Contents

The Input Component Produces Graded

Local Signals 28

Preface xxxv Acknowledgments xxxvii	The Trigger Component Makes the Decision to Generate an Action Potential 29
Contributors xxxix	The Conductile Component Propagates an All-or-None Action Potential 31
Part I	The Output Component Releases Neurotransmitter 31
The Neurobiology of Behavior 1 The Brain and Behavior	The Transformation of the Neural Signal From Sensory to Motor is Illustrated by the Stretch Reflex Pathway 32
Eric R. Kandel	Nerve Cells Differ Most at the Molecular Level 33
Two Opposing Views Have Been Advanced on the Relationship Between Brain and Behavior 6	Nerve Cells Are Able to Convey Unique Information Because They Form Specific Networks 33
The Brain Has Distinct Functional Regions 7	The Modifiability of Specific Connections Contributes to the Adaptability of Behavior 34
Cognitive Functions Are Localized Within the Cerebral Cortex 9	Selected Readings 34
Affective Traits and Aspects of Personality Are Also Anatomically Localized 14	References 35
Mental Processes Are Represented in the Brain by Their Elementary Processing Operations 15	3 Genes and Behavior
Selected Readings 17	T. Conrad Gilliam, Eric R. Kandel, Thomas M. Jessell
References 17	Genetic Information Is Stored in Chromosomes 37
2 Nerve Cells and Behavior19	Gregor Mendel's Work Led to the Delineation of the Relationship Between Genotype and Phenotype 38
Eric R. Kandel	The Genotype Is a Significant Determinant of Human Behavior 40
The Nervous System Has Two Classes of Cells 20	Single Genes Alleles Can Encode Normal Behavior
Glial Cells Are Support Cells 20	Variations in Worms and Flies 42
Nerve Cells Are the Main Signaling Units of the Nervous System 21	Mutations in Single Genes Can Affect Certain Behaviors in Flies 42
Nerve Cells Form Specific Signaling Networks That Mediate Specific Behaviors 25	Defects in Single Genes Can Have Profound Effects on Complex Behaviors in Mice 47
Signaling Is Organized in the Same Way in All Nerve Cells 27	Mutations in the Gene Encoding Leptin Affect Feeding Behavior 47

Mutations in the Gene Encoding a Serotonergic

Receptor Intensify Impulsive Behavior 50

References 86

Deletion of a Gene That Encodes an Enzyme Important for Dopamine Production Disrupts Locomotor Behavior and Motivation 50	5 Synthesis and Trafficking of Neuronal Protein
Single Genes Are Critical Factors in Certain Human	James H. Schwartz, Pietro De Camilli Most Pretains Are Synthesized in the Call Body. 88
Behavioral Traits 51	Most Proteins Are Synthesized in the Cell Body 88 Proteins May Be Modified During or After Synthesis 92
Mutations in a Dopamine Receptor May Influence Novelty-Seeking Behavior 51	Some Proteins Are Synthesized in the Cytosol
Mutations in Opsin Genes Influence Color Perception 51	and Actively Imported by the Nucleus, Mitochondria, and Peroxisomes 93
Mutations in the Huntingtin Gene Result in Huntington Disease 52	Secretory Proteins and Proteins of the Vacuolar Apparatus and Plasmalemma Are Synthesized and Modified in the Endoplasmic Reticulum 94
Most Complex Behavioral Traits in Humans Are Multigenic 55	Secretory Proteins Are Processed Further in the Golgi Complex and Then Exported 96
An Overall View 59	Surface Membrane and Extracellular Substances Are
Selected Readings 60	Taken Up Into the Cell by Endocytosis 97
References 61	Proteins and Organelles Are Transported Along the Axon 99
Part II Pransformation of the Neural Signal From III Part II	Fast Axonal Transport Carries Membranous Organelles 100
Cell and Molecular Biology of the Neuron	Slow Axonal Transport Carries Cytosolic Proteins and Cytoskeletal Elements 103
of the realist	An Overall View 103
4 The Cytology of Neurons67	Selected Readings 103
James H. Schwartz, Gary L. Westbrook	References 104
The Structural and Functional Blueprint of Neurons Is Similar to Epithelial Cells 69	
Membranous Organelles Are Selectively Distributed Throughout the Neuron 69	6 Ion Channels
The Cytoskeleton Determines the Shape of the Neuron 72	Ion Channels Are Important for Signaling in the Nervous System 105
The Neurons That Mediate the Stretch Reflex Differ in Morphology and Transmitter Substance 76	Ion Channels Are Proteins That Span the Cell Membrane 107
The Sensory Neuron Conducts Information From the Periphery to the Central Nervous System 76	Ion Channels Can Be Investigated Using Functional Methods 109
The Motor Neuron Conveys Central Motor Commands to the Muscle Fiber 77	Ion Channels in All Cells Share Several Characteristics 110
A Single Motor Neuron Forms Synapses With Several	The Flux of Ions Through the Ion Channel is Passive 110
Muscle Cells 78 Pyramidal Neurons in the Cerebral Cortex Have	The Opening and Closing of a Channel Involve Conformational Changes 112
More Extensive Dendritic Trees Than Spinal Motor Neurons 85	The Structure of Ion Channels Is Inferred From Biophysical, Biochemical, and Molecular Biological
Glial Cells Produce the Insulating Myelin Sheath Around	Studies 116
Signal-Conducting Axons 85	Ion Channels Can be Grouped Into Gene Families 118
An Overall View 86 Selected Readings 86	The Structure of a Potassium-Selective Ion Channel Has Been Solved by X-ray Crystallography 120

An Overall View 123

Selected Readings 123	An Overall View 148
References 123	Selected Readings 149
An Overall Vigger 2025 or one	References 149
7 Membrane Potential	9 Propagated Signaling: The Action Potential
Separation of Charges Across the Cell Membrane 126 The Resting Membrane Potential Is Determined by	The Action Potential Is Generated by the Flow of Ions
Resting Ion Channels 126	Through Voltage-Gated Channels 150
Resting Channels in Glial Cells Are Selective for Potassium Only 128	Sodium and Potassium Currents Through Voltage-Gated Channels Are Recorded With the Voltage Clamp 151
Resting Channels in Nerve Cells Are Selective for Several Ion Species 129	Voltage-Gated Sodium and Potassium Conductances Are Calculated From Their Currents 154
Passive Flux of Sodium and Potassium Is Balanced by Active Pumping of the Ions 131	The Action Potential Can Be Reconstructed From the Properties of Sodium and Potassium Channels 155
Chloride Ions May Be Passively Distributed 131	Variations in the Properties of Voltage-Gated Ion
The Balance of Ion Fluxes That Gives Rise to the Resting Membrane Potential Is Abolished During the Action Potential 132	Channels Increase the Signaling Capabilities of Neurons 158
The Contributions of Different Ions to the	The Nervous System Expresses a Rich Variety of Voltage-Gated Ion Channels 158
Resting Membrane Potential Can Be Quantified by the Goldman Equation 132	Gating of Voltage-Sensitive Ion Channels Can Be Influenced by Various Cytoplasmic Factors 159
The Functional Properties of the Neuron Can Be Represented in an Electrical Equivalent Circuit 134	Excitability Properties Vary Between Regions of the Neuron 159
Each Ion Channel Acts as a Conductor and Battery in Parallel 134	Excitability Properties Vary Among Neurons 160
An Equivalent Circuit Model of the Membrane Includes Batteries, Conductors, a Capacitor, and a Current	The Signaling Functions of Voltage-Gated Channels Can Be Related to Their Molecular Structures 160
Generator 138	Opening of Voltage-Gated Channels is All-or-None 161
An Overall View 138	Redistribution of Charges Within Voltage-Gated Sodium
Selected Readings 139 Market Super Market Su	Channels Controls Channel Gating 162
References 139	The Voltage-Gated Sodium Channel Selects for Sodium on the Basis of Size, Charge, and Energy of Hydration of the Ion 163
8 Local Signaling: Passive Electrical Properties of the Neuron140	Genes Encoding the Potassium, Sodium, and Calcium Channels Stem From a Common Ancestor 164
John Koester, Steven A. Siegelbaum	Various Smaller Subunits Contribute to the Functional
Input Resistance Determines the Magnitude of Passive Changes in Membrane Potential 140	Properties of Voltage-Gated Sodium, Calcium, and Potassium Channels 166
Membrane Capacitance Prolongs the Time Course of Electrical Signals 142	The Diversity of Voltage-Gated Channel Types Is Due to Several Genetic Mechanisms 167
Membrane and Axoplasmic Resistance Affect the Efficiency of Signal Conduction 143	Mutations in Voltage-Gated Channels Cause Specific Neurological Diseases 167
Large Axons Are More Easily Excited Than Small Axons by Extracellular Current Stimuli 146	An Overall View 169
Passive Membrane Properties and Axon Diameter Affect	Selected Readings 169
the Velocity of Action Potential Propagation 147	References 170

