80
 - sequencing costs and, 24

- Humanized transgenic mouse technology, 54
- Hunter, JE, 98
- Huntington's disease, 223
- Hybrids, 5–7
- Hyman, BT, 123
- Hyperphagia, 12
- Hypothalamic-pituitary-adrenal (HPA) axis
function, 148
- Identical by descent (IBD) alleles, 30, 36–37
- Imprinting, 12, 29
- Inducer sites, 9
- Inductible transgenic mouse technology, 53–54
- Inheritance, 3
chromosomes and, 6–8
crossover events and, 8
eye color and, 5
heritability concept and, 3–4 (*see also*
Heritability)
- Jacob/Laban account and, 5
- linkage analysis and, 27–29, 34–37
- meiosis and, 6–8
- Mendel and, 5–6
- pair exchange and, 7–8
- Inhibitor sites, 9, 12
- Inlow, JK, 109
- Insertion, 8
bacterial artificial chromosome (BAC) clones
and, 52–53
drug resistance and, 56–57
genetically altered mice and, 51–58, 68–81
- Inspection time, 104
- Instrumental learning, 64–65
- Insulin degrading enzyme (IDE), 233
- Intelligence, 16–17
academic success and, 98
ADHD and, 109
adoption studies and, 98–100
aging and, 98–101, 110, 159–171
Alzheimer's disease and, 223–225
animal models and, 109
brain functioning and, 103–105
brain volume and, 101–103
candidate gene approach and, 109–112
children and, 98–114
CHRM2 gene and, 111
COMT gene and, 110–111
crystallized, 167
definition of, 97
DTNBP1 gene and, 111–112
dyslexia and, 177–186
environmental factors and, 98–101, 105–107
factor analysis and, 97
family studies and, 98–114
gender and, 102
general cognition factor and, 97–98
genetic amplification and, 98
genome-wide association (GWA) and,
107–109
G x E interactions and, 105–107
heritability and, 98–105, 112
human genome and, 112–114
individual differences in, 97
information processing speed and, 103–105,
167
inspection time and, 104
job success and, 98
linkage analysis and, 108–109
longevity and, 98
molecular genetics and, 107–112
multivariate studies of, 101–105
performance, 102
phenotypic correlation and, 104–107
pooled association and, 107–109
premorbid, 251
reaction time and, 103–105
rGE correlations and, 105–107
schizophrenia and, 112, 196–197, 200,
251–252, 254
SNAP-25 gene and, 111–112
socioeconomic status and, 98
structural equation modeling and, 102
twin studies and, 98–106, 111
verbal, 102
Wechsler Adult Intelligence Scale (WAIS),
27, 102, 104, 199–200

- whole genome approach and, 107–109
Wisconsin Card Sorting Test, 67, 128, 199, 202, 205, 230
- Interaction OR, 44
- Interclass correlation coefficient (ICC), 30–31
- International HAPMAP Project, 21, 23, 131–132
- Intertrial delay, 61
- Intertrial intervals (ITIs), 66
- Intratrial delay, 61
- Introns, 9, 57
- Inversions, 8
- Inverted-U functional response curve, 249
- Iowa Gambling Task, 68
- IQ tests, 16–17, 97. *See also* Intelligence
academic success and, 98
age and, 98
environmental factors and, 105
Flynn effect and, 160
job success and, 98
literature on, 98
longevity and, 98
multivariate studies of, 101–105
phenotypic correlations and, 104
Raven's Matrices and, 103–104
reaction time and, 104–105
singletons and, 101
twin studies and, 98–101
- Irish study, 252
- Iversen, SD, 66
- Izquierdo, A, 65
- Jacob (Biblical person), 5
- Jacoby, AS, 74
- Jaffee, SR, 124
- Jamot, L, 72
- Jang, CG, 72
- Janka, Z, 201
- Japan, 21, 131, 226
- Javitt, DC, 197
- Jensen, M, 102
- Johannsen, Wilhelm, 6
- Jones, KR, 65–66
- Joober, R, 71, 199
- Jordan, BD, 232
- Jorm, A, 168
- Jung, MY, 70
- Kachiwala, SJ, 169
- Kamil, AC, 79
- Kamprath, K, 73
- Karayiorgou, M, 132
- Karlinsky, H, 226
- Karmiloff-Smith, A, 123, 133
- Katsanis, J, 126
- Keefe, RS, 201, 246–247
- Keenan, JM, 178
- Keilp, JG, 200
- Kellendonk, C, 62, 70
- Kempf, Lucas, 3–26
- Kendler, KS, 148, 150
- Kennedy, AM, 229
- Kenyon, C, 161
- Keri, S, 198, 201
- Kernie, SG, 75
- Ketamine, 249
- Kiely, JL, 100
- Killcross, AS, 68
- Kim, JJ, 59
- Kimmel, G, 40
- Kinney, JW, 74
- Klotho, 110, 169
- Knock-in mouse technology, 57–58, 69
- Knockout mice, 52, 54–58, 73–74, 182–183
- Kooy, RF, 73
- κ -opioid receptor (KOR), 72
- Kovas, Y, 108, 112, 208
- Kovelowski, CJ, 128
- Krabbendam, L, 198
- Krawczak, M, 46
- Kremen, WS, 185
- Laban (Biblical person), 5
- Lange, C, 46
- Lange, KW, 128
- Language impairment (LI), 183
- Laplante, F, 74

