COURSE BOOK

Introduction to natural sciences: Neuroscience

Academic year 2020–2021

МИНИСТЕРСТВО ОБРАЗОВАНИЯ И НАУКИ РФ
НАЦИОНАЛЬНЫЙ ИССЛЕДОВАТЕЛЬСКИЙ ТОМСКИЙ ГОСУДАРСТВЕННЫЙ УНИВЕРСИТЕТ
САЕ ИНСТИТУТ «УМНЫЕ МАТЕРИАЛЫ И ТЕХНОЛОГИИ»

INTRODUCTION TO NATURAL SCIENCES: NEUROSCIENCE
COURSE BOOK
ВВЕДЕНИЕ В НЕЙРОНАУКИ

Методическое руководство по курсу «Введение в естественные науки: нейронаука» для студентов автономной образовательной программы бакалавриата «Tomsk International Science Program» по направлению подготовки 27.03.05 Инноватика

Томск 2020

РАССМОТРЕНО И УТВЕРЖДЕНО методической комиссией САЕ Институт «Умные материалы и технологии»
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Председатель МК И.А. Курзина

Методическое руководство составлено в соответствии с тематикой семинарских занятий и программой курса «Введение в естественные науки: нейронаука» для студентов автономной образовательной программы бакалавриата «Tomsk International Science Program» (TISP) по направлению подготовки 27.03.05 Инноватика. Особое внимание уделено основным функциям отделов головного мозга и симптоматике патологических состояний и болезней ЦНС. Методическое руководство содержит кейсы для семинарских занятий, методические указания к их решению, а также их оценки с использованием рейтингового контроля.
Для студентов и слушателей курсов TISP, а также для студентов биологических и медицинских специальностей.

СОСТАВИТЕЛИ: Е.А. Соломина, И. А. Жукова, Х. Кингма

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1. GENERAL INFORMATION

1.1. Objectives

- To introduce the students to the field of neuroscience, the study of the nervous system.
- To provide fundamental basis of the anatomy, development, and physiology of the nervous system.

1.2. Overview

This course begins with the study of the nervous system structure, ranging from the macroscopical to microscopical level, and its development. This includes the aspects of neuron and synapse structure, membrane permeability, action potential generation and propagation, synaptic transmission, post-synaptic mechanisms of signal integration. You will learn to identify the major features of the brain and spinal cord and to understand the structural and functional relationships between these structures. Also included will be the psychological aspects of disorders associated with specific brain regions, including neurodegenerative diseases like Parkinson's disease and Alzheimer's disease.

1.3. Study material

Required literature

- *Books*

In this course we will make use of one course textbook, and several additional sources. The course book is **Principles of Neural Science – Kandel E.R., 5th edition.** This is a very good basic book, and we will be covering quite a large amount of the book throughout the course.

Other good sources of information are Neuroscience: Exploring the Brain (4th edition) by Bear, Neuroscience by Purves, Fundamental Neuroscience by Squire. These books cover the required content at a much more advanced level. For those who want to go a little deeper into the content, these are good sources. I would not advise purchasing these books. Tutors have electronic versions of them.

- *Articles*

Some tasks require also some specific readings that are not covered sufficiently in Handbooks. Therefore we will provide a selection of interesting articles via Moodle. Although textbooks are very valuable in providing a proper basic academic knowledge, articles provide an essential and indispensable addition.

Searching for your own literature

One important feature of PBL, is to let students select their own literature to a great extent. Throughout the course, I expect that you supplement the given literature with your own choice. In searching for literature, I would however like to urge you to carefully consider the selection you make. Literature ought to be trustworthy, of sufficient academic level, credible, relevant to the subject at hand and referenced when used. Some good sources are: Research Library of Tomsk State University Maastricht University Library, www.sciencedirect.com, www.pubmed.org etc.

- *Moodle*

Please check Moodle on a daily basis. There, study material such as PDF-copies of lectures and additional literature will be offered to the students. In addition, this is where changes to the schedule will be announced. Additional information concerning the content of the assignments and tasks will also be provided at Moodle.

1.4. Assessment

Summative assessment

Students will be assessed in two different manners. Students will have to make an oral presentation and to complete a written exam. At the beginning of the course, students will receive additional information concerning the assessments.

- *Oral presentation*

Each student will have to give an oral presentation that summary one case.
The grade of the presentation will count for **30%** towards your final grade.

- *Exam*

The exam will consist of 9 open questions, one per case. The exam will test both factual knowledge and insight into the material. The content of the cases as well as the lectures are part of the exam.
The grade of the exam will count for 70 % towards your final grade.