Part III	A Single Macromolecule Forms the Nicotinic
Elementary Interactions Between Neurons: Synaptic Transmission	Acetylcholine Receptor and Channel 197 An Overall View 201
9 Propagated Signaling: The Action	Postscript: The End-Plate Current Can Be Calculated From an Equivalent Circuit 202
10 Overview of Synaptic	Selected Readings 205
Transmission	References 205
Synapses Are Either Electrical or Chemical 175	
Electrical Synapses Provide Instantaneous	Secretory Proteins and Proteinsanthelbannas of games a
Signal Transmission 177	12 Synaptic Integration207 Eric R. Kandel, Steven A. Siegelbaum
Gap-Junction Channels Connect Communicating Cells at an Electrical Synapse 178	A Central Neuron Receives Both Excitatory and
Electrical Transmission Allows the Rapid and Synchronous Firing of Interconnected Cells 180	Inhibitory Signals 209 Excitatory and Inhibitory Synapses Have
Gap Junctions Have a Role in Glial Function and Disease 180	Distinctive Ultrastructures 209 Excitatory Synaptic Action Is Mediated
Chemical Synapses Can Amplify Signals 182	by Glutamate-Gated Channels That Conduct Sodium and Potassium 212
Chemical Transmitters Bind to Postsynaptic Receptors 183	Inhibitory Synaptic Action Is Usually Mediated by GABA- and Glycine-Gated Channels That
Postsynaptic Receptors Gate Ion Channels Either	Conduct Chloride 214
Directly or Indirectly 185 Selected Readings 185	Currents Through Single GABA- and Glycine-Gated Channels Can Be Recorded 217
References 185	How Does the Opening of Chloride Channels Inhibit the Postsynaptic Cell? 217
11 Signaling at the Nerve-Muscle Synapse:	Synaptic Receptors for Glutamate, GABA, and Glycine Are Transmembrane Proteins 219
Directly Gated Transmission187	GABA and Glycine Receptors 219
Eric R. Kandel, Steven A. Siegelbaum	Glutamate Receptors 219
The Neuromuscular Junction Is a Well-Studied Example of Directly Gated Synaptic Transmission 187	Other Receptor-Channels in the Central Nervous System 221
The Motor Neuron Excites the Muscle by Opening Ion Channels at the End-Plate 190	Excitatory and Inhibitory Signals Are Integrated Into a Single Response by the Cell 222
The Synaptic Potential at the End-Plate Is Produced by Ionic Current Flowing Through Acetylcholine-Gated Channels 190	Synapses On a Single Central Neuron Are Grouped According to Function 223
The Ion Channel at the End-Plate Is Permeable to Both	Synapses on Cell Bodies Are Often Inhibitory 224
Sodium and Potassium 191	Synapses on Dendritic Spines Are Often
The Current Flow Through Single Ion Channels Can Be Measured by the Patch Clamp 192	Excitatory 224 Synapses on Axon Terminals Are Often
Individual Acetylcholine-Gated Channels Conduct a Unitary Current 193	Modulatory 226 An Overall View 226
Four Factors Determine the End-Plate Current 194	Selected Readings 227

References 228

The Molecular Properties of the Acetylcholine-Gated Channel at the Nerve-Muscle Synapse Are Known 196

Voltage-Gated Channels 196

Ligand-Gated Channels for Acetylcholine Differ From

Modulation of Synaptic Transmission: Second Messengers	Exocytosis Involves the Formation of a Fusion Pore 264
Steven A. Siegelbaum, James H. Schwartz,	Synaptic Vesicles Are Recycled 267
Eric R. Kandel	A Variety of Proteins Are Involved in the Vesicular Release of Transmitter 270
Second-Messenger Pathways Activated by Metabotropic Receptors Share a Common Molecular Logic 230	The Amount of Transmitter Released Can Be Modulated
The Cyclic AMP Pathway Involves a Polar and Diffusible Cytoplasmic Messenger 231	by Regulating the Amount of Calcium Influx During the Action Potential 274
IP ₃ , Diacylglycerol, and Arachidonic Acid Are Generated Through Hydrolysis of Phospholipids 236	Intrinsic Cellular Mechanisms Regulate the Concentration of Free Calcium 274
Arachidonic Acid Is Metabolized to Produce Other Second Messengers 236	Axo-axonic Synapses on Presynaptic Terminals Regulate Intracelluar Free Calcium 275
The Tyrosine Kinase Pathway Utilizes Both Receptor	An Overall View 276
and Cytoplasmic Kinases 238	Selected Readings 277
The Gaseous Second Messengers, Nitric Oxide and Carbon Monoxide, Stimulate cGMP Synthesis 239	References 278
The Physiological Actions of Ionotropic and Metabotropic Receptors Differ: Second Messengers Can Close As Well As Open Ion Channels 240	15 Neurotransmitters
Cyclic AMP-Dependent Protein Kinase Can Close Potassium Channels 243	Chemical Messengers Must Fulfill Four Criteria To Be Considered Transmitters 280
Arachidonic Acid Metabolites Open the Same Channels Closed by cAMP 243	Only a Few Small-Molecule Substances Act as Transmitters 282
G Proteins Can Modulate Ion Channels	Acetylcholine 282
Directly 244	Biogenic Amine Transmitters 282
Second-Messenger Pathways Interact With One Another 248	Amino Acid Transmitters 284
Phosphoprotein Phosphatases Regulate the Levels of Phosphorylation 249	ATP and Adenosine 285 Small-Molecule Transmitters Are Actively Taken Up
Second Messengers Can Endow Synaptic Transmission	Into Vesicles 285
With Long-Lasting Consequences 249	Many Neuroactive Peptides Serve as Transmitters 286
An Overall View 250	Peptides and Small-Molecule Transmitters Differ in Several Ways 290
Selected Readings 251	Peptides and Small-Molecule Transmitters Can Coexist
References 251	and Be Coreleased 290
14 Transmitter Release253	Removal of Transmitter From the Synaptic Cleft Terminates Synaptic Transmission 294
Eric R. Kandel, Steven A. Siegelbaum	An Overall View 295
Transmitter Release is Regulated by Depolarization	Selected Readings 296
of the Presynaptic Terminal 253	References 296
Transmitter Release is Triggered by Calcium Influx 255	16 Diseases of Chemical Transmission
Transmitter Is Released in Quantal Units 258	at the Nerve-Muscle Synapse:
Transmitter Is Stored and Released by Synaptic Vesicles 262	Myasthenia Gravis298 Lewis P. Rowland
Synaptic Vesicles Discharge Transmitter	Myasthenia Gravis Affects Transmission at the
by Exocytosis 262	Nerve-Muscle Synapse 299

Physiological Studies Showed a Disorder of Neuromuscular Transmission 299

Immunological Studies Indicated That Myasthenia Is an Autoimmune Disease 300

Identification of Antibodies to the Acetylcholine Receptor Initiated the Modern Period of Research 300

Immunological Changes Cause the Physiological Abnormality 302

Antibody Binds to the α -Subunit of the Acetylcholine Receptor in Myasthenia Gravis 303

The Molecular Basis of the Autoimmune Reaction Has Been Defined 304

Current Therapy for Autoimmune Myasthenia Gravis Is Effective but Not Ideal 306

Congenital Forms of Myasthenia Gravis 306

Other Disorders of Neuromuscular Transmission: Lambert-Eaton Syndrome and Botulism 307

An Overall View 308

Selected Readings 308

References 308

Part IV

The Neural Basis of Cognition

David G. Amaral

The Central Nervous System Has Seven Major Divisions 319

Spinal Cord 319

Medulla 320

Pons 322

Midbrain 322

Cerebellum 322

Diencephalon 322

Cerebral Hemispheres 322

Five Principles Govern the Organization of the Major Functional Systems 323

Each Functional System Involves Several Brain Regions That Carry Out Different Types of Information Processing 323

Identifiable Pathways Link the Components of a Functional System 323

Each Part of the Brain Projects in an Orderly Fashion Onto the Next, Thereby Creating Topographical Maps 323

Functional Systems Are Hierarchically Organized 324

Functional Systems on One Side of the Brain Control the Other Side of the Body 324

The Cerebral Cortex Is Concerned With Cognitive Functioning 324

The Cerebral Cortex Is Anatomically Divided Into Four Lobes 325

The Cerebral Cortex Has Functionally Distinct Regions 325

The Cerebral Cortex Is Organized in Layers 327

The Layers Organize Inputs and Outputs 327

The Cerebral Cortex Has Two Major Neuronal Cell Types: Projection Neurons and Interneurons 329

Subcortical Regions of the Brain Contain Functional Groups of Neurons Called Nuclei 331

Modulatory Systems in the Brain Influence Motivation, Emotion, and Memory 333

The Peripheral Nervous System Is Anatomically But Not Functionally Distinct From the Central Nervous System 334

An Overall View 335

Selected Readings 336

References 336

18 The Functional Organization of Perception and Movement337

David G. Amaral

Sensory Information Processing Is Illustrated in the Somatosensory System 338

Somatosensory Information From the Trunk and Limbs Is Conveyed to the Spinal Cord 338

The Primary Sensory Neurons of the Trunk and Limbs Are Clustered in the Dorsal Root Ganglia 340

The Central Axons of Dorsal Root Ganglion Neurons Are Arranged to Produce a Map of the Body Surface 340

Each Somatic Submodality is Processed in a Distinct Subsystem From the Periphery to the Brain 341

The Thalamus Is an Essential Link Between Sensory Receptors and the Cerebral Cortex for All Modalities Except Olfaction 341

Sensory Information Processing Culminates in the Cerebral Cortex 344

Voluntary Movement Is Mediated by Direct Connections Between the Cortex and Spinal Cord 347

An Overall View 348

Selected Readings 348

References 348

19 Integration of Sensory and Motor Function: The Association Areas of the Cerebral Cortex and the Cognitive Capabilities of the Brain349

Clifford B. Saper, Susan Iversen, Richard Frackowiak

Three Multimodal Association Areas Are Concerned With Integrating Different Sensory Modalities and Linking Them to Action 350

Three Principles Govern the Function of the Association Areas 353

Sensory Information is Processed Both Sequentially and in Parallel 353

Sensory Information From Unimodal Areas of Cortex Converges in Multimodal Areas 354

The Sequence of Information Processing Is Reversed in the Motor System 355

The Prefrontal Association Areas Illustrate the Function of Association Cortex 356

Lesions of the Prefrontal Association Area in Monkeys Interfere With Motor Planning 356

The Cortex Surrounding the Principal Sulcus Is Concerned With Tasks That Require Working Memory 357

Lesions of the Prefrontal Association Area Disturb Behavioral Planning in Humans 361

Interaction Among Association Areas Leads to Comprehension, Cognition, and Consciousness 362

Consciousness and the Sensory Processing Streams Are Not Distributed Symmetrically in the Two Cerebral Hemispheres 363

An Overall View 365

Postscript: Functional Imaging Offers a Unique Window on Cognitive Function 366

Functional MRI Is an Adaptation of MRI That Records Changes Related to Tissue Function in Successive Images 374