- LaRusse, S, 234
Laurent, A, 201
Lavretsky, H, 167
Ledent, C, 72
LeDoux, J, 59
Lefly, D, 179
Lencz, T, 246
Leonardo, ED, 148
Lesch, KP, 149–150
LeTurco, Joseph, 182
Leukemia, 54
Levy, E, 197, 226
Lewontin, R, 34, 185
Li, Y, 55
Lichtman, AH, 73
Likelihood ratio test (LRT), 43, 45
Lin, DY, 40
Linkage analysis, 19–21. *See also* Family studies
 affected sib pairs (ASP) and, 36
 allele-sharing values and, 29
 Alzheimer's disease and, 225–226
 autism and, 109
 dyslexia and, 185–186
 Hasemen-Elston regression and, 37
 intelligence and, 108–109
 LOD score and, 34–36, 46, 183–184
 molecular biology techniques and, 34
 monogenic genes and, 28
 multiplex families and, 28
 nonparametric, 27–29
 parametric, 27–28, 36
 pedigree structure and, 34–35
 quantitative traits and, 37
 relative pair method and, 36
 schizophrenia and, 198–200, 203
 Solar software and, 37
 statistical genetics and, 27–29, 34–37
 within-family association and, 34–36
Linkage disequilibrium (LD), 15–16, 21
 attention and, 131–132
 candidate gene approach and, 109
 genome-wide association (GWA) and, 39–40
 intelligence and, 109–110
 permutation procedures and, 40
 statistical genetics and, 33–34, 38
Linnarson, S, 75
Lippa, CF, 226, 229, 231
Listening comprehension, 178–181
Liu, L, 249
Local FDR, 40
Local Global Task, 201–202
LOD score, 34–36, 46, 183–184
Loehlin, JC, 99
Logistic regression, 31–32, 38, 40, 170
Logue, SF, 59
Lohmueller, J, 127–128
Longevity
 APOE and, 167–168
 BDNF and, 170–171
 caloric restriction and, 161
 cognitive aging and, 160–171
 COMT and, 168–169
 SLC64A and, 169–170
 Werner's syndrome and, 161, 169
Loo, SK, 184
Lopera, F, 229
Lothian birth cohort (LBC), 110
Lowenberg, K, 225
LoxP element, 55–56
Luciano, M, 99, 104, 108
Lucki, I, 149–150
Luellen, BA, 152
Lynch, M, 32
Lyons, MJ, 75

McCarron, MO, 232
McClearn, GE, 99
McCrae, RR, 17
McCroy, E, 181
McDaniel, MA, 102
MacDonald, AW, 125, 197
McDonald, C, 195
McDonald, RJ, 63
McEwen, BS, 134
McGrath, Lauren M., 177–193
McGue, M, 98

- McKeith, IG, 224
MacLulich, AMJ, 102
McMahon, RP, 252
McNemar method, 29
Macular degeneration, 19
Magnetic resonance imaging (MRI), 23,
102–103, 123–124, 130
Magyar, O, 67
Mahley, RW, 233
Maier, SF, 151
Major depression, 19
Malhotra, Anil K., 71, 199, 245–249
Manic depression, 146
Mann, JJ, 225, 227
Manuck, SB, 148, 150
Marchini, J, 39, 45
Marino, C, 182
Marjaux, E, 229
Marker statistics, 123
affected sib pairs (ASP) and, 36
allele frequency and, 32
candidate gene association studies and, 37–39
Delta measure and, 33–34
genome-wide association (GWA) and, 27,
29, 39–43
Hardy-Weinberg equilibrium and, 32–33
high-throughput genotyping platforms and, 39
linkage analysis and, 27–29, 33–37
LOD score and, 34–36
phenotypes and, 27, 29, 32–34, 39–43
transmission disequilibrium test (TDT) and,
29, 38–39
Marrocco, RT, 124, 129
Marsicano, G, 72
Martin, P, 79
Martinowich, K, 223
Mattay, Venkata S., 159–174, 249
Mauldin, JE, 79
Mayeux, R, 234
Mayford, M, 52, 54, 60, 69
Mazes
Barnes, 60, 69
Morris water, 58–60, 69–70, 73–78
radial, 62–63, 71, 75–76, 79
shifting task and, 67
T, 61–62, 67–68, 70–71, 76
technical problems and, 79
Y, 60
Medial frontal cortex, 67
Medial temporal lobe, 59
Mega, MS, 226
Mehmet, H, 134
Meiosis, 6–8
Mekel-Bobrov, N, 110
Membrane metallo-endopeptidase (MME), 136
Memory
Alzheimer's disease and, 221–235
APOE and, 161–162, 167–168
aversive, 73
brain volume and, 101–103
calcium/calmodulin-dependent protein
kinase II and, 52, 68–69
cognitive aging and, 159–171
complex phenotypes and, 16–17
declarative, 58–61, 202–203
dopamine system and, 11, 70–72
endocannabinoid system and, 72–73
episodic, 195, 202
extinction and, 73
gene coding and, 8–9
molecular genetics and, 203–205
nicotinic receptors and, 77–78
olfactory, 74
postural mediation and, 80
prefrontal cortex (PFC) and, 61–62
recall and, 203–205
recognition, 63–68
schizophrenia and, 197–205, 248–249
statistical association and, 8
storage subsystems and, 197
verbal, 203–204
visual, 203
working, 61–65, 195, 197–200, 205, 248–249
Mendel, Gregor, 5–6
Mendelian traits, 6, 19
Meng, H, 182