Formative assessment

- In order to be able to take the exam, student have to obtain not less than 170 points during the course, which include attendance of tutorials and lectures, active participation during tutorial, using correct terminology and additional sources for post-discussion;
- The group process and the functioning of the tutor will be evaluated at mid-term and at the end of the course by both students and tutors.
- The performance of the discussion leader and the scribe will be shortly evaluated at the end of each session.
- Peers and tutors will provide formative feedback on the presentation of one learning goal by individual students at every session.
- Peers and tutors will provide formative feedback on the final oral presentation of one case.

1.5. Attendance, Additional Assignments and Resit Policy

This course has an 85 % attendance requirement. Students must attend a minimum of 12 of the 14 tutorial meetings. If you cannot attend an individual session, please contact your tutor and e-mail your assignment (e.g. preparation for the PBL case) to your tutor and course coordinator. Students who have attended 11 meetings may apply for a compensation assignment according to MSC procedures. Please note that additional assignments are only granted when students have a *valid reason* for missing *all* meetings. Students who attend 10 meetings or less will fail the course.

When a student fails the course he or she is entitled to a resit on the exam if, and only if, they made a reasonable effort to pass the course. This means that if you do not show up for the exam, or do not hand in your essay, you are not allowed to take the resit.

1.6. Staff

Course coordinator

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Tutors

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2. CASES

Case1. How special is the human brain?

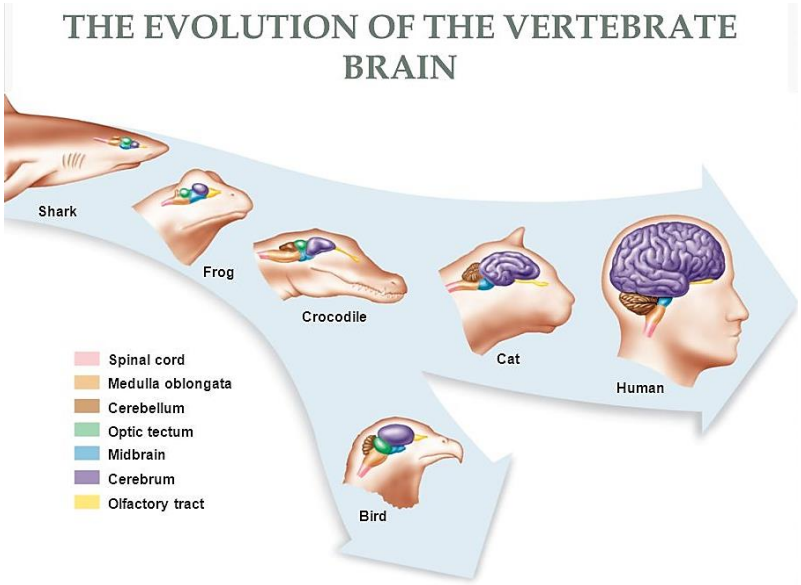
The first neurons were connected in a diffuse network across the body, forming nerve nets and ganglia. Later, groups of neurons began to appear – a central nervous system, consisting of the spinal cord and the brain. In the vertebrate animals, the brain is playing crucial roles in behavior. Although the structure and function of the brains are diverse, they are maintaining a lot of commonality. For example, the brains of vertebrates conserved the basic structures such as the forebrain (telencephalon and diencephalon), midbrain, and hindbrain in the early stage of evolution, and have changed the function of each region.

The relationship between brain size and body size is highly ordered. In most vertebrates, brain size varies approximately 10-fold, and brain size increases with body size, although this increase is not proportional. Among amphibians, frogs generally have relatively larger brains than salamanders, and the brains of reptiles are generally two to three times larger than the brains of most amphibians of the same body size.

Both birds and mammals have brains that are 6–10 times larger than the brains of reptiles of the same body size. Among birds, the largest brains for body size are seen in perching birds, woodpeckers, and parrots, while the relatively smallest brains are found in pigeons. Primates and cetaceans have the largest brains for their body size.

A progressive enlargement of the hominid brain led to a threefold increase in volume of human brain. The modern human brain came into existence in Africa by about 200,000 years ago. Many of the core structures such as amygdala, parts of the limbic system and basal ganglia found in human brain evolved. Different regions of the brain such, as cerebellum and cerebral cortex, have become specialised with functions.

Thus, in some cases selection may have acted for a change in body size, and the increased/decreased brain size may only reflect this general change. In other cases, a change in brain size may have been selected for directly, with little or no change in body size. In any case, when relative brain size has increased, what are the organizational consequences of that increase?



Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Chapter "The Organization of the Central Nervous System". 2013. P. 337.

2. Bear M.F., Connors B.W., Paradiso M.A. Neuroscience: Exploring the brain (4th edition), Chapter 7 as well as the appendix "The structure of the nervous system" Chapter 1 "Neuroscience: Past, Present, and Future" of the same book will give information about brain evolution.

3. The following link https://www.brainfacts.org/3d-brain#intro=false&focus=Brain is an interactive didactic website that students can explore to go insight into neuroanatomy of human brain.

Case 1. Post-discussion worksheet

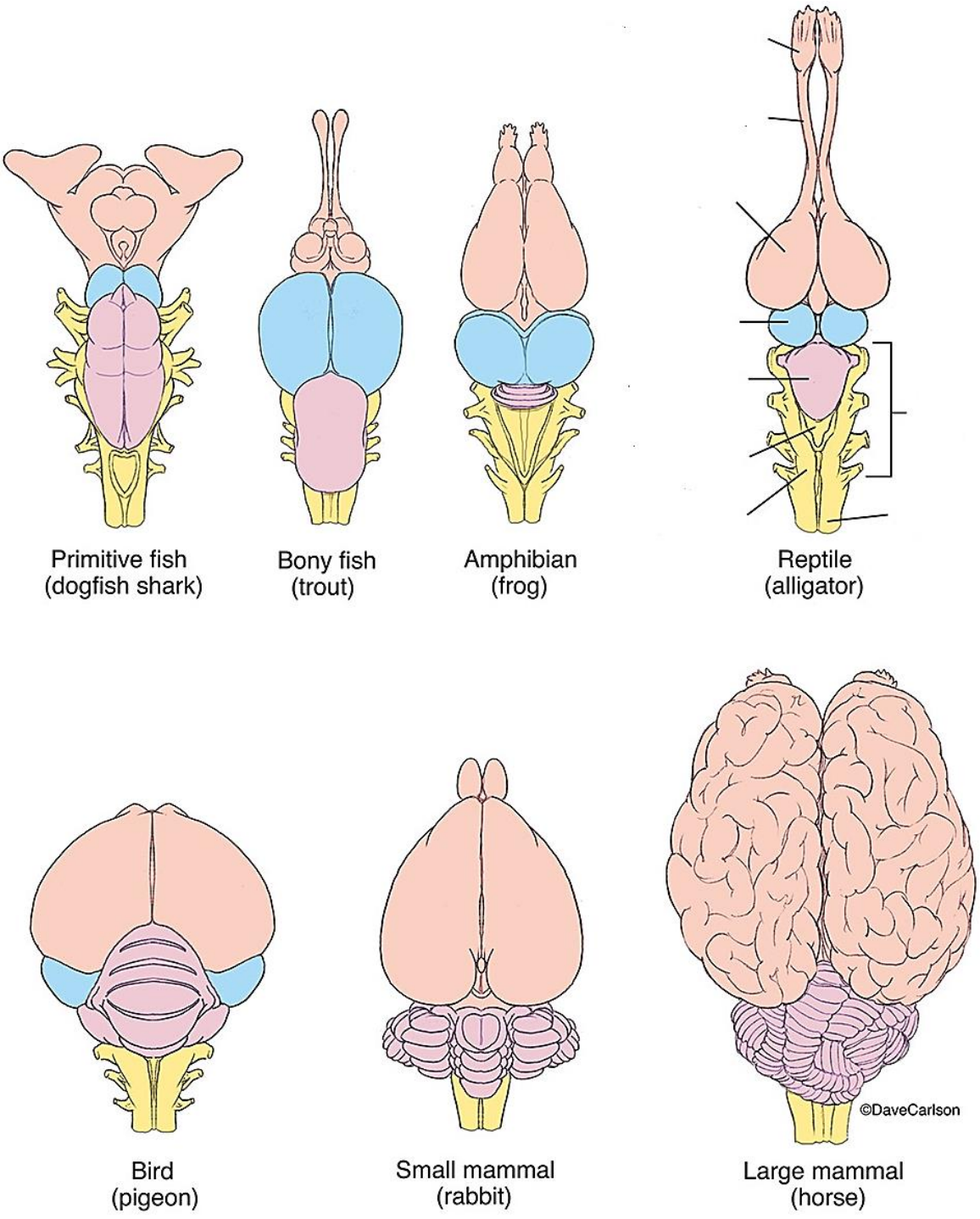


Fig. 1. Compare mammals. Name main divisions and components of the brains

Table 1

Fill in the table

Brain component	Brain division	Function
…	…	…

Case 2. The Brain's Forest

The discovery of the neuron was a milestone in brain research, and paved the way for modern neuroscience.