Use of Radioactive Tracers Yields Images of Biochemical Processes in the Living Brain 375

Selected Readings 379

References 380

Eric R. Kandel

The Major Goal of Cognitive Neural Science Is to Study the Neural Representations of Mental Acts 382

Cognitive Neural Science Integrates Five Major Approaches to the Study of Cognitive Function 383

The Brain Has an Orderly Representation of Personal Space That Can Be Studied on the Cellular Level 384

The Cortex Has a Map of the Body for Each Submodality of Sensation 387

The Orderliness of the Cortical Maps of the Body Is the Basis of the Accuracy of Clinical Neurological Examinations 388

The Internal Representation of Personal Space Is Modifiable by Experience 388

The Cortical Representation of the Human Hand Area Can Be Modified 389

The Phantom Limb Syndrome May Result From Rearrangements of Cortical Inputs 390

Real as Well as Imagined and Remembered Extrapersonal Space Is Represented in the Posterior Parietal Association Cortex 392

Is Consciousness Accessible to Neurobiological Analysis? 396

Consciousness Poses Fundamental Problems for a Biological Theory of the Mind 396

Despite Philosophical Cautions, Neurobiologists Have Adopted a Reductionist Approach to Consciousness 398

Selective Attention Is a Testable Component of Consciousness 400

An Overall View 402

Selected Readings 402

References 402

Part V

Perception

21 Coding of Sensory Information 411

Esther P. Gardner, John H. Martin

Sensory Systems Mediate Four Attributes of a Stimulus That Can Be Correlated Quantitatively With a Sensation 412

Sensory Modality Is Determined by the
Stimulus Energy 414
Modality is Encoded by a Labeled Line Code 414
Receptors Transduce Specific Types of Energy Into an Electrical Signal 416
Each Receptor Responds to a Narrow Range of Stimulus Energy 416
The Spatial Distribution of Sensory Neurons Activated by a Stimulus Conveys Information About the Stimulus Location 418
The Receptive Fields of Sensory Neurons in the Somatosensory and Visual Systems Define the Spatial Resolution of a Stimulus 418
The Sensory Neurons for Hearing, Taste, and Smell Are Spatially Organized According to Sensitivity 419
Intensity of Sensation Is Determined by the Stimulus Amplitude 419
Psychophysical Laws Govern the Perception of Stimulus Intensity 421
Stimulus Intensity Is Encoded by the Frequency of Action Potentials in Sensory Nerves 421
The Duration of a Sensation is Determined in Part by the Adaptation Rates of Receptors 423
Sensory Systems Have a Common Plan 425
Sensory Information Is Conveyed by Populations of Sensory Neurons Acting Together 426
Sensory Systems Process Information in a Series of Relay Nuclei 426
Inhibitory Interneurons Within Each Relay Nucleus Help Sharpen Contrast Between Stimuli 427
An Overall View 428
Selected Readings 428
References 428
22 The Bodily Senses

Esther P. Gardner, John H. Martin, Thomas M. Jessell The Dorsal Root Ganglion Neuron Is the Sensory Receptor in the Somatic Sensory System 431 Touch Is Mediated by Mechanoreceptors in the Skin 432 Mechanoreceptors Differ in Morphology and Skin Location 432 Mechanoreceptors in the Superfield and Deep Layers of

Skin Have Different Receptive Fields 435

Mechanoreceptors Varies 436

The Spatial Resolution of Stimuli on the Skin Varies Throughout the Body Because the Density of

Mechanoreceptors Differ in Adaptation Properties and Sensory Thresholds 438 The Spatial Characteristics of Objects Are Signaled by Populations of Mechanoreceptors 438 Other Somatic Sensations Are Mediated by a Variety of Specialized Receptors 441 Warmth and Cold Are Mediated by Thermal Receptors 441 Pain Is Mediated by Nociceptors 442 Proprioception Is Mediated by Mechanoreceptors in Skeletal Muscle and Joint Capsules 443 The Viscera Have Mechanosensory and Chemosensory Receptors 443 The Afferent Fibers of Different Receptors Conduct Action Potentials at Different Rates 444 Afferent Fibers Conveying Different Somatic Sensory Modalities Have Distinct Terminal Patterns in the Spinal Cord and Medulla 446 The Dorsal Column-Medial Lemniscal System Is the Principal Pathway for Perception of Touch and Proprioception 446 The Anterolateral System Mediates Sensations of Pain and Temperature 448

An Overall View 449 Selected Readings 449

References 450

23 Touch

Esther P. Gardner, Eric R. Kandel

Tactile Information About an Object Is Fragmented by Peripheral Sensors and Must Be Integrated by the Brain 452

The Primary Somatic Sensory Cortex Integrates Information About Touch 452

Cortical Neurons Are Defined by Their Receptive Fields as Well as by Modality 454

The Properties of Cortical Receptive Fields Are Due to Convergent and Divergent Connections in the Relay Nuclei 456

Inputs to the Somatic Sensory Cortex Are Organized in Columns by Receptive Field and Modality 456

The Body Surface Is Represented in the Brain by the Somatotopic Arrangement of Sensory Inputs 458

Spatial Resolution in the Cortex Is Correlated With the Innervation Density of the Skin 459

Cortical Receptive Fields Are Altered by Use of the Hand 462

Inhibitory Networks Sharpen Spatial Resolution by Restricting the Spread of Excitation 462

Lateral Inhibition Can Aid in Two-Point Discrimination 462

Spatial Detail Is Accurately Represented in the Cortex 462

Neurons in Higher Cortical Areas Have Complex Feature-Detecting Properties 463

Stimulus Features Are Processed in Parallel by Distinct Areas of Cortex 465

The Behavioral Relevance of a Tactile Stimulus Modifies Cortical Responses 468

Lesions in Somatosensory Areas of the Brain Produce Specific Sensory Deficits 468

An Overall View 469

Selected Readings 470

References 470

Allan I. Basbaum, Thomas M. Jessell

Noxious Insults Activate Nociceptors 473

Nociceptive Afferent Fibers Terminate on Neurons in the Dorsal Horn of the Spinal Cord 475

Nociceptive Afferent Fibers Use Glutamate and Neuropeptides as Neurotransmitters 477

Hyperalgesia Has Both Peripheral and Central Origins 477

Changes in Nociceptor Sensitivity Underlie Primary Hyperalgesia 477

The Hyperexcitability of Dorsal Horn Neurons Underlies Centrally Mediated Hyperalgesia 479

Nociceptive Information Is Transmitted From the Spinal Cord to the Thalamus and Cerebral Cortex Along Five Ascending Pathways 480

Thalamic Nuclei Relay Afferent Information to the Cerebral Cortex 480

The Cerebral Cortex Contributes to the Processing of Pain 481

Pain Can Be Controlled by Central Mechanisms 482

The Balance of Activity in Nociceptive and Nonnociceptive Primary Afferent Fibers Can Modulate Pain: The Gate Control Theory 482

Direct Electrical Stimulation of the Brain Produces Analgesia 483

Opiated-Induced Analgesia Involves the Same Pathways as Stimulation-Produced Analgesia 483

Opioid Peptides Contribute to the Endogenous Pain Control System 483

Endogenous Opioid Peptides and Their Receptors Are Located at Key Points in the Pain Modularity System 483

Activation of Opioid Receptors by Morphine Controls Pain 486

Tolerance and Addiction to Opioids Are Distinct Phenomena 489

Stress Induces Analgesia Through Both Opioid and Nonopioid Mechanisms 489

An Overall View 489

Selected Readings 490

References 490

25 Constructing the Visual Image 492

Eric R. Kandel, Robert H. Wurtz

Visual Perception Is a Creative Process 492

Visual Information is Processed in Multiple Cortical Areas 496

Different Cortical Areas Make Different Contributions to the Processing of Motion, Depth, Form, and Color 497

Parallel Pathways Convey Information From the Retina to Parietal and Temporal Cortical Areas 500

Visual Attention May Facilitate Coordination Between Separate Visual Pathways 501

The Analysis of Visual Attention May Provide Important Clues About Conscious Awareness 504

An Overall View 505

Selected Readings 505

References 506

26 Visual Processing by the Retina507

Marc Tessier-Lavigne

The Retina Contains the Eye's Receptor Sheet 508

There Are Two Types of Photoreceptors:Rods and Cones 508

Rods Detect Dim Lights 509

Cones Mediate Color Vision 509

Light Is Absorbed by Visual Pigments in the Photoreceptors 510

Phototransduction Results From a Three-Stage Cascade of Biochemical Events in the Photoreceptors 510

Stage 1: Light Activates Pigment Molecules in the Photoreceptors 511

W Cerlifeh Bullijovicish

Stage 2: Activation of Pigment Molecules Reduces the Cytoplasmic Concentration of Cyclic GMP 512
Stage 3: The Reduction in Cyclic GMP Concentration Closes cGMP-Gated Ion Channels, Thus Hyperpolarizing the Photoreceptor 514
Photoreceptors Slowly Adapt to Changes in Light Intensity 515
The Output of the Retina is Conveyed by the Ganglion Cells 517
The Receptive Field of the Ganglion Cell Has a Center and an Antagonistic Surround 517
Ganglion Cells Are Specialized for the Detection of Contrasts and Rapid Changes in the Visual Image 519
Specialized Ganglion Cells Process Different Aspects of the Visual Image 520
Signals From Photoreceptors Are Relayed to Ganglion Cells Through a Network of Interneurons 520
Bipolar Cells Convey Cone Signals to Ganglion Cells Through Direct or Indirect Pathways 520
The Receptive Fields of Bipolar Cells Have a Center-Surround Organization 521
Different Classes of Bipolar Cells Have Excitatory Connections With Corresponding Classes of Ganglion Cells 521
An Overall View 521
Selected Readings 522
References 522
27 Central Visual Pathways523
Robert H. Wurtz, Eric R. Kandel
The Retinal Image Is an Inversion of the Visual Field 524
The Retina Projects to Subcortical Regions in the Brain 526
The Superior Colliculus Controls Saccadic Eye Movements 526
The Pretectum of the Midbrain Controls Pupillary Reflexes 527
The Lateral Geniculate Nucleus is the Main Terminus for Input to the Visual Cortex 528
Magnocellular and Parvocellular Pathways Convey