- Mensah, FK, 38
- Mental retardation, 8, 12
 attention and, 132, 136
 dyslexia and, 179
 fragile X protein and, 73–74, 133
 intelligence and, 109
- Mental retardation syndrome, 228
- Mesulam, MM, 124
- Methuselah, 161
- Methyl-CpG-binding protein (MeCP2), 222–223
- Meyer-Lindenberg, A, 12, 130, 133–134, 161, 196, 199–201, 208
- Meyers, EN, 56
- Mice, 43
 age-dependent performance deterioration and, 78
 attention and, 65–66
 avoidance and, 60, 77–78
 Barnes maze and, 60, 69
 brain-derived neurotrophic factor (BDNF), 75–76
 breeding and, 51
 calcium/calmodulin-dependent protein kinase II and, 52, 68–69
 cognitive aging and, 160–161
 conditioned punishment and, 68
 confounding and, 75, 78–80
 corticotropin-releasing factor (CRF) system and, 69–70
 decision making and, 68
 declarative memory and, 58–61
 delayed matching to sample (DMTS) and, 64–65
 delayed nonmatching to sample (DNMTS) and, 64–65
 demonstrator, 61
 dopamine system and, 70–72
 drug resistance and, 56–57
 embryonic stem (ES) cells and, 54–58
 endocannabinoid system and, 72–73
 environmental factors and, 80
 extinction and, 66
 fear conditioning and, 59, 69, 73–75, 78
 flexibility and, 67
 fragile X, 73–74
 galanin system and, 74–75
 genetically altered, 51–58, 68–81
 habituation-dishabituation paradigm and, 64
 instrumental learning and, 64–65
 knock-in, 57–58
 knockout, 52, 54–58, 73–74, 182–183
 Morris water maze and, 58–60, 69–70, 73–78
 neuregulin 1 and, 76–77
 nicotinic receptors and, 77–78
 NMDA receptor and, 76
 object recognition and, 63–64
 odor span task and, 63
 opioid system and, 72
 oxytocin and, 76–77
 proline dehydrogenase and, 76
 radial maze and, 62–63, 71, 75–76, 79
 rat studies and, 51
 reaction time and, 68
 recognition memory and, 63–68
 reversal learning and, 66, 73
 schizophrenia 1 and, 76
 shifting and, 67
 social discrimination paradigm and, 64
 social recognition and, 63–64, 77
 social transmission of food preference (STFP) and, 60–61
 species effects and, 78–79
 T-maze and, 61–62, 67–68, 70–71, 76
 training time and, 80
 transgenic, 51–54, 74, 80–81, 234–235
 vasopressin and, 76–77
 working memory and, 61–65
 Y-maze and, 60
- Microcephalin (MCPH1), 110
- MicroRNAs, 14
- Migrant studies, 27–28, 127
- Miksys, SL, 54
- Miller, S, 69
- Milner, B, 202
- Mineur, YS, 73
- Minichiello, L, 76

- Mini-Mental state Examination (MMSE), 230
- Mini Mental task, 169
- Minnesota Study of Twins Reared Apart, 99
- Mishkin, M, 66
- Mismatch negativity, 197
- Mobini, S, 68
- ModBase, 22
- Moffitt, TE, 153
- Moghaddam, B, 61
- Mohn, AR, 76
- Moldin, SO, 146
- Molecular genetics
- Continuous Performance Tasks (CPT) and, 200–202
 - dyslexia and, 177–186
 - intelligence and, 107–112
 - memory recall and, 203–205
 - schizophrenia and, 201–205
 - whole genome approach and, 107–109
- Monoamine oxidase a (MAOA), 128–130, 151
- Monoamine oxidase (MAO), 72
- Monogenic disease genes, 28
- Monozygotic (MZ) twins
- attention and, 126
 - cognitive aging and, 161, 167
 - intelligence and, 99, 102–106
 - schizophrenia and, 198, 202–203
 - statistical genetics and, 28, 30
- Monteggia, LM, 75
- Montkowski, A, 75
- Morgan, Thomas, 7
- Morris, RG, 59
- Morris water maze, 58–60, 69–70, 73–78
- Morrow, BA, 64
- Motor skills
- animal models and, 58–60, 70
 - Alzheimer's disease and, 222–224
 - attention and, 136
 - complex phenotypes and, 17
 - schizophrenia and, 255
- Moulard, B, 232
- MPTP, 128
- mRNA (messenger RNA), 9, 22
- attention and, 136
 - corticotropin-releasing factor (CRF) system and, 69–70
 - functional variation effects and, 12–16
- Muir, JL, 65, 80
- Mullan, M, 226
- Muller-Myhsok, B, 40
- Multiple sclerosis, 19
- Multiple testing, 39–41
- Multiplex families, 28
- Multivariate studies, 101–105
- Mumby, DG, 64
- Munafo, MR, 148–149, 151
- μ -opioid receptor (MOR), 72
- Murphy, DL, 149
- Mutsuddi, M, 205
- Myles-Worsley, M, 126, 198
- Nachman, MW, 127
- Nackley, AG, 13
- Narrow sense heritability, 30, 32
- Nathan, BP, 101, 233
- Nation, K, 178
- National Collaborative Perinatal Project, 105
- National Institute of Mental Health, 247
- National Institutes of Health (NIH), 58
- Natriuretic peptide precursor C (NPPC), 135–136
- N-back task, 201, 206, 248, 254
- NCBI cd3d structures, 22
- Need, AC, 69
- Neisser, U, 98, 185
- NEOAC (Neuroticism, Extroversion, Openness to Experience, Agreeableness, and Conscientiousness), 17
- Nestin, 52
- Netherlands, 108, 110–111
- Neubauer, AC, 104
- Neural networks
- attention and, 123–137
 - neuroimaging and, 123–124
 - Stroop task and, 125