The Spanish neuroanatomist Santiago Ramón y Cajal (1852–1934) is considered the father of modern neuroscience, as important in his field as Charles Darwin or Louis Pasteur are in theirs. His discoveries, made during the last dozen years of the 19th-century, concern the way neurons, the building blocks of the brain, spinal cord and nervous system, communicate with one another. His theory – immediately accepted by most, but not strictly proven until the 1950s – was that neurons are in touch without touching. They communicate across infinitesimal gaps known as synaptic clefts. Through a chemical and electrical transmission, the single-stemmed axon of one neuron talks to the branched root-like dendrite of another. It is largely because of his work that the Neuron Doctrine eventually came to be accepted.

However, attempts at reconstructing a three-dimensional structure of the nervous system were frustrated by the impossibility of determining the exact relationships between cell bodies (somas), neuronal protoplasmic processes (dendrites) and nervous fibres. What do we know about neurons today? Are they the only type of cells of the nervous system?

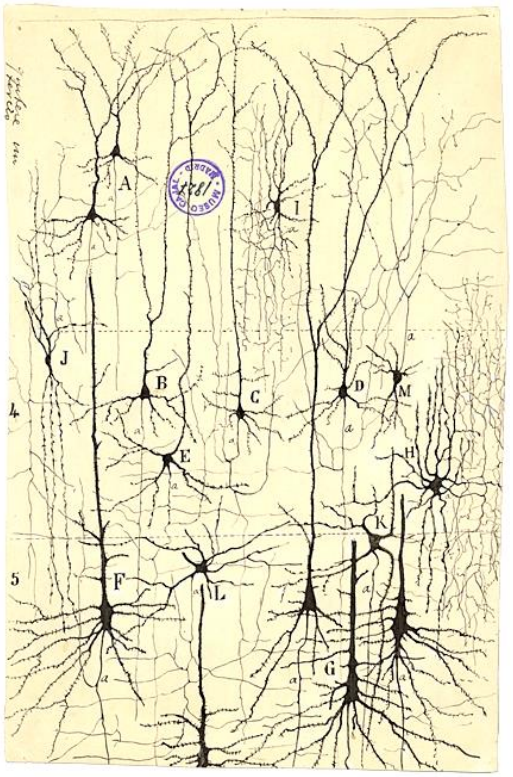


Fig. 2. Cajal's graceful drawings of neurons show them as separate, individual cells. He was the first to realize that the nervous system is not a network of continuous fibers, as was widely believed at the time

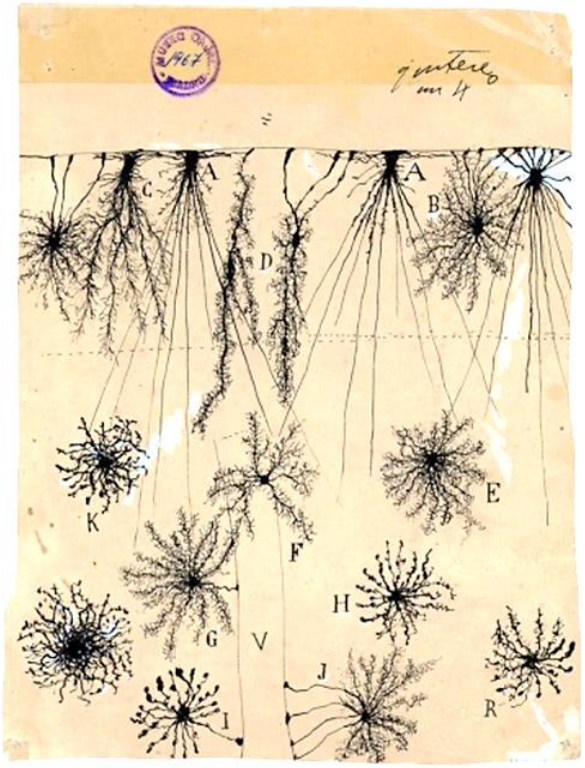


Fig. 3. Glial cells of the cerebral cortex of a child, a drawing from 1904.Credit: Cajal Institute, Madrid