Different Information to the Visual Cortex 529

of a Visual Image Into Short Line Segments

of Various Orientations 533

The Primary Visual Cortex Organizes Simple Retinal

Inputs Into the Building Blocks of Visual Images 532

Simple and Complex Cells Decompose the Outlines

Some Feature Abstraction Is Accomplished by Progressive Convergence 535 The Primary Visual Cortex Is Organized Into Functional Modules 537 Neurons With Similar Receptive Fields Are Organized in Columns 537 A Hypercolumn Represents the Visual Properties of One Region of the Visual Field 539 Columnar Units Are Linked by Horizontal Connections 540 Lesions in the Retino-Geniculate-Cortical Pathway Are Associated With Specific Gaps in the Visual Field 543 An Overall View 545 Selected Readings 545 References 546 28 Perception of Motion, Depth, and Form Robert H. Wurtz, Eric. R. Kandel The Parvocellular and Magnocellular Pathways Feed Into Two Processing Pathways in Extrastriate Cortex 549 Motion Is Analyzed Primarily in the Dorsal Pathway to the Parietal Cortex 552 Motion Is Represented in the Middle Temporal Area 553 Cells in MT Solve the Aperture Problem 553 Control of Movement Is Selectively Impaired by Lesions of MT 556 Perception of Motion Is Altered by Lesions and Microstimulation of MT 556 Depth Vision Depends on Monocular Cues and Binocular Disparity 558 Monocular Cues Create Far-Field Depth Perception 558 Stereoscopic Cues Create Near-Field Depth Perception 560

Information From the Two Eyes Is First Combined in the

Random Dot Stereograms Separate Stereopsis From

Object Vision Depends on the Ventral Pathway to the

Recognition of Faces and Other Complex Forms Depends Upon the Inferior Temporal Cortex 564

Cells in V2 Respond to Both Illusory and

Cells in V4 Respond to Form 563

Primary Visual Cortex 560

Object Vision 561

Inferior Temporal Lobe 562

Actual Contours 562

xix

in the Cochlea 599
Neural Processing of Auditory Information 601
Ganglion Cells Innervate Cochlear Hair Cells 601
Cochlear Nerve Fibers Encode Stimulus Frequency and Intensity 601
Sound Processing Begins in the Cochlear Nuclei 603
Relay Nuclei in the Brain Stem Mediate Localization
of Sound Sources 606
Auditory Information Is Processed in Multiple Areas of
the Cerebral Cortex 608
Sensorineural Hearing Loss Is Common But Can Often Be Overcome 610
An Overall View 612
Selected Readings 613
References 613
Hactory Aculty Varies in Humans of the weit lisrayo and
31 Sensory Transduction in the Ear61
A. J. Hudspeth
Hair Cells Transform Mechanical Energy Into Neural Signals 616
Deflection of the Hair Bundle Initiates Mechanoelectrical Transduction 616
Mechanical Force Directly Opens and Closes
Transduction Channels 617
Direct Mechanoelectrical Transduction Is Rapid 619
The Temporal Responsiveness of Hair Cells Determines
Their Sensitivity to Stimuli 619
Hair Cells Adapt to Sustained Stimuli 619
Hair Cells Are Tuned to Specific Stimulus Frequencies 620
Synatptic Transmission From Hair Cells is Triggered at
Low-Amplitude Receptor Potentials 622
An Overall View 623
Selected Readings 624
References 624
32 Smell and Taste: The Chemical Senses
Linda B. Buck
Odors Are Detected by Nasal Olfactory Sensory Neurons 626
Different Odorants Stimulate Different Olfactory Sensory Neurons 627

A Large Family of Odorant Receptors Permits
Discrimination of a Wide Variety of Odorants 627
The Interaction Between Odorant and Receptor
Activates a Second-Messenger System That Leads to
Depolarization of the Sensory Neuron 629
Different Olfactory Neurons Express Different
Odorant Receptors 630

Odorant Information Is Encoded Spatially in the Olfactory Bulb 630

Odorant Information Is Transmitted From the Olfactory Bulb to the Neocortex Directly and via the Thalamus 633

Pheromones Are Species-Specific Chemical Messengers 633

The Vomeronasal Organ Transmits Information About Pheromones 634

Sensory Transduction in the Vomeronasal Organ Differs From That in the Nose 634

Olfactory Acuity Varies in Humans 634

Invertebrates and Vertebrates Use Different Strategies to Process Chemosensory Information 635

Taste Stimuli Are Detected by Taste Cells in the Mouth 636

Taste Cells Are Clustered in Taste Buds 636

The Four Different Taste Qualities Are Mediated by a Variety of Mechanisms 637

Information About Taste Is Relayed to the Cortex via the Thalamus 642

Different Taste Sensations Derive From Variations in Patterns of Activity in the Afferent Fiber Population 644

The Sensation of Flavors Results From a Combination of Gustatory, Olfactory, and Somatosensory Inputs 644

An Overall View 644 Selected Readings 645

References 645

Part VI

Movement

33 The Organization of Movement 653

Claude Ghez, John Krakauer

The Motor Systems Generate Reflexive, Rhythmic and Voluntary Movements 654

Reflexive and Rhythmic Movements Are Produced by Stereotyped Patterns of Muscle Contraction 654

Voluntary Movements Are Goal-Directed and Improve With Practice as a Result of Feedback and Feed-Forward Mechanisms 656

Voluntary Movements Obey Psychophysical Principles 658

Voluntary Movements Have Certain Invariant Features and Are Governed By Motor Programs 659

Reaction Time Varies With the Amount of Information Processed 661

Voluntary Movements Trade Speed for Accuracy 662

The Motor Systems Are Organized Hierarchically 663

The Spinal Cord, Brain Stem, and Forebrain Contain Successively More Complex Motor Circuits 663

The Cerebellum and Basal Ganglia Influence Cortical and Brain Stem Motor Systems 663

Lesions of the Motor Pathways Produce Positive and Negative Signs 666

Spinal Motor Neurons Execute Movement 667

The Brain Stem Modulates the Action of Spinal Motor Circuits 668

The Cerebral Cortex Modulates the Action of Motor Neurons in the Brain Stem and Spinal Cord 669

The Cerebral Cortex Acts on Spinal Motor Neurons Both Directly and Indirectly 669

The Cerebral Cortex Acts on Brain Stem Motor Neurons Through the Corticobulbar Tract 671

The Motor Cortex Is Influenced by Both Cortical and Subcortical Inputs 671

An Overall View 671

Selected Readings 672

References 673

34 The Motor Unit and Muscle Action

Gerald E. Loeb, Claude Ghez

Motor Neurons Convey Commands to Muscle Fibers 676

The Contractile Machinery of Muscle Fibers Is Organized Into Sarcomeres and Cross Bridges 676

Sarcomeres Are Composed of Interdigitated Thick and Thin Filaments 676

Contractile Force Is Produced by Cross Bridges 678

Noncontractile Components in Muscle Fibers Provide Stability for the Contractile Elements 678

Contractile Force Depends on the Level of Activation of Each Muscle Fiber and Its Length and Velocity 680
Formation of Cross Bridges Depends on Calcium 680
The Number of Cross Bridges Depends on the Degree of Overlap Between Actin and Myosin Filaments 681
The Force Produced by Cross Bridges Depends on the Velocity of the Sarcomere 683
Repeated Activation of Muscle Causes Fatigue 683
Three Types of Motor Units Differ in Speed, Strength of Contraction, and Fatigability 683
Motor Units Are Recruited in Fixed Order 686
The Electrical Properties of Motor Neurons Determine Their Responses to Synaptic Input 686
The Force of Contraction Depends on the Number of Recruited Motor Neurons and Their Individual Firing Rates 687
Movements Are Produced by the Coordinated Work of Many Muscles Acting on Skeletal Joints 687
Muscles Have Different Actions at Individual Joints 687
Rapid Changes in Joint Torque Require Sequential Activation of Agonist and Antagonist Muscles 688
Muscle Force Is Required to Overcome Inertia 688
Muscle Force May Be Used to Create Stiffness at Joints 689
Muscles Act on More than One Joint 690
An Overall View 693
Selected Reading 693
References 693
35 Diseases of the Motor Unit695 Lewis P. Rowland
Neurogenic and Myopathic Diseases Are Distinguished by Clinical and Laboratory Criteria 696
Clinical Criteria Help to Identify Neurogenic and Myopathic Conditions 696
Laboratory Criteria Also Assist in Making the Diagnosis 697
Diseases of Motor Neurons Are Acute or Chronic 700
Motor Neuron Diseases Do Not Affect Sensory Neurons 700
Motor Neuron Disease Is Characterized by Fasciculation and Fibrillation 701

Diseases of Peripheral Nerves Are Also Acute or Chronic 701

Neuropathies Can Cause Positive or Negative Signs

and Symptoms 703

Demyelination Leads to Slowing of Conduction Velocity 703 Diseases of Skeletal Muscle Can Be Inherited or Acquired 704 Muscular Dystrophies Are the Most Common Inherited Myopathies 704 Dermatomyositis Exemplifies Acquired Myopathy 704 Weakness in Myopathies Need Not Be Due to Loss of Muscle Fibers 705 Molecular Genetics Has Illuminated the Physiology and Pathology of Neurogenic and Myopathic Diseases 705 The Membrane Protein Dystrophin is Lacking in Duchenne Muscular Dystrophy 707 Dystrophin-Normal Muscular Dystrophy and Limb-Girdle Muscular Dystrophy are Associated With Mutations of Genes for Sarcoglycans 707 Myelin Proteins Are Affected in Some Hereditary Peripheral Neuropathies 709 An Overall View 710 Selected Readings 710 References 710 36 Spinal Reflexes Keir Pearson, James Gordon Reflexes Are Highly Adaptable and Control Movements in a Purposeful Manner 714 Spinal Reflexes Produce Coordinated Patterns of Muscle Contraction 715 Cutaneous Reflexes Produce Complex Movements That Serve Protective and Postural Functions 715 The Stretch Reflex Acts to Resist the Lengthening of a Muscle 717 Neuronal Networks in the Spinal Cord Contribute to the Purposeful Integration of Reflex Responses The Stretch Reflex Involves a Monosynaptic Pathway 717 **Inhibitory Interneurons Coordinate Muscles**