- Neural nicotinic cholinergic receptor (CHRNA4), 129
- Neuregulin 1 (NRG1), 13–14, 76–77, 195, 200, 206, 253
- Neurexophilin 3 (NXPH3), 135–136
- Neurofibrillary triangles (NFTs), 223–225, 227
- Neuroimaging
- anterior cingulate cortex (ACC) and, 125, 130–131, 134–137
 - attention networks and, 129–130
 - candidate gene approach and, 129–130
 - chromosomes and, 123
 - corticolimbic function and, 145
 - false positives/negatives and, 124
 - functional magnetic resonance imaging (fMRI) and, 23, 124–125, 129, 145, 150–152
 - magnetic resonance imaging (MRI) and, 23, 102–103, 123–124, 130
 - positron emission tomography (PET) and, 150, 153
 - schizophrenia and, 195
 - serotonin and, 145
 - statistical genetics and, 123–124
- Neuropsychiatric genetics
- Alzheimer's disease and, 221–235
 - animal models and, 51–81
 - brain-derived neurotrophic factor (BDNF) and, 75–76
 - calcium/calmodulin-dependent protein kinase II and, 52, 68–69
 - candidate gene association studies and, 37–39 (*see also* Candidate gene approach)
 - component determination and, 30–32
 - corticotropin-releasing factor (CRF) system and, 69–70
 - dopamine system and, 70–72
 - endocannabinoid system and, 72–73
 - environmental factors and, 43–46
 - epistasis and, 43–46
 - familial correlation and, 30–31
 - family-based association test (FBAT) and, 39 (*see also* Family studies)
 - fear conditioning and, 59, 69, 73–75, 78
 - Fisher's exact test and, 29, 33
 - galanin system and, 74–75
 - haplotype analysis and, 38
 - Hardy-Weinberg equilibrium (HWE) and, 32–33, 36–38
 - linkage analysis and, 34–37 (*see also* Linkage analysis)
 - LOD scores and, 34–36, 46, 183–184
 - McNemar test and, 29
 - marker statistics and, 27–29, 32–43
 - neuregulin 1 and, 76–77
 - nicotinic receptors and, 77–78, 129
 - NMDA and, 56, 76, 204, 249–250
 - opioid system and, 72
 - oxytocin and, 77
 - Pearson's test and, 29–30, 33, 37
 - pharmacogenetics and, 245–255
 - power calculation and, 46–47
 - proline dehydrogenase and, 76
 - regressive model and, 31–32
 - sample size and, 46–47
 - schizophrenia and, 76, 195–208, 245–255
 - statistical methods in, 27–47
 - vasopressin and, 77
- Neuropsychological genetics
- animal models and, 51–81
 - complex phenotypes and, 16–19
 - defined, 3
 - emotion and, 3
 - picking genes for study, 19–24
 - transgenic mice and, 51–54
- Newman, SK, 229
- Nicastrin, 110
- Nicodemus, Kristin K., 27–50
- Nicotinic receptors, 77–78, 129
- Niendam, TA, 196
- Nieuwenstein, MR, 196
- Nigeria, 21
- Niwa, H, 57
- N-methyl-D-aspartate (NMDA), 56, 76, 204, 249–250
- Noblett, KL, 147
- Nolan, KA, 71, 199

- Nonparametric linkage, 27
Norepinephrine system, 124
Norton, N, 250
Notch receptor, 199
Novel arm, 60
Nucleus accumbens, 68
Nucleus basalis magnocellularis lesions, 65
Nucleus basalis of Meynert, 224
- Obesity, 12
Object recognition, 63–64
O'Brien, C, 100
Occult functions, 23
Octo Twin project, 99
Odor span task, 63
Ogden, CA, 136
Olanzapine, 247, 250
Old Testament, 5
Olfactory discrimination, 63, 69
Olfactory memory, 74
Olson, RK, 179, 182
OMIM (Online Mendelian Inheritance in Man), 22
Onchocerciasis, 19
Operant conditioning chamber, 64
Opioid system, 72
Oppenheim, JS, 126
Oral comprehension, 178–181
Oral pontine nucleus, 130–131
Orienting, 125, 129
Origin of Species, The (Darwin), 5
Orthographic coding (OC), 179
Out-of-bag test, 46
Owen, MJ, 206–207
Oxytocin (OT), 77
- Pain
 avoidance and, 60
 shocks and, 60–61, 66, 68, 79
Paired helical filaments (PHFs), 223–224
Pair exchange, 7–8
Papaleo, Francesco, 51–94
Paracchini, S, 182
Paradee, W, 74
Parametric linkage, 27
Parasuraman, R, 168
Pardo, PJ, 126, 135
Parietal lobe, 125
Park, S, 198
Parkinson's disease, 70, 128, 224, 232
Parsey, RV, 150
Passingham, RE, 66
Passive avoidance, 60
Passive rGE, 106
Pastor, P, 232
Paterlini, M, 76
Paunio, T, 203
Pavlovian conditioning, 78
Payton, A, 169
PBAT software, 46
Pea hybrids, 5–7
Pearson, Karl, 5
Pearson test, 29–30, 33, 37
Pedersen, NL, 99, 167
Pedigree structure, 34–35
Pedunculopontine tegmental nucleus lesions, 65
Peier, AM, 74
Pennington, Bruce F., 101–102, 177–193
Perirhinal cortex, 59
Perphenazine, 247
Personality
 affective disorders and, 148
 broad bandwidth measures of, 148
 complex phenotypes and, 16–19
 corticolimbic function and, 147–148
 dopamine system and, 146–148
 emotional regulation and, 145–153
 environmental effects and, 3–4
 extraversion and, 146–147
 measures for, 17
 NEOAC measure and, 17
 serotonin and, 145–153
 threshold disorders and, 17, 19
 trait inheritance and, xi (*see also* Traits)
- Petersen, RC, 224
Petersen, SE, 124

- Petrill, SA, 99
- Pezawas, L, 134–135, 151–152
- Pharmacogenetics, 51
 advantages of, 245–246
 affective symptoms and, 245
 COMT and, 248–249
 confounds and, 253–255
 dopamine system and, 248–249
 ease of DNA sampling and, 245–246
 glutamate and, 249–253
 large-scale clinical trials and, 247, 254
 phenotypic candidates for, 246–248
 psychiatry and, 245–246
 second-generation antipsychotics (SGAs)
 and, 247, 250
 side effects and, 245–255
 technological advancements in, 245
 waiting game of, 245
- Pharoah, PD, 40
- Phase, 38
- Phenocopies, 206
- Phenotypes, xii
 Alzheimer's disease and, 221–235
 attentional deficits and, 200
 binary characteristics and, 27
 candidate gene association studies and, 37–39
 categorical analysis and, 27
 comorbidity and, 183–184
 complex, 16–19, 27
 component determination and, 30–32
 continuous characteristics and, 27
 dyslexia and, 177–181
 environmental factors and, 3–4, 43–46 (*see also* Environmental factors)
 epigenetic function control and, 12
 epistasis and, 43–46
 familial correlation and, 30–31
 family-based association test (FBAT) and, 39
 (*see also* Family studies)
 Fisher's exact test and, 29
 genome-wide association (GWA) and, 27,
 29, 39–43
 haplotype analysis and, 38
 Hardy-Weinberg equilibrium (HWE) and,
 32–33, 36–38
 heritability and, 3–4 (*see also* Heritability)
 high-throughput genotyping platforms and, 39
 intelligence and, 97–114
 interclass correlation coefficient (ICC) and,
 30–31
 intermediate, 195–197, 202–203
 linkage analysis and, 27–29, 34–37 (*see also*
 Linkage analysis)
 LOD scores and, 34–36, 46, 183–184
 McNemar test and, 29
 marker statistics and, 27–29, 32–43
 Pearson test and, 29–30, 33, 37
 pharmacogenetics and, 246–248
 regressive model and, 31–32
 schizophrenia and, 195–208, 245–255
 statistical genetics and, 27–47
 threshold disorders and, 17, 19
 transmission disequilibrium test (TDT) and,
 29, 38–39
 variance in, 3–4
- Phillips, AG, 62
- Philosophers, 3
- Phonological awareness (PA), 179
- Phonological coding (PC), 179
- Picciotto, MR, 55
- Placebos, 250
- Pleiotropy, 205
- PLINK, 39
- Plomin, R, 4, 98, 106–108, 112, 146, 208
- Plougham, LM, 46
- Pluripotent stage, 54
- Poets, 3
- Polderman, TJC, 98
- Pollard, KS, 109
- Polymerase chain reaction, 54
- Polymorphisms, 9–15, 19
 Alzheimer's disease and, 233
 animal models and, 71
 attention and, 128–133
 cognitive aging and, 159, 167–170
 dyslexia and, 182