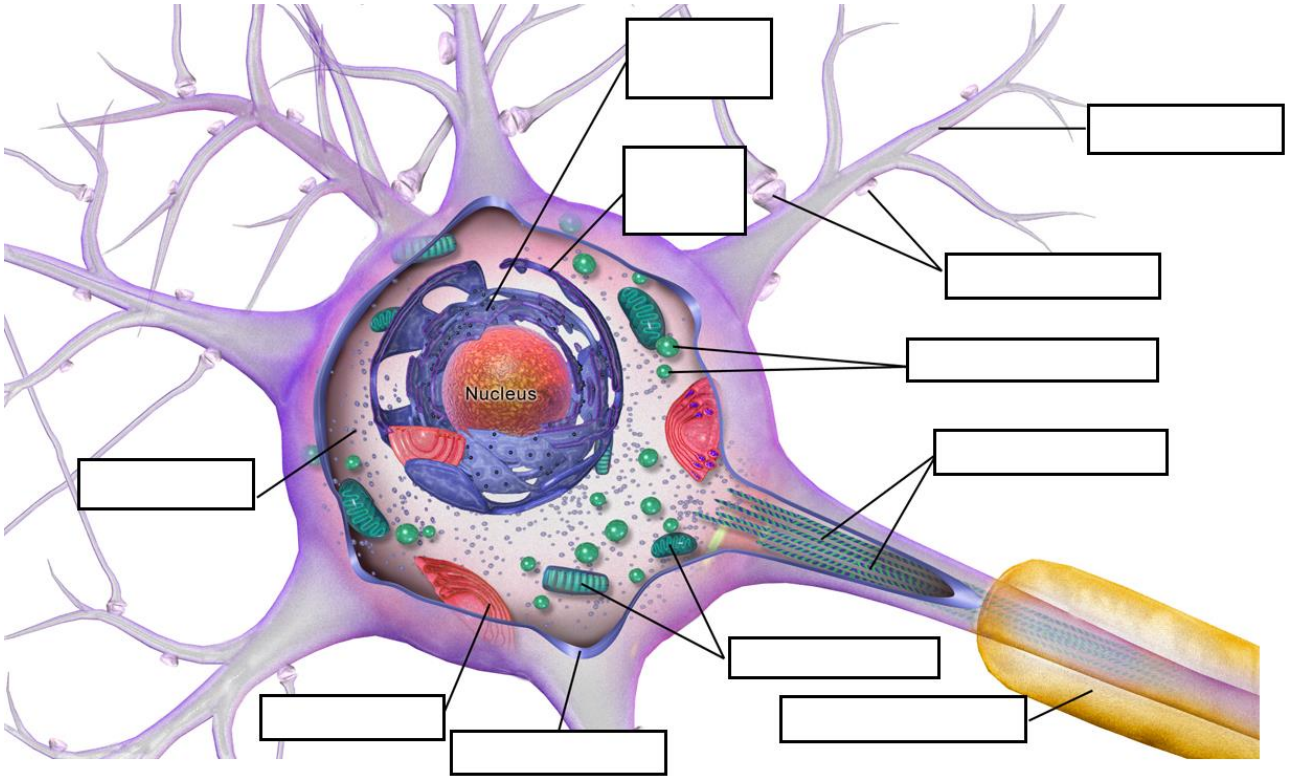


Fig. 4. Drawing of a 'typical' neuron. Fill in all the blank lines

Table 2

Types of neuronal cells and their functions. Fill in the table

Cell type	Function
Neuron	
Glial cells (Neuroglia)	

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science, Part II. Cell and Molecular Biology of the Neuron. 2013. Pp. 71–98; 5th ed. McGraw-Hill, New York.

2. Costandi M. The discovery of the neuron. Neurophilosopy. 2006. URL: https://neurophilosophy.wordpress.com/2006/08/29/the-discovery-of-the-neuron/

3. Mazzarello P. A unifying concept: the history of cell theory. Nature Cell Biology 1, E13–E15 (1999) doi:10.1038/8964

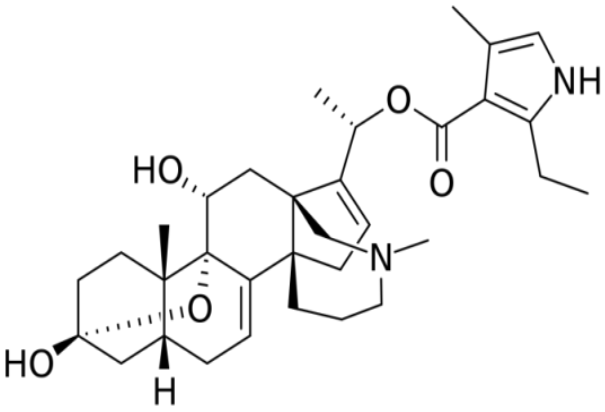
4. Molnar C., Gair J. Concepts of Biology – 1st Canadian Edition, 16.1 Neurons and Glial Cells, BC Open Textbooks.