Surrounding a Joint 717

of Spinal Reflexes 724

Flexibility of Reflex Responses 721

Centrally Generated Motor Commands Can Alter

Transmission in Spinal Reflex Pathways 724

Divergence in Reflex Pathways Amplifies Sensory Inputs and Coordinates Muscle Contractions 721 Convergence of Inputs on Interneurons Increases the

Tonic and Dynamic Mechanisms Regulate the Strength

Gamma Motor Neurons Provide a Mechanism for Adjusting the Sensitivity of Muscle Spindles 724

Proprioceptive Reflexes Play an Important Role in the Regulation of Both Voluntary and Automatic Movements 726

Reflexes Involving Limb Muscles Are Mediated Through Spinal and Supraspinal Pathways 727

Stretch Reflexes Reinforce Central Commands for Movements 728

Damage to the Central Nervous System Produces Characteristic Alterations in Reflex Responses and Muscle Tone 730

Interruption of Descending Pathways to the Spinal Cord Frequently Produces Spasticity 730

Transection of the Spinal Cord in Humans Leads to a Period of Spinal Shock Followed by Hyperreflexia 730

An Overall View 735

Selected Readings 735

References 735

Keir Pearson, James Gordon

A Complex Sequence of Muscle Contractions Is Required for Stepping 740

The Motor Pattern for Stepping Mammals Is Produced at the Spinal Level 740

Neuronal Networks Within the Spinal Cord Generate Rhythmic Alternating Activity in Flexor and Extensor Muscles 742

The Rhthym-Generating System in the Spinal Cord Can Generate Complex Motor Patterns 743

Sensory Input From Moving Limbs Regulates Stepping Patterns 747

Proprioception Regulates the Timing and Amplitude of the Stepping Patterns 747

Sensory Input From the Skin Allows Stepping to Adjust to Unexpected Obstacles 749

Descending Pathways Are Necessary for Initiation and Adaptive Control of Walking 750

Descending Pathways From the Brain Stem Initiate Walking and Control Its Speed 750

The Descending Signals That Initiate Locomotion Are Transmitted via the Reticulospinal Pathway 751

The Motor Cortex Is Involved in the Control of Precise Stepping Movements in Visually Guided Walking 752 The Cerebellum Fine-Tunes the Locomotor Pattern by Regulating the Timing and Intensity of Descending Signals 753

Human Walking May Involve Spinal Pattern Generators 753

An Overall View 754

Selected Readings 754

References 754

John Krakauer, Claude Ghez

Voluntary Movement Is Organized in the Cortex 758

The Primary Motor Cortex Controls Simple Features of Movement 758

Premotor Cortical Areas Project to the Primary Motor Cortex and Spinal Cord 760

Each Cortical Motor Area Receives Unique Cortical and Subcortical Inputs 760

The Somatotopic Organization of the Motor Cortex Is Plastic 761

Corticospinal Axons Influence Spinal Motor Neurons Through Direct and Indirect Connections 763

The Primary Motor Cortex Executes Movements and Adapts Them to New Conditions 764

Activity in Individual Neurons of the Primary Motor Cortex Is Related to Muscle Force 764

Direction of Movement is Encoded by Populations of Cortical Neurons 765

Neurons in the Primary Motor Cortex Are Activated Directly by Peripheral Simulation Under Particular Conditions 767

Individual Movement of Digits Is Controlled by Patterns of Activity in a Population of Cortical Neurons 767

Each Premotor Area Contributes to Different Aspects of Motor Planning 770

The Supplementary and Presupplementary Motor Areas Play an Important Role in Learning Sequences of Discrete Movements 771

The Lateral Premotor Areas Contribute to the Selection of Action and to Sensorimotor Transformations 774

Reaching and Grasping Are Mediated by Separate Parieto-Premotor Channels 777

An Overall View 778

Selected Readings 779

References 779

39 The Control of Gaze782	An Overall View 797
Michael E. Goldberg	Selected Readings 798
Six Neuronal Control Systems Keep the Fovea on Target 783	References 798
An Active Fixation System Keeps the Eyes on the Stationary Target 784	
The Saccadic System Points the Fovea Toward Objects of Interest 784	40 The Vestibular System801 Michael E. Goldberg, A.J. Hudspeth
The Smooth Pursuit System Keeps Moving Targets on the Fovea 784	The Vestibular Labyrinth Houses Five Receptor Organs 802
The Vergence Movement System Aligns the Eyes to Look at Targets at Different Depths 785	Hair Cells Transduce Mechanical Stimuli into Receptor Potentials 802
The Eye Is Moved by Six Muscles 785	The Vestibular Nerve Transmits Sensory Information
Eye Movements Rotate the Eye in the Orbit 785	From the Vestibular Organs 803
The Six Extraocular Muscles Form Three Complementary Pairs 786	The Utricle and the Saccule Detect Linear Accelerations 804
Extraocular Muscles Are Controlled by Three Cranial Nerves 787	The Semicircular Canals Detect Angular Accelerations 805
Extraocular Motor Neurons Signal Eye Position and Velocity 788	Most Movements Elicit Complex Patterns of Vestibular Stimulation 806
The Motor Circuits for Saccades Lie in the Brain Stem 789	Menière Disease Affects the Vestibular Labyrinth 807
Horizontal Saccades Are Generated in the Pontine Reticular Formation 789	Vestibular Reflexes Stabilize the Eyes and the Body When the Head Moves 808
Vertical Saccades Are Generated in the Mesencephalic Reticular Formation 792	The Vestibulo-Ocular Reflexes Compensate for Head Movement 808
Patients With Brain Stem Lesions Have Characteristic Deficits in Eye Movements 792	Vestibular Nystagmus Resets Eye Position During Sustained Rotation of the Head 809
Saccades Are Controlled by the Cerebral Cortex 792	The Otolith Reflexes Compensate for Linear
The Superior Colliculus Integrates Visual and Motor Information Into Oculomotor Signals to the	Motion and Head Deviation Relative to Gravity 809
Brain Stem 792 The Rostral Superior Colliculus Facilitates	The Optokinetic System Supplements the Vestibulo-Ocular Reflexes 809
Visual Fixation 793 The Basal Ganglia Inhibit the Superior Colliculus 793	Vestibulospinal Reflexes Are Important in Maintaining Vertical Posture 810
The Parietal Cortex Controls Visual Attention 794	Central Connections of the Vestibular Apparatus Integrate
The Frontal Eye Field Sends a Specific Movement Signal	Vestibular, Visual, and Motor Signals 810
to the Superior Colliculus 794	The Vestibular Nerve Signals Head Velocity to the Vestibular Nuclei 810
The Control of Saccades Can Be Modified By Experience 795	Subcortical and Cortical Structures Contribute to the Optokinetic Reflex 812
Smooth Pursuit, Vergence, and Gaze Are Controlled by Distinct Systems 795	The Vestibular Projection to the Cerebral Cortex Allows Perception of Rotation and Vertical
Smooth Pursuit Involves the Cerebral Cortex, the Cerebellum, and the Pons 795	Orientation 813
Vergence Is Organized in the Midbrain 796	An Overall View 813
Gaze Involves Combined Head and	Selected Readings 814

References 814

Eye Movements 796

The Vestibulocerbellum Regulates Balance and
Eye Movements 841
The Spinocerebellum Regulates Body and Limb Movements 841
Somatosensory Information Reaches the
Spinocerebellum Through Direct And Indirect Mossy Fiber Pathways 841
The Spinocerebellum Contains Sensory Maps 842
The Spinocerebellum Modulates the Descending Motor Systems in the Brain Stem and Cerebral Cortex 843
The Spinocerebellum Uses Feed-Forward Mechanisms
to Regulate Movements 843
The Cerebrocerebellum Is Involved in Planning
Movement and Evaluating Sensory Information for Action 845
The Cerebrocerebellum Is Part of a High-Level Internal Feedback Circuit That Regulates
Cortical Motor Programs 845
Lesions of the Cerebrocerebellum Disrupt Motor Planning and Prolong Reaction Time 846
The Cerebrocerebellum Also Has Purely Cognitive Functions 846
The Cerebellum Participates in Motor Learning 847
Cerebellar Diseases Have Distinctive Symptoms and Signs 849
An Overall View 850
Selected Readings 850
References 851
43 The Basal Ganglia85
Mahlon R. DeLong
The Basal Ganglia Consist of Four Nuclei 854
The Striatum, the Input Nucleus to the Basal Ganglia, I Heterogeneous in Both Its Anatomy and Function 856
The Straitum Projects to the Output Nuclei via Direct and Indirect Pathways 856
The Basal Ganglia Are the Principal Subcortical Components of a Family of Parallel Circuits Linking the
Thalamus and Cerebral Cortex 857
The Skeletomotor Circuit Engages Specific Portions of the Cerebral Cortex, Basal Ganglia, and Thalamus
Single Cell Recording Studies Provide Direct Insight into the Role of the Motor Circuits 859
Studies of the Oculomotor Circuit Provided Important Insight Into How the Skeletomotor Circuit Operates 86

Some Movement Disorders Result From Imbalances in the Direct and Indirect Pathways in the Basal Ganglia 861

Overactivity in the Indirect Pathway Is a Major Factor in Parkinsonian Signs 862

The Level of Dopamine in the Basal Ganglia Is Decreased in Parkinson Disease 864

Underactivity in the Indirect Pathway Is a Major Factor in Hyperkinetic Disorders 864