- emotion and, 145–153
- intelligence and, 107–111
- schizophrenia and, 199–207, 249
- SNPs and, 11 (*see also* SNPs (single nucleotide polymorphisms))
- statistical genetics and, 22–24, 29
- Pontecorvo, MJ, 80
- Populations
 - candidate gene approaches and, 20
 - complex phenotypes and, 16–19
 - defined, 5
 - family studies and, 29–31 (*see also* Family studies; Twin studies)
 - International HAPMAP Project and, 21
 - linkage analysis and, 19–21 (*see also* Linkage analysis)
 - marker statistics and, 27–29, 32–43
 - quantitative traits and, 16–17
 - stratification and, 41, 43
 - subpopulation data and, 41–43
 - substructure and, 41
 - threshold disorders and, 17, 19
- Porteous, DJ, 205
- Positive FDR (pFDR), 40
- Positron emission tomography (PET), 150, 153
- Posner, Michael I., 123–144
- Posterior cortical atrophy, 223
- Posthuma, Danielle, 97–121
- Poulos, AM, 59
- Power calculation, 46–47
- Powers, WF, 100
- Prader-Willi syndrome, 12
- Prasher, VP, 227, 232
- Prefrontal cortex (PFC)
 - animal models and, 59, 61–62, 66
 - attention and, 128–129
 - decision making and, 68
 - dopamine system and, 71
 - schizophrenia and, 248–249, 254
 - shifting tasks and, 67
- Prelimbic cortex, 62
- Presenilins, 228–231
- Price, AL, 42
- Price, CJ, 181
- Pritchard, JK, 43
- Privacy issues, 125
- Proline dehydrogenase (PRODH), 76–78
- Promoter-inhibitor sites, 12–14
- Proteins. *See also* Specific protein
 - Alzheimer's disease and, 221–235
 - amyloid precursor, 52
 - corticotropin-releasing factor (CRF) system and, 69–70
 - DNA coding and, 8–10
 - endocannabinoid system and, 72–73
 - functional variations and, 12–16
 - gene coding and, 9
 - posttranslational modification and, 15
 - transgenic mice and, 51–54
- Psychosis susceptibility gene, 13
- Punnett square, 6
- Purcell, S, 39
- p values, 40

- Qin, W, 161
- Quantitative trait loci (QTLs), 107
- QUANTO software, 46
- Quetiapine, 247
- Quraishi, S, 195
- q values, 40

- Race, 20
 - Alzheimer's disease and, 230–231
 - intelligence and, 105, 109
 - migratory patterns and, 127
- Radial maze, 62–63, 71, 75–76, 79
- Ragozzino, ME, 67
- Raitano, NA, 183
- Ramakers, GJ, 109
- Rampon, C, 76
- Random-effect logistic models, 31
- Random foraging task, 62–63
- Random forest, 45
- Raphe nuclei, 130–131
- Rapid serial naming (RSN), 179, 184
- Rats, 51, 68, 160

- Raven's Matrices, 103–104
- Raz, N, 102, 160, 200
- Reaction time
 animal models and, 65–66, 68
 attention and, 128
 delayed response task and, 128
 inspection time and, 104
 intelligence and, 103–105
- Reading comprehension, 177–181
- Recessive traits, 6, 43
- Recognition memory,
 attention and, 65–66
 change in habits and, 66
 decision making and, 68
 delayed comparison procedures and, 65
 extinction and, 66
 flexibility and, 67
 instrumental learning and, 64–65
 object, 63–64
 reaction time and, 68
 reversal learning and, 66
 shifting tasks and, 67
 social, 64
- Recombination, 34
- Record, RG, 101
- Recursive partitioning, 46
- Redon, R, 107
- Reduced model, 43
- Regression analysis, 31–32, 38, 40, 170
- Reibaud, M, 72
- Reich, DE, 127
- Reif, A, 149
- Reiman, EM, 232
- Relative pair linkage method, 36
- Religion, 4, 20
- Renner, JA, 223
- Ren-Patterson, RF, 152
- Restifo, LL, 109
- Retinoblastoma, 19
- Rett syndrome (RS), 222–223
- Reuter, M, 111, 133
- Reversal learning, 66, 73
- Reverse tTA (rtTA), 54
- Reynolds, CA, 99
- rGE correlations, 105–107
- RGS4, 199
- Rijsdijk, FV, 99, 103
- Ringman, John M., 222–244
- Risch, N, 33
- Risk Evaluation and Education for
 Alzheimer's Disease study, 234
- Risperidone, 247, 250
- RNA (ribonucleic acid)
 attention and, 136
 corticotropin-releasing factor (CRF) system
 and, 69–70
 functional variation effects and, 12–16
 messenger, 9, 12–16, 22, 69–70, 136
 small interfering, 9
 splicing and, 10
- RNA interference technology, 182
- Robbins, TW, 65
- Robertson, IH, 196
- Rogaeva, E, 228, 234
- Romeo, RD, 134
- Ronalds, GA, 101
- Rondi-Reig, L, 76
- Rosa, A, 199, 248
- Rosen, C, 124
- Ross, MH, 227
- Ross, RS, 61
- Rosselli, MC, 229
- Rossor, MN, 226
- Rovelet-Lecrux, A, 225
- Rowe, DC, 105, 185
- Rowe, J, 228
- Rubenstein, M, 137
- Rueda, MR, 126, 133
- Russia, 231
- Rutter, M, 185
- Ryan, CN, 68
- Rybakowski, JK, 199
- Rypma, B, 160
- Sabeti, PC, 109
- Sabol, SZ, 128