Case 3. Neurotoxicity

After recovering from his tetrodotoxin (TTX) poisoning, Dr. Marshall Westwood decided to take a vacation. An avid birder, he decided to go to Papua New Guinea with Bill Whitlatch, an ornithologist friend of his from Montana Technical Institute.

Three days into their trip, Bill netted a bird with an orange body and black wings and head for closer study. Dr. Westwood was very curious and asked Bill if he could have a closer look at the bird. After handling the bird and later touching his mouth with his hand,

Dr. Westwood noticed that his fingers and lips were going numb. Luckily, the symptoms faded before they progressed into anything more serious. His friend Bill used a key to identify the animal as a pitohui. The pitohui are small, social songbirds that live in Papua New Guinea. They are generally about 23 centimeters long with strong legs and a powerful beak.



Homobatrachotoxin

Before releasing the bird, Dr. Westwood collected feather and tissue samples to bring back to the lab. After returning to Montana, he set out to isolate the toxic compound that he believed was being produced by the pitohui. It appeared that the active ingredient was a homobatrachotoxin. Homobatrachotoxin is a steroidal alkaloid (a molecule with a steroid structure) that is similar to batrachotoxin (BTX), the toxic principle of the Central American poison arrow frog Phyllobates aurotaenia. Batrachotoxin and homobatrachotoxin are both known to act on voltage-sensitive sodium channels in excitable tissues.

You and your colleagues received a call from Dr. Westwood asking if you could help elucidate the mechanism of action of this toxic compound. One of the hypotheses is that this toxin acts similarly to TTX.

In your first experiment, you generated action potentials in axons of large neurons obtained from squid in the presence of this new toxin. You found that after depolarizing, the membrane potential remained positive for an extended length of time and the repolarization was often extremely delayed. Draw a graph (membrane potential in mV vs. time) to illustrate this effect.

As you continued to experiment with higher concentrations of the toxin, you found cases when the cell could not repolarize at all, or if it began to repolarize, it would immediately depolarize again. Using this description and the description in the previous question, describe how this toxin acts on voltage-gated sodium ion channels.

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part II. Cell and Molecular Biology of the Neuron, Ion Channels. 2013. Pp. 100–171; 5th ed. McGraw-Hill, New York.

2. Molnar C., Gair J. Concepts of Biology – 1st Canadian Edition, 12.4 The Action Potential, BC Open Textbooks.

3. Raghavan M., Fee D., Barkhaus, P.E. Generation and propagation of the action potential. Handbook of Clinical Neurology. 2019. Pp. 3–22. doi:10.1016/b978-0-444-64032-1.00001-1

4. Lorentz M.N., Stokes A.N., Rößler D.C., Lötters S. Tetrodotoxin. Current Biology. 2016. 26(19), R870–R872. doi:10.1016/j.cub.2016.05.067

Case 4. Neurotransmitter diseases

Depression is highly prevalent worldwide and associated with significant morbidity and mortality. Approximately 340 million people worldwide suffer from depression at any given time. Based on estimates from the World Health Organization (WHO), depression is responsible for the greatest proportion of burden associated with non-fatal health outcomes and accounts for approximately 12% total years lived with disability. The exact causes of major depression are unknown and likely include both genetic and environmental risk factors. There are several classes of antidepressant medications that work through different mechanisms. For example, monoamine oxidase inhibitors (MAO inhibitors) block the enzyme that degrades many neurotransmitters (including dopamine, serotonin, norepinephrine), resulting in increased neurotransmitter in the synaptic cleft. Selective serotonin reuptake inhibitors (SSRIs) block the reuptake of serotonin into the presynaptic neuron. This blockage results in an increase in serotonin in the synaptic cleft. Other types of drugs such as norepinephrine-dopamine reuptake inhibitors and norepinephrine-serotonin reuptake inhibitors are also used to treat depression.

Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which cause unintended or uncontrollable movements of the body. The precise cause of PD is unknown, but some cases are hereditary while others are thought to occur from a combination of genetics and environmental factors that trigger the disease. At present, there is no cure for PD, but a variety of medications provide dramatic relief from the symptoms. Usually, affected individuals are given levodopa combined with carbidopa. Carbidopa delays the conversion of levodopa into dopamine until it reaches the brain. Although levodopa helps most people with PD, not everyone responds equally to the drug. Anticholinergic drugs may help control tremor and rigidity.