Huntington Disease Is a Heritable Hyperkinetic Disorder 864

The Gene for Huntington Disease Has Been Identified 864

Glutamate-Induced Neuronal Cell Death Contributes to Huntington Disease 865

The Basal Ganglia Also Have a Role in Cognition, Mood, and Nonmotor Behavior Function 866

An Overall View 867

Selected Readings 867

References 867

Part VII

Arousal, Emotion, and Behavioral Homeostasis

44 Brain Stem, Reflexive Behavior, and the Cranial Nerves

Clifford B. Saper

The Cranial Nerves Are Functionally Homologous to the Spinal Nerves 876

The Cranial Nerves Leave the Skull in Groups and Therefore Are Likely to Be Injured Together 876

The Cranial Nerves Supply the Sensory and Motor Functions of the Face and Head and Autonomic Functions of the Body 877

The Cranial Nerve Nuclei Follow the Basic Plan for Sensory and Motor Structures in the Spinal Cord 880

The Sensory Nuclei 880

The Motor Nuclei 883

The Brain Stem Deviates From the Organization of the Spinal Cord in Two Important Ways 885

Neuronal Ensembles in the Brain Stem Reticular Formation Coordinate Reflexes and Simple Behaviors Mediated by the Cranial Nerves 885

An Overall View 887

Selected Readings 888

References 888

45 Brain Stem Modulation of Sensation, Movement, and Consciousness889

Clifford B. Saper

Cell Groups in the Brain Stem With Long Projections Can Be Defined by Their Neurotransmitters 889

Descending Projections from the Brain Stem to the Spinal Cord Modulate Sensory and Motor Pathways 896

Pain Is Modulated by Descending Monoaminergic Projections 896

Posture, Gait, and Muscle Tone Are Modulated by Two Reticulospinal Tracts 896

Ascending Projections From the Brain Stem Modulate Arousal and Consciousness 896

Consciousness Represents the Summated Activity of the Cerebral Cortex 897

The EEG Reflects Two Modes of Firing of Thalamic Neurons 897

Damage to Either Branch of the Ascending Arousal System May Impair Consciousness 899

Bilateral Forebrain Damage May Cause Coma or Persistent Vegetative State or Be Symptomatic of Brain Death 900

An Overall View 900

Postscript: Examination of the Comatose Patient 901

States of Consciousness Are Assessed Clinically in Terms of Responsiveness to the Environment 901

Loss of Consciousness May Be Either Structural or Metabolic in Origin 901

Testing Four Functional Systems Gives Important Clues to the Cause of Structural Coma 902

Emergency Care of the Comatose Patient Can Be Lifesaving 905

Selected Readings 908

References 908

46 Seizures and Epilepsy910

Gary L. Westbrook

Classification of Seizures and the Epilepsies Is Important for Pathogenesis and Treatment 911

The Electroencephalogram Represents the Collective Behavior of Cortical Neurons 913

Sleep Periods Change Over the Life Span 943

The Functions of Sleep and Dreaming

Are Not Yet Known 944

There Are Phylogenetic Variations in Sleep 944

Partial Seizures Originate Within a Small Group of Neurons Known as a Seizure Focus 917	An Overall View 946
Neurons in a Seizure Focus Have Characteristic Activity 917	Selected Readings 947 References 947
Synchronization Results From the Breakdown of Surround Inhibition 919 The Spread of Seizure Activity Involves Normal Cortical Circuitry 920	48 Disorders of Sleep and Wakefulness
Generalized Seizures Evolve From Thalamocortical Circuits 922	A Variety of Medical Disorders Are Associated With Excessive Sleepiness 949
Locating the Seizure Focus Is Critical to the Surgical Treatment of Epilepsy 925	Persistant Daytime Sleepiness Is the Most Prominent Symptom of Narcolepsy 949
Prolonged Seizures Can Cause Brain Damage 927 Repeated Convulsive Seizures (Status Epilepticus) Are a	Breathing Is Compromised in Obstructive Sleep Apnea Syndrome 951
Medical Emergency 927 Excitotoxicity Underlies Seizure-Related	Chronic Insufficient Sleep Syndrome Reflects a Failure to Obtain Sufficient Sleep 953
Brain Damage 927	Insomnia Can Be Transient or Persistent 954
The Factors Leading to Development of the Epileptic Condition Are an Unsolved Mystery 930	Insomnia Is the Most Frequent of All Complaints About Sleep and Wakefulness 954
An Overall View 933	Disturbed Circadian Rhythm Causes Insomnia 954
Selected Readings 934 References 934	Periodic Limb Movement Disorder Is a Primary Sleep Pathology 955
System May Impair Consequences System May Consequence Consequence Coma or Bilateral Forebrain Damage May Cause Coma or	Parasomnias Are Disorders of Arousal From Non-REM and REM Sleep 955
47 Sleep and Dreaming936 Allan Rechtschaffen, Jerome Siegel	REM Behavior Disorder Gives Rise to Violent Dream Enactment During Sleep 956
Sleep Follows a Circadian Rhythm 937	Abrupt Arousal from Non-REM Sleep Gives Rise to a
Sleep Is Not Uniform But Is Organized in Cycles of	Variety of Dysfunctional Behaviors 956
Non-REM and REM Stages 937	An Overall View 958
Non-REM Sleep Comprises Four Stages 937	Selected Readings 958
REM Sleep Is an Active Form of Sleep 938	References 958
Different Neural Systems Promote Arousal and Sleep 939	
Non-REM Sleep Is Regulated by Interacting Sleep-Inducing and Arousal Mechanisms 940	49 The Autonomic Nervous System and the Hypothalamus960
REM Sleep Is Regulated Primarily by Nuclei Located at the Junction of the Midbrain and Pons 940	Susan Iversen, Leslie Iversen, Clifford B. Saper The Autonomic Nervous System Is a Visceral and Largely
Several Endogenous Substances Affect Sleep 943	Involuntary Sensory and Motor System 961

Various Theories of the Function of Sleep Have Been
Proposed 944

Modern Research Has Increased Our Knowledge
About Dreaming 945

to Ganglia Alongside the Spinal Cord 963

Parasympathetic Pathways Convey Outputs from the
Brain Stem Nuclei and Sacral Spinal Cord to Widely
Dispersed Ganglia 963

Each of the Three Divisions of the Autonomic Nervous

Lie Outside the Central Nervous System 962

System Has a Distinctive Anatomical Organization 962

The Motor Neurons of the Autonomic Nervous System

Sympathetic Pathways Convey Thoracolumbar Outputs

The Enteric Nervous System Is Largely Autonomous 964

Sensory Inputs Produce a Wide Range of Visceral Reflexes 965

Discrete Autonomic Reflexes Produce Both Slow and Rapid Visceral Responses 966

Autonomic Neurons Use a Variety of Chemical Transmitters 969

Ganglionic Transmission Involves Both Fast and Slow Synaptic Potentials 970

Norepinephrine and Acetylcholine Are the Predominant Transmitters in the Autonomic Nervous System 970

ATP and Adenosine Have Potent Extracellular Actions 970

Many Different Neuropeptides Are Present in Autonomic Neurons 970

A Central Autonomic Network Coordinates **Autonomic Function 972**

The Hypothalamus Integrates Autonomic and Endocrine Functions With Behavior 974

The Hypothalamus Contains Specialized Groups of Neurons Clustered in Nuclei 977

The Hypothalamus Controls the Endocrine System 978

Magnocellular Neurons Secrete Oxytocin and Vasopressin Directly From the Posterior Pituitary Gland 979

Parvocellular Neurons Secrete Peptides That Regulate Release of Anterior Pituitary Hormones 979

An Overall View 980

Selected Readings 980

References 981

50 Emotional States and Feelings982

Susan Iversen, Irving Kupfermann, Eric R. Kandel

The Peripheral Components of Emotion Prepare the Body for Action and Communicate Our Emotional States to Other People 983

A Theory of Emotion Must Explain the Relationship of Cognitive and Physiological States 983

In the James-Lange Theory Emotions Are Cognitive Responses to Information From the Periphery 983

The Cannon-Bard Theory Emphasizes the Importance of the Hypothalamus and Other Subcortical Structures in Meditating Both the Cognitive and Peripheral Aspects of Emotion 984

According to the Schachter Theory Feelings Are Cognitive Translations of Ambiguous Peripheral Signals 984

In the Arnold Theory Autonomic Responses Are Not an Essential Component of Emotion 985

The Hypothalamus Coordinates the Peripheral Expression of Emotional States 986

The Search for Cortical Representation of Feeling Has Led to the Limbic System 986

The Amygdala Is the Part of the Limbic System Most Specifically Involved With Emotional Experience 988

Learned Emotional Responses Are Processed in the Amygdala 990

The Amygdala May be Involved in Both Pleasurable and Fearful Responses to Stimuli 992

The Amygdala Mediates Both the Autonomic Expression and the Cognitive Experience of Emotion 992

The Frontal, Cingulate, and Parahippocampal Cortices Are **Involved in Emotion 993**

The Hippocampus Has Only an Indirect Role in Emotion 994

An Overall View 995

Selected Readings

References 996

51 Motivational and Addictive States ... 998

Irving Kupfermann, Eric R. Kandel, Susan Iversen

Drive States Are Simple Cases of Motivational States That Can be Modeled as Servo-Control Systems 999

Temperature Regulation Involves Integration of Autonomic, Endocrine, and Skeletomotor Responses 1000

Feeding Behavior Is Regulated by a Variety of Mechanisms 1002

Dual Controlling Elements in the Hypothalamus Contribute to the Control of Food Intake

Food Intake Is Controlled by Short-Term and Long-Term Cues 1004

Specific Genes Are Involved in the Control of Food Intake 1005

Drinking Is Regulated by Tissue Osmolality and Vascular Volume 1006

Motivational States Can Be Regulated by Factors Other Than Tissue Needs 1007

Ecological Constraints 1007

Anticipatory Mechanisms 1007

Hedonic Factors 1007

The Mesolimbic Dopaminergic Pathways Important for Reinforcement Are Also Recruited by Some Drugs of Abuse 1009