- Sakai, N, 54
- Salthouse, TA, 159
- Sample size
- combination of samples and, 29
 - Fisher's exact test and, 29
 - importance of calculating, 46
 - LOD scores and, 46
 - statistical genetics and, 29, 46–47
- Sanders, MJ, 72
- Saoud, M, 201
- Sarcosine, 250
- Saura, CA, 229
- Savatti, C, 40
- Savitz, J, 111, 168
- Savolainen, P, 4
- Sawaguchi, T, 128
- Scarborough, HS, 179, 181
- Scerif, G, 133
- Scerri, TS, 182
- Schacter, DL, 171
- Schaid, DJ, 38
- Schaie, KW, 160
- Schellenberg, GD, 228
- Scheuner, D, 224, 226, 229
- Schinka, JA, 147, 149
- Schizoaffective disorder, 250–251
- Schizophrenia, xi, 9, 19
- age-dependent performance deterioration and, 78
 - attention and, 123, 127, 135, 195–196, 200–202
 - BDNF and, 203, 206
 - body mass index and, 207
 - California Verbal Learning Test and, 202
 - candidate gene approach and, 195–208
 - childhood-onset, 109
 - cognitive genes and, 200
 - COMT and, 199, 201, 203, 206–207, 248–249, 253–254
 - confounds and, 205–206
 - Continuous Performance Tasks (CPT) and, 200–205
 - CVLT and, 204
 - DAOA and, 195–196, 199, 201, 204–205, 207–208, 252
 - DARPP-32 and, 199–200
 - declarative memory and, 202–203
 - description of, 195
 - DISC1 and, 8, 76, 79, 169, 195–196, 199, 204–206, 208, 253
 - dopamine system and, 70, 199, 248–249, 254–255
 - dysbindin and, 195, 199, 201, 206, 208, 250–252
 - episodic memory and, 195, 202
 - false positives and, 205
 - family studies and, 192, 196, 198, 200–205, 246, 248–249
 - flexible switching and, 201–202
 - G72 and, 195
 - genetic heterogeneity and, 205
 - genome-wide association (GWA) and, 253–254
 - GRM3 and, 201, 204, 206
 - hallucinations and, 224
 - heritability and, 192, 198, 201–205
 - heterogeneous symptoms of, 195–196
 - independent living and, 246
 - information processing and, 196–197
 - intelligence and, 112, 196–197, 200, 251–252, 254
 - linkage analysis and, 198–200, 203
 - literature findings on, 197–205
 - Local Global Task and, 201–202
 - marker identification and, 245
 - memory and, 197–205, 248–249
 - molecular genetics and, 201–205
 - multiple testing and, 205
 - N-back task and, 201, 206, 248, 254
 - neuregulin 1 and, 76–77, 200, 253
 - neurofibrillary tangles (NFTs) and, 223–225
 - neuroimaging and, 195
 - nicotinic receptors and, 78
 - NMDA and, 195, 204, 249–250
 - Notch4 and, 199
 - NRG1 and, 195–196, 206
 - pharmacogenetics and, 245–255

- Schizophrenia (cont.)
 phenotype identification methods and, 196–197
 pleiotropy and, 205
 proline dehydrogenase and, 76
 putative susceptibility genes for, 233–235
 RGS4 and, 199, 206
 second-generation antipsychotics (SGAs) and, 247, 250
 senile plaques and, 223–224
 statistical issues and, 205–206
 study conclusions on, 206–208
 susceptibility genes and, 195–196, 206–208
 task diversity and, 205
 twin studies and, 198, 202–203, 205, 248–249
 Warrington facial recognition subtest and, 202
 Wechsler tests and, 198–204
 Wisconsin Card Sorting Task and, 199, 202, 205
- Schmidt, FL, 98
- Schneider, JS, 128
- Schoepp, DD, 253
- Schork, NJ, 34
- Schumacher, J, 182, 196
- Schupf, N, 228
- Schweimer, J, 68
- Scottish studies, 97–98, 110, 169, 170–171
- Scoville, WB, 202
- Screening methods, 23
- Seaman, SR, 40
- Seamans, JK, 62, 128
- Seattle Longitudinal Study, 160
- Sebat, J, 11
- Second-generation antipsychotics (SGAs). *See* Pharmacogenetics
- Secreted frizzled-related protein 2 (sFRP2), 135–136
- Seidenberg, MS, 179
- Seidman, LJ, 202
- Selective breeding, 4–5
- Sen, S, 149
- Senile plaques, 223–224, 227
- Sensorimotor gating, 126
- Sensory cortex, 59
- Serotonin, 129
 animal models and, 152–153
 anxiety and, 145–153
 attention and, 130, 133–134
 cognitive aging and, 169–170
 corticolimbic function and, 147–153
 emotional regulation and, 145–153
 extraversion and, 147–148
 individual differences and, 150
 neuroimaging and, 145
 personality and, 147–148
- Sesack, SR, 130
- Sex, 6–8
- Shamir, R, 40
- Sheep, 5
- Shenkin, SD, 100
- Sherrington, R, 228, 231
- Shields, J, 196
- Shimizu, E, 76
- Shioe, K, 150
- Shocks, 60–61, 66, 68, 79
- Sib pairs
 affected, 36, 46
 Hasemen-Elston regression and, 37
 linkage analysis and, 36–37
 transmission disequilibrium test (TDT) and, 38–39
- Sidekick (SDK1), 136
- Silberg, J, 185
- Silva, AJ, 69
- Sin3A-associated protein (SAP18), 136
- Singleton studies, 100–101
- SIR2 gene, 160
- siRNA (small interfering RNAs), 9
- Skin cancer, 5
- Skinner box, 64
- Skin pigmentation, 5, 43
- SLC64A gene, 169–170
- Slice variants, 10
- Small, B, 110
- Small, GW, 232
- Smith, DR, 70