Alzheimer's disease (AD) is an age-related, non-reversible brain disorder that develops over a period of years. AD is one of a group of disorders called dementias that are characterized by cognitive and behavioral problems. AD ultimately leads to a severe loss of mental function. These losses are related to the worsening breakdown of the connections between certain neurons in the brain and their eventual death. It is the most common cause of dementia among people age 65 and older. Currently there are no medicines that can slow the progression of AD. However, four FDA-approved medications are used to treat AD symptoms. Donepezil (Aricept), rivastigmine (Exelon), and galantamine (Razadyne) are prescribed to treat mild to moderate AD symptoms. Donepezil was recently approved to treat severe AD as well. The newest AD medication is memantine (Namenda), which is prescribed to treat moderate to severe AD symptoms.

Why these diseases are called “neurotransmitter diseases”?

Table 3

Types of neurotransmitters and their functions. Fill in the table

Neurotransmitter	Type of neurotransmitter	Functions	Problems, caused by imbalance
…	…	…	…

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part III. Synaptic Transmission. 2013. Pp. 177–188, 289–305; 5th ed. McGraw-Hill, New York.

2. Kenhub anatomy tool. URL: https://www.kenhub.com/en/library/anatomy/neuro-transmitters

Case 5. Exploring the Interrelation between the Nervous and Muscular Systems

Kathy, a 20-year-old woman, awakens one morning to a tingling, numb sensation covering both of her feet. This has happened to her a number of times throughout the year. In the past, when experiencing this sensation, within a couple of days to a week the numbness would subside, and so she is not too concerned. About a week later, she notices that the numbness and tingling not only persists, but has also spread up to her knees. Again, she ignores the abnormal sensation. By the end of a month's time, the numbness spreads to the midline of her body. At this point, she becomes alarmed.

Kathy sees the nurse at her college who tells her that she should see a doctor. Kathy calls her doctor's office to schedule an appointment, but the soonest slot is in two weeks. She makes the appointment and goes about her daily routine.

The next morning, Kathy wakes, but when she attempts to get out of bed, she comes crashing to the floor. Because she is still groggy from sleep, she doesn't really understand what has just happened. As she tries to stand up, the muscles of her left leg engage, but as she also attempts pushing up with her right leg, she again falls to the floor. She sits in bewilderment as she tries to make sense of what has just happened and realizes that she has seriously scraped her knee in her fall. She does not feel the pain from her wound.

Kathy thinks about how odd this year has been. She remembers another medical issue she had earlier in the year when she had lost hearing in her right ear and wonders if there is a connection to her current condition. At that time, Kathy underwent extensive testing, but the ear, nose, and throat specialist remained baffled. He thought that a severe inner ear infection could have destroyed her ability to hear on that side, but there was no conclusive evidence to support this. In an attempt to recover any hearing he could, the doctor prescribed very high dosages of steroids; he told Kathy that she probably wouldn't see a change, but there were rare occurrences where steroids helped. To both Kathy and her doctor's surprise, after about a week of steroids, she completely regained hearing in her right ear. It was a "miracle."

Kathy wonders whether she can count on a new miracle to heal her current medical issues.

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part V. Perception, Sensory Coding. 2013. Pp. 456–473.
2. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part VI. Movement. Chapter 34. The Motor Unit and Muscle Action. 2013. Pp. 768–772.
3. Leddy S., Dobson R. Multiple Sclerosis, Medicine. URL: https://doi.org/10.1016/j.mpmed.2020.06.008
4. Dobsona R., Giovannoni G. Multiple sclerosis – a review // European Journal of Neurology. 2019, 26: 27–40, doi:10.1111/ene.13819
5. Kenhub anatomy tool. URL: https://www.kenhub.com/en/library/anatomy/the-myelin-sheath-and-myelination
6. Brain Facts. 8th edition. Chapters 11–15. Pp. 71–104.

Case 6. Perception I

Every day, you smell many things, like freshly baked cookies, stinky shoes, or smoke from a nearby fire. Have you ever wondered what life would be like without the sense of smell?