The Limbic Dopaminergic Neurons Are Involved in Behavioral Activation 1009

Drugs of Abuse Increase the Level of Dopamine Released in the Brain 1010

An Overall View 1012

Selected Readings 1012

References 1013

Part VIII

The Development of the Nervous System

Thomas M. Jessell, Joshua R. Sanes

The Entire Nervous System Arises From the Ectoderm 1021

Inductive Signals Control Neural Cell Differentiation 1022

The Neural Plate Is Induced by Signals From Adjacent Mesoderm 1023

Neural Induction Involves Inhibition of Bone Morphogenetic Protein Signals 1024

The Neural Plate Is Patterned Along Its Dorsoventral Axis by Signals From Adjacent Nonneural Cells 1027

The Ventral Neural Tube Is Patterned by Sonic Hedgehog Secreted From the Notochord and Floor Plate 1027

The Dorsal Neural Tube Is Patterned by Bone Morphogenetic Proteins Secreted From the Epidermal Ectoderm and Roof Plate 1029

Inductive Signaling in the Two Halves of the Neural Tube Depends on a Common Principle 1029

Dorsoventral Patterning Is Maintained Throughout the Rostrocaudal Length of the Neural Tube 1029

The Rostrocaudal Axis of the Neural Tube Is Patterned in Several Stages 1030

The Hindbrain is Organized in Segmental Units by *Hox* Genes 1030

The Midbrain is Patterned by Signals From a Neural Organizing Center 1034

The Developing Forebrain Is Subdivided Along Its Rostrocaudal Axis 1035

Regional Differentiation of the Cerebral Cortex Depends on Afferent Input As Well As Intrinsic Programs of Cell Differentiation 1036

An Overall View 1038

Selected Readings 1038

References 1039

53 The Generation and Survival of Nerve Cells1041

Thomas M. Jessell, Joshua R. Sanes

The Molecular Basis of Neurona Generation Is Similar Throughout Phylogeny 1041

Neuronal and Glial Fates Are Controlled by Local Signaling 1047

Secreted Factors Direct the Differentiation of Neural Crest Cells into Neurons and Glia 1048

Glial Cell Differentiation in the Central Nervous System Is Also Controlled by Diffusible Factors 1049

Neuronal Fate in The Mammalian Cortex Is Influenced by the Timing of Cell Differentiation 1049

The Neurotransmitter Phenotype of a Neuron Is Controlled by Signals From the Neuronal Target 1051

The Survival of a Neuron Is Also Regulated by Signals From the Neuronal Target 1052

Target Cells Secrete a Variety of Neurotrophic Factors 1055

Elimination of Neurotrophic Factors and Their Receptors Leads to Neuronal Death 1057

Deprivation of Neurotrophic Factors Activates a Cell Death Program in Neurons 1058

An Overall View 1061

Selected Readings 1061

References 1061

54 The Guidance of Axons to Their Targets1063

Joshua R. Sanes, Thomas M. Jessell

Specific Molecular Cues Guide Axons to Their Targets 1063

Axons Reach Their Destinations in a Series of Discrete Steps 1067

Retinal Axons React to Intermediate Cues en Route to Their Targets 1067

Motor Axons Grow Through Peripheral Nerves to Muscles 1069

The Cellular Environment Provides a Complex Set of Commands to the Growing Axon 1069

The Growth Cone Is a Sensory-Motor Structure That Recognizes and Responds to Guidance Cues 1070

Pathway Guidance Cues Act in Diverse Ways 1074

Integrins on Growth Cones Interact With Laminins in the Extracellular Matrix 1074

Molecules That Mediate Cell-Cell Adhesion Also Promote Neurite Outgrowth 1074

Netrins Are Chemoattractant Factors 1078

Ephrins and Semaphorins Guide Growth Cones by Providing Inhibitory Signals 1081

Soluble Factors Attract Some Growth Cones and Repel Others 1081

Molecules of Different Families Interact to Guide Axons to Their Destinations 1081

An Overall View 1084

Selected Readings 1084

References 1085

Joshua R. Sanes, Thomas M. Jessell

Interactions Between Motor Neurons and Skeletal Muscles Organize the Development of the Neuromuscular Junction 1089

The Motor Nerve Organizes Differentiation of the Postsynaptic Muscle Membrane 1091

Agrin Triggers the Clustering of Acetylcholine Receptors 1092

Neuregulin Stimulates Synthesis of Acetylcholine Receptors 1094

Neural Activity Represses Synthesis of Acetylcholine Receptors in Nonsynaptic Areas 1096

Several Aspects of Postsynaptic Differentiation Are Controlled by the Motor Axon 1098

The Muscle Fiber Organizes the Differentiation of Motor Nerve Terminals 1098

Many Neuromuscular Junctions That Form in the Embryo Are Eliminated After Birth 1100

Central Synapses and Neuromuscular Junctions Develop in Similar Ways 1101

Central Nerve Terminals Develop Gradually and Are Subject to Elimination 1101

Neurotransmitter Receptors Cluster at Central Synapses 1103

The Synaptic Cleft Differs at Central and Neuromuscular Synapses 1103

The Recognition of Synaptic Targets Is Highly Specific 1105

New Neural Connections Can Reform Following Nerve Injury 1108

Both Neurons and Cells Around Them Are Affected by Damage to the Axon 1108

Regenerative Capacity Is Greater in the Peripheral Than in the Central Nervous System 1109

Therapeutic Interventions May Promote Axonal Regeneration in the Injured Central Nervous System 1110

Restoration of Function Requires Synaptic Regeneration 1111

An Overall View 1112

Selected Readings 1113

References 1113

56 Sensory Experience and the Fine-Tuning of Synaptic Connections 1115

Eric R. Kandel, Thomas M. Jessell, Joshua R. Sanes

Development of Visual Perception Requires Sensory Experience 1115

Development of Binocular Circuits in the Cortex Depends on Postnatal Neural Activity 1117

Ocular Dominance Columns Are Organized After Birth 1118

Synchronized Activity in the Pathways From Each Eye Organizes the Ocular Dominance Columns 1119

Segregation of Retinal Inputs to the Thalamus Is Driven by Spontaneous, Synchronized Neural Activity in Utero 1123

Synchronous Presynaptic Activity May Enhance the Release of Neurotrophic Factors From Target Neurons 1123

Early Intracortical Connections May Direct the Development of Orientation Columns 1125

Activity-Dependent Refinement of Connections Is a General Feature of Circuits in the Central Nervous System 1125

There Is a Critical Period in the Development of Social Behavior 1127

An Overall View 1128

Selected Readings 1129

References 1129

57 Sexual Differentiation of the Nervous System 1131

Roger A. Gorski

Sexual Differentiation of the Reproductive System Is a Fundamental Characteristic of Development 1131

Development of the Testes Depends on a Testis Determining Factor 1132

Sexual Differentiation of the Internal and External Genitalia Depends on Hormones Produced by the Testes 1132

The Brain Also Undergoes Hormonally Dependent Sexual Differentiation 1134

Gonadal Hormones Exert Permanent Effects on the Developing Central Nervous System and Transient Effects on the Adult Brain 1136

Exposure to Testicular Hormones During Development Produces Sex Differences in the Central Nervous System 1136

Estradiol Is the Masculinizing Hormone for Many Sexually Dimorphic Brain Characteristics 1138

Hormones Exert Diverse Actions on the Development of the Central Nervous System 1140

Estradiol May Prevent Apoptotic Cell Death in the Sexually Dimorphic Nucleus of the Preoptic Area 1140

Gonadal Hormones May Induce Apoptotic Cell Death in the Anteroventral Periventricular Nucleus 1140

The Action of Testosterone on Peripheral Muscles May Prevent Neuronal Death in the Spinal Nucleus of the Bulbocavernosus 1141

Hormone-Induced Modifications in the Brain Structure Are Not Limited to Development 1141

Specific Sex Differences in the Brain Control Behavior 1141

There May Be a Genetic and Anatomical Basis for Homosexuality 1143

An Overall View 1146

Selected Readings 1146

References 1146

Donald L. Price

Several Hypotheses Have Been Proposed for the Molecular Mechanisms of Aging 1149

Changes in the Function and Structure of the Brain Are Associated With Aging 1150

A Variety of Senile Dementias Afflict the Elderly 1151

Alzheimer Disease Is Characterized by Several Structural Abnormalities in the Brain 1153

Alzheimer Disease Is Associated With Cytoskeletal Abnormalities in Neurons 1154

Amyloid Deposits Are One of the Hallmarks of Alzheimer Disease 1155

Several Genetic Risk Factors for Alzheimer Disease Have Been Identified 1156

Certain Mutations Increase the Risk of Early-Onset Alzheimer Disease 1156

Alleles of Genes Increase the Risk of Late-Onset Alzheimer Disease 1156

Animal Models Provide Insight Into the Molecular Mechanisms of the Disease 1157

Treatment of Alzheimer Disease 1158

An Overall View 1158

Selected Readings 1159

References 1159

Part IX

Language, Thought, Mood, and Learning, and Memory

59 Language and the Aphasias 1169

Nina F. Dronkers, Steven Pinker, Antonio Damasio

Language Is the Ability to Encode Ideas Into Signals and Must be Distinguished From Thought, Literacy, and Correct Usage 1169

Language Has a Universal Design 1170

Complex Language Develops Spontaneously in Children 1171

Languages Are Learned and the Capacity to Learn Language Is Innate 1172

Other Animals Appear to Lack Homologs of Human Language, but Language May Nonetheless Have Evolved by Darwinian Natural Selection 1173

The Study of Aphasia Led to the Discovery of Critical Brain Areas Related to Language 1174

Broca Aphasia Results From a Large Frontal Lobe Lesion 1175

People With Broca Aphasia Have Trouble Understanding Grammatically Complex Sentences 1177

Wernicke Aphasia Results From Damage to Left Temporal Lobe Structures 1179 Conduction Aphasia Results From Damage to Structures That Interact With Major Language Areas of the Brain 1180