- Smith, JD, 184
- Smith, Shelley D., 177–193
- SNAP-25 gene, 111–112
- Snijders, T, 31
- Snitz, BE, 200, 202
- Snowdon, DA, 225
- SNPs (single nucleotide polymorphisms), 11
- anxiety and, 151–152
 - association studies and, 29
 - attention and, 131
 - cognitive aging and, 169, 171
 - CpG islands and, 23
 - functional variations and, 12–16
 - gene picking methods and, 21–23
 - genome-wide association (GWA) and, 27, 29, 39–43
 - high-throughput genotyping platforms and, 39
 - International HAPMAP Project and, 21
 - likelihood ratio test (LRT) and, 43
 - linkage disequilibrium (LD) and, 33–34
 - marker statistics and, 27–29, 32–43
 - multiple testing and, 39–41
 - schizophrenia and, 204–205, 207
 - tag, 23
 - training set and, 45–46
 - trend tests and, 38
 - whole genome approach to intelligence and, 107–109
- Sobin, C, 132
- Social discrimination paradigm, 64
- Social recognition, 64, 77
- Social transmission of food preference (STFP) task, 60–61, 74
- Solar (sequential oligogenic linkage analysis routines) software, 37
- Soreq, H, 70
- Southern blotting, 54
- Span of Apprehension task, 126
- Span task, 126, 169
- Spearman, Charles, 5, 16, 97
- Specific Language Impairment (SLI)-Consortium, 183
- Speech sound disorder (SSD), 183–186
- Speed-of-processing theory of intelligence, 103–105
- Sperm, 6–8
- Spielman, RS, 29, 38
- Spinath, FM, 98, 103
- Spine density, 160
- Splicing, 10
- Spontaneous Selective Attention Task, 126
- Squire, LR, 59, 202
- Staal, WG, 202
- Standard deviation (SD), 17, 101, 110, 247, 251–252
- Standard error, 44
- Stanton, ME, 61
- Statistical genetics
- allele frequency and, 32
 - candidate gene association studies and, 37–39
 - chi-square test and, 33, 37–38
 - confidence interval (CI) and, 44–45
 - confounding and, 41
 - data mining algorithms and, 45
 - epistasis and, 43–46
 - familial correlation and, 27–31
 - family-based association test (FBAT) and, 39
 - fine mapping and, 27
 - Fisher's exact test and, 29, 33
 - gene-environment interaction and, 43–46
 - genetic component determination and, 8–10, 30–32
 - genome-wide association (GWA) and, 27, 29, 39–43
 - haplotype analysis and, 38
 - Hardy-Weinberg equilibrium (HWE) and, 32–33, 36–38
 - high-throughput genotyping platforms and, 39
 - interclass correlation coefficient (ICC) and, 30–31
 - likelihood ratio test (LRT) and, 43, 45
 - linkage analysis and, 27–29, 34–37
 - linkage disequilibrium (LD) and, 33–34
 - LOD score and, 34–36, 46
 - marker, 32–34 (*see also* Marker statistics)
 - migrant studies and, 27–28

- Statistical genetics (cont.)
 multiplex families and, 28
 neuroimaging and, 23, 102–103, 123–124
 nonparametric linkage and, 27
 parametric linkage and, 27
 Pearson test and, 29–30, 33, 37
 power calculations and, 46–47
 random forest and, 45
 recursive partitioning and, 46
 regressive model and, 31–32
 sample size and, 46–47
 schizophrenia and, 205–206
 standard deviation (SD) and, 17, 101, 110, 247, 251–252
 standard error and, 44
 training set and, 45–46
 transmission disequilibrium test (TDT) and, 29, 38–39
 twin studies and, 27–28
 variance component and, 27
 Staubli, U, 61
 Stefanis, NC, 200, 207
 Steiner, RA, 52, 74
 Stern, CE, 66, 227
 Sternberg, RJ, 97
 Stolnick, SD, 171
 Storey, JD, 40
 Storfer, M, 102
 Stough, C, 104
 Stranger, BE, 40
 Striatum, 70–71
 Strobel, A, 147
 Stroop task, 125
 Structural equation modeling, 102
 STRUCTURE, 42–43
 Stutzmann, GE, 131, 134
 Su, AI, 136
 Subiculum, 59
 Sugino, K, 135
 Sun, L, 40
 Superior temporal lobe, 125
 Supralemniscal group, 130–131
 Sur, M, 137
 Survival of the fittest, 5
 Swearer, JM, 226
 Swedish Adoption Twin Study of Aging, 99
 Swedish Twin Registry, 99
 Tachykinin precursor 1 (TAC1), 135–136
 Taghzouti, K, 66
 Tag markers, 21, 23
 Taipale, M, 182
 Takeda, A, 136
 Tan, HY, 206, 253
 Tan, W, 14
 Tan, YL, 203
 Tang, MX, 231
 Tanzi, RE, 233
 TaqIA polymorphism, 131–132
 Tatum, EL, 9
 Techykinin, 135
 Tesseur, I, 233
 Tetracycline transactivator (tTA), 53–54
Tgf-alpha, 134
 Thomas, DC, 40–41
 Thomas, KR, 54
 Thompson, PM, 101, 110, 126
 Thompson, R, 61
 Threshold disorders, 17, 19
 Tibshirani, R, 40
 Tillerson, JL, 71
 Tischfield, JA, 137
 Tissue-specific transgenic mouse technology, 52–53
 T-maze, 61–62, 67–68, 70–71, 76
 Tokuda, T, 227
 Tomie, JA, 78–79
 Touloupoulou, T, 202
 Tournoy, J, 229
 Tower test, 168
 Traditional knockout technology, 54–55
 Trails Making Test, 199, 230
 Training set, 45–46
 Traits
 Alzheimer's disease and, 221–235
 brain reaction diversity and, 10–11