Sometimes in meetings we are asked to share a little-known fact about ourselves as an "icebreaker." (I hate icebreakers, by the way.) But my fact is always the same and I think it's pretty interesting: I can't detect odorants. Now, if I stick my nose right up to an open bottle of ammonia or acetone and snort, I can smell that, but that's pretty much all I can ever smell. If I ever had a sense of smell, I was too little to remember it, so it's not like I "remember" what oranges smell like or anything like that. I had surgery to remove some polyps (really gross) when I was in eighth grade, but all that resulted in was a completely random, gushing bloody nose that ruined my brand new Z-Cavaricci shirt in the middle of Mr. Zimmerman's science class. I had to go to the nurse and she gave me a replacement t-shirt from the lost and found. I still have that t-shirt actually; sometimes I wear it to bed. But anyway... It wasn't until college that I found out that this problem actually has a name: anosmia and it can be a sign of Parkinson's or Alzheimer's disease. I am afraid I might be at risks. Why this happened to me?

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part V. Perception, Smell and Taste: The Chemical Senses. 2013. Pp. 712–734; 5th ed. McGraw-Hill, New York.

2. Interactive web-site about brain and diseases. URL: https://www.brainfacts.org/thinking-sensing-and-behaving/smell/2016/smell-an-overview

Case 7. Perception II

Patient I. Frank is a 71-year-old, right-handed male. He has come to his doctor complaining of an increasing difficulty with recognizing familiar people, including family members. In one instance, a woman started a conversation with him on the street, and it was not until he recognized her voice that he realized she was an ex-wife of his and that they'd had a child! Frank was found to have normal visual acuity, and was referred to a neurologist and neuropsychologist team. After extensive testing, Frank's results were compiled. Here are some of them:

- Superior on both verbal and non-verbal abilities.
- Performed poorly on the object decision and silhouette tasks, but well on dot counting and other spatial tasks.
- Able to correctly perceive age, sex, and emotions in the faces. However, his matching performance was in the low to average range. It seemed he was most able to correctly match faces when focusing on specific features of each face (such as a mustache) and not the entire face.

Frank's overall language and executive functioning skills were normal, however.

Frank also showed a reduced ability to distinguish between famous and non-famous faces when shown photographs. He was only able to name four out of 40 celebrities by looking at their photographs.

Patient II. Laura has recently experienced what her doctors call a "bilateral posterior vascular abnormality." This resulted in some brain damage. While her rehabilitation has gone well, she has been left with some strange, specific visual difficulties.

As she described the problems to her doctors, Laura was clearly uncomfortable with the conversation. When asked why, she said, "I'm sorry, but it looks to me like your lips are just hopping up and down. It's very distracting. I hope you don't mind if I just close my eyes while we talk".

After being told that this was all right, Laura went on to tell of how she sometimes felt like she was a blind person. "I can't pour tea anymore unless I have my finger in the cup …

otherwise I can't tell when the tea has reached the rim and I end up with hot tea in my lap! If I watch it pour from the pot, all I see is something like an icicle that goes from the spout to my cup. And what's more, the tea doesn't look right anymore; everything is just yucky and colorless … a nasty grey".

When asked about her everyday life, Laura seemed quite dejected. "I can't go anywhere by myself. If I have to go where there are crowds of people I just feel like I'm in some kind of horror movie. People just disappear and suddenly reappear right in front of me … and I never see them move! It's terrifying! And what's more … I almost got run over by a car yesterday … Somebody had to grab me before I stepped out into traffic. I swear I thought they had all stopped!"

Standard neuropsychological testing yielded no deficits in her reading or writing abilities. She could recognize objects well, and showed no problems with complex movements.

Strangely enough, her world has also become "washed out" and "colorless." Not only did her tea look colorless, but people appeared to have nasty grey skin, foods were unappealing (everything appeared grey, dead, and tasteless), and she could no longer imagine things in color.

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part V. Perception, The Constructive Nature of Visual Processing. 2013. Pp. 556–564; Chapter "Low-Level Visual Processing: The Retina". Pp. 577–580; Chapter "Intermediate-Level Visual Processing and Visual Primitives". P. 619; Chapter "High-Level Visual Processing: Cognitive Influences". Pp. 624–626, 399–402; 5th ed. McGraw-Hill, New York.

2. Sacks O. The man who mistook his wife for a hat. A book with short real stories about deficits of perception; Picador, 2011; ISBN: 9780330523622.

3. The Brain from Top to Bottom: From Tought to Language. Broca's Area, Wernicke's Area, and Other Language-Processing Areas in the Brain. URL: http://thebrain.mcgill.ca/

After this case you will have a mid-term evaluation: an open test about previous cases and a feedback session.

Case 8. Movement Disorders I

The patient is a 65-year-old, right-handed male presenting with a 10-year history of tremor. He had tremor involving both hands and head, which he felt had progressed in severity over time. The tremors interfered