Transcortial Motor and Sensory Aphasias Result From Damage to Areas Near Broca's and Wernicke's Areas 1180

Global Aphasia Is a Combination of Broca, Wernicke, and Conduction Aphasias 1181

Beyond the Classical Language Areas: Other Brain Areas Are Important for Language 1181

The Right Cerebral Hemisphere Is Important for Prosody and Pragmatics 1182

Alexia and Agraphia Are Acquired Disorders of Reading and Writing 1183

Developmental Dyslexia is a Difficulty in Learning to Read 1184

An Overall View 1185

Selected Readings 1186

References 1186

Eric R. Kandel

Mental Illnesses Can Be Diagnosed Using Classical Medical Criteria 1188

Schizophrenia Is Likely to Be Several Related Disorders 1189

Psychotic Episodes Are Preceded by Prodromal Signs and Followed by Residual Symptoms 1192

Genetic Predisposition Is an Important Factor 1193

Prominent Anatomical Abnormalities in the Brain Occur in Some Cases of Schizophrenia 1195

A Two-Step Model Seems Most Consistent With the Pathogenesis of Schizophrenia 1196

Antipsychotic Drugs Effective in the Treatment of Schizophrenia Act on Dopaminergic Systems 1197

Abnormalities in Dopaminergic Synaptic Transmission Are Thought to Be Associated With Schizophrenic Symptoms 1200

Excess Synaptic Transmission of Dopamine May Contribute to the Expression of Schizophrenia 1200

Distinct Anatomical Components of the Dopaminergic System Are Implicated in Schizophrenia 1201

Abnormalities in Dopaminergic Transmission Do Not Account for All Aspects of Schizophrenia 1204

An Overall View 1206

Selected Readings 1207 References 1207

Eric R. Kandel

The Major Mood Disorders Can Be Either Unipolar or Bipolar 1209

Unipolar Depression Is Most Likely Several Mood Disorders 1210

Bipolar Depressive (Manic-Depressive) Disorders Give Rise to Alternating Euphoria and Depression 1211

Mood Disorders Have a Strong Genetic Predisposition 1211

Familial Unipolar and Bipolar Depressions May Reflect an Abnormality in the Functioning of the Subgenual Region of the Frontal Cortex 1212

Unipolar Depressive and Manic-Depressive Disorders Can Be Treated Effectively 1213

Drugs Effective in Depression Act on Serotonergic and Noradrenergic Pathways 1216

An Abnormality in Biogenic Amine Transmission May Contribute to the Disorders of Mood 1216

Unipolar Depression May Involve Disturbances of Neuroendocrine Function 1220

There Are at Least Four Major Types of Anxiety Disorders 1220

Panic Attacks Are Brief Episodes of Terror 1221

Post-Traumatic Stress Disorder Reflects Persistent Traces Of Anxiety That Follow Traumatic Episodes 1222

Generalized Anxiety Disorder Is Characterized by Long-Lasting Worries 1222

In Obsessive-Compulsive Disorder Obtrusive Thoughts Are a Source of Anxiety and Compulsion 1223

An Overall View 1224

Selected Readings 1225

References 1225

62 Learning and Memory1227

Eric R. Kandel, Irving Kupfermann, Susan Iversen

Memory Can Be Classified as Implicit or Explicit on the Basis of How Information Is Stored and Recalled 1228

The Distinction Between Explicit and Implicit Memory Was First Revealed With Lesions of the Limbic Association Areas of the Temporal Lobe 1229

Animal Studies Help to Understand Memory 1231

Damage Restricted to Specific Subregions of the Hippocampus Is Sufficient to Impair Explicit Memory Storage 1233

Explicit Memory Is Stored in Different Association Cortices 1233

Semantic (Factual) Knowledge Is Stored in a Distributed Fashion in the Neocortex 1233

Episodic (Autobiographical) Knowledge About Time and Place Seems to Involve the Prefrontal Cortex 1237

Explicit Knowledge Involves at Least Four Distinct Processes 1237

Working Memory Is a Short-Term Memory Required for Both the Encoding and Recall of Explicit Knowledge 1238

Implicit Memory Is Stored in Perceptual, Motor, and Emotional Circuits 1239

Implicit Memory Can Be Nonassociative or Associative 1240

Classical Conditioning Involves Associating Two Stimuli 1240

Operant Conditioning Involves Associating a Specific Behavior With a Reinforcing Event 1242

Associative Learning Is Not Random But Is Constrained by the Biology of the Organism 1242

Certain Forms of Implicit Memory Involve the Cerebellum and Amygdala 1243

Some Learned Behaviors Involve Both Implicit and Explicit Forms of Memory 1243

Both Explicit and Implicit Memory are Stored in Stages 1244

An Overall View 1245

Selected Readings 1245

References 1245

Eric R. Kandel

Short-Term Storage of Implicit Memory for Simple Forms of Learning Results From Changes in the Effectiveness of Synaptic Transmission 1248

Habituation Involves an Activity-Dependent Presynaptic Depression of Synaptic Transmission 1248

Sensitization Involves Presynaptic Facilitation of Synaptic Transmission 1250

Classical Conditioning Involves Presynaptic Facilitation of Synaptic Transmission That Is Dependent on Activity in Both the Presynaptic and the Postsynaptic Cell 1252

Long-Term Storage of Implicit Memory for Sensitization and Classical Conditioning Involves the cAMP-PKA-MAPK-CREB Pathway 1254

Molecular Biological Analysis of Long-Term Sensitization Reveals a Role for cAMP Signaling in Long-Term Memory 1254

Genetic Analyses of Implicit Memory Storage for Classical Conditioning Also Implicate the cAMP-PKA-CREB Pathway 1257

Explicit Memory in Mammals Involves Long-Term Potentiation in the Hippocampus 1259

Long-Term Potentiation in the Mossy Fiber Pathway Is Nonassociative 1260

Long-Term Potentiation in the Schaffer Collateral and Perforant Pathways Is Associative 1260

Long-Term Potentiation Has a Transient Early and a Consolidated Late Phase 1262

Genetic Interference With Long-Term Potentiation Is Reflected in the Properties of Place Cells in the Hippocampus 1264

Associative Long-Term Potentiation Is Important for Spatial Memory 1267

Is There a Molecular Alphabet for Learning? 1272

Changes in the Somatotopic Map Produced by Learning May Contribute to the Biological Expression of Individuality 1274

Neuronal Changes Associated With Learning Provide Insights Into Psychiatric Disorders 1275

An Overall View 1277

Selected Readings 1277

References 1277

Appendices

A Current Flow in Neurons 1280

John Koester

Definition of Electrical Parameters 1280

Potential Difference (V or E) 1280

Current (I) 1280

Conductance (g) 1281

Capacitance (C) 1281

Rules for Circuit Analysis 1282

Conductance 1282

Current 1283

Capacitance 1284	Clinical Vascular Syndromes May Follow Vessel Occlusion, Hypoperfusion, or Hemorrhage 1306
Potential Difference 1284	Infarction Can Occur in the Middle
Current Flow in Circuits With Capacitance 1285	Cerebral Artery Territory 1306 Infarction Can Occur in the Anterior
Circuit With Capacitor 1285	
Circuit With Resistor and Capacitor in Series 1285	Cerebral Artery Territory 1308
Circuit With Resistor and Capacitor in Parallel 1285	Infarction Can Occur in the Posterior Cerebral Artery Territory 1308
B Ventricular Organization of Cerebrospinal Fluid: Blood-Brain Barrier, Brain Edema, and Hydrocephalus	The Anterior Choroidal and Penetrating Arteries Can Become Occluded 1308 The Carotid Artery Can Become Occluded 1309
John Laterra, Gary W. Goldstein	The Brain Stem and Cerebellum Are Supplied by
Differentiated Properties of Brain Capillary Endothelial	Branches of the Vertebral and Basilar Arteries 1309
Cells Account for the Blood-Brain Barrier 1288	Infarcts Affecting Predominantly Medial or
Anatomy of the Blood-Brain Barrier 1288	Lateral Brain Stem Structures Produce Characteristic Syndromes 1311
Selectivity of the Blood-Brain Barrier 1289	
The Metabolic Blood-Brain Barrier 1293	Bilateral Brain Stem Lesions Can Have
Some Areas of the Brain Do Not Have a Blood-Brain Barrier 1293	Devastating Consequences 1312 Infarction Can Be Restricted to the Cerebellum 1313
Brain-Derived Signals Induce Endothelial Cells to	Infarction Can Affect the Spinal Cord 1313
Express Blood-Brain Barrier Properties 1293	Diffuse Hypoperfusion Can Cause Ischemia
Disorders of the Blood-Brain Barrier 1294	or Infarction 1313
Cerebrospinal Fluid Has Several Functions 1295	Cerebrovascular Disease Can Cause Dementia 1314
Cerebrospinal Fluid Is Secreted by the Choroid Plexus 1295	The Rupture of Microaneurysms Causes Intraparenchymal Stroke 1315
The Composition of Cerebrospinal Fluid May be Altered in Disease 1297	The Rupture of Saccular Aneurysms Causes Subarachnoid Hemorrhage 1315
Increased Intracranial Pressure May Harm the Brain 1298	Stroke Alters the Vascular Physiology of the Brain 1316
Brain Edema Is a State of Increased Brain Volume Due to Increased Water Content 1299	Selected Readings 1316
Hydrocephalus Is an Increase in the Volume of the	
Cerebral Ventricles 1299	D Consciousness and the Neurobiology
Selected Readings 1300	of the Twenty-First Century131
References 1300	James H. Schwartz
	Early Ideas About Consciousness Were Dualistic 1317
C Circulation of the Brain	The Modern View of Consciousness Arose in the Nineteenth Century 1317
The Blood Supply of the Brain Can Be Divided Into Arterial Territories 1302	Modern Thinking About Consciousness Is Materialistic 1318
The Cerebral Vessels Have Unique Physiological Responses 1305	Can Consciousness Be Explained? 1318
A Stroke Is the Result of Disease Involving	Selected Readings 1319
Blood Vessels 1306	Index 1321