- brain volume and, 101–103
brief history of genetics and, 4–24
chromosomes and, 6–8 (*see also*
Chromosomes)
complex phenotypes and, 16–19, 27
component determination and, 30–32
crossover events and, 8
cross-trait cross-twin correlation and, 102
dominant, 6, 43
environmental factors and, 11, 43–46
epistasis and, 43–46
familial correlation and, 27–31
family-based association test (FBAT) and, 39
(*see also* Family studies)
genetic component determination and, 30–32
genetic distance and, 7
intelligence and, 97–114
linkage analysis and, 34–37
Mendel and, 6, 19
NEOAC measure and, 17
Punnet square and, 6
quantitative, 16–17, 107
random distribution and, 7, 31
recessive, 6, 43
regressive model and, 31–32
schizophrenia and, 195–208, 245–255
selective breeding and, 4–5
statistical genetics and, 27–47
Tramo, MJ, 126
Trandafir, A, 246
Transcription phase, 13–14, 23
Transgenic mice, 51–54, 74, 80–81, 234–235
Translocations, 8
Transmission disequilibrium test (TDT), 29,
38–39
Trend test, 38
Trisomy 18, 8
Trisomy 21, 8
Trommer, BL, 232
Tryptophan hydroxylase (TPH), 133, 151–152
Tsai, G, 250
Tsai, SJ, 71, 111, 199, 248
Tsien, JZ, 76
Tubby homologue (TUB), 136
Tulving, E, 202
Tunick, RA, 183
Turkheimer, E, 105, 185
Tuulio-Henriksson, A, 198
Twin-singleton studies, 100–101
Twin studies, 4, 27
attention and, 126
cognitive aging and, 161, 167, 170
cross-trait cross-twin correlation and, 102
dizygotic (DZ) twins, 28, 30, 99, 102–106,
161, 167, 169, 198, 203
environmental factors and, 98–99
heterozygotic twins, 32, 38, 69, 71, 75, 77,
111
homozygotic twins, 32, 51, 75, 77, 79, 111,
136, 169–171, 204, 248–249
intelligence and, 98–106, 111
monozygotic (MZ) twins, 28, 30, 99,
102–106, 126, 161, 167, 198, 202–203
schizophrenia and, 198, 202–203, 205,
248–249
separate rearing and, 99
socioeconomic status and, 98
Tyrosine kinase receptor (TrkB), 75–77

Ubiquilin, 233
UCSC genome browser, 22–23
United Kingdom, 226
U.S. National Institute on Aging Late-Onset
Alzheimer
Disease study, 233
Utah, 131
Utermann, G, 231

Valine allele, 129
van Baal, GCM, 98
van Gaalen, MM, 68
Van Valen, L, 102
van Veen, V, 135
Variable number tandem repeats (VNTRs)
bioinformatics and, 11
marker statistics and, 27–29, 32–43

- Variance components
family studies and, 30–31
linkage analysis and, 34–37
marker statistics and, 27–29, 32–43
regressive model and, 31–32
- Variance-covariance matrix, 44–45
- Variance-variance matrix, 44–45
- Varvel, SA, 63, 73
- Vasopressin (AVP), 77
- Ventral striatum, 66
- Verbal learning task, 169
- Vernon, PA, 103
- Vision
Alzheimer's disease and, 223
attention and, 123–137
inspection time and, 104
macular degeneration and, 19
mazes and, 58–63, 67–79
memory and, 203
shifting tasks and, 67
smooth pursuit eye tracking and, 126
Span of Apprehension task and, 126
- Vitamin D, 5
- Vogt, BA, 135
- Voight, BF, 109
- von Melchner, H, 57
- Vyssotski, AL, 76
- Waggoner, SG, 225
- Wainwright, MA, 108
- Wakutani, Y, 226
- Walsh, B, 32
- Walton, ME, 68
- Wang, H, 69
- Warren, DM, 37
- Warrington facial recognition subtest, 202
- Wassink, TH, 199
- Watanabe, K, 128
- Watkins, LR, 151
- Webbink, D, 101
- Wechsler Adult Intelligence Scale (WAIS), 27, 102, 104, 199–200
- Wechsler Memory Scale (WMS), 198–199, 201, 203–204
- Wechsler Working Memory tasks, 198
- Weickert, CS, 251
- Weickert, TW, 248–249
- Weight, 16
- Weighted FDR, 40
- Weinberger, Daniel R.
animal models and, 51–94
attention and, 123, 133
emotion and, 150
molecular genetics and, 3–26
schizophrenia and, 196–197, 248
- Werner's syndrome, 161, 169
- Westminster Dog Show, 5
- Wetter, SR, 232
- Whishaw, IQ, 78–79
- White, NM, 63
- Whittemore, AS, 40
- Whyte, MC, 203
- Wickett, JC, 102
- Wiedenmayer, CP, 69
- Wijsman, EM, 232
- Willcutt, E, 183
- Willerman, L, 102
- Williams, GV, 249
- Williams, NM, 252
- Williams-Beuren syndrome, 11–12
- Williams syndrome, 109, 123, 133
- Win-shift radial maze, 71
- Winstanley, CA, 68
- Winterer, G, 70
- Wisconsin Card Sorting Test, 67, 128, 199, 202, 205, 230
- Wisniewski, K, 224
- Witte, EA, 124
- Woodward, 248–249
- Working memory (WM)
animal models and, 61–65
schizophrenia and, 195, 197–200, 205, 248–249
- Wrenn, CC, 74
- WRN gene, 161
- Wyatt, RJ, 245
- Xu, K, 123

Y-maze, 60
Young, JW, 63, 65, 78
Young, LJ, 77

Zaykin, DV, 40
Zhang, Fengyu, 27–50
Zhang, H, 112
Zhang, J, 109
Zhang, Y, 61
Zheng, G, 46
Zhivotovsky, LA, 40
Zimmer, A, 72
Zinc transporter (SLC39A5), 136
Ziprasidone, 247
Zola, SM, 59, 202
Zygotes, 8. *See also* Twin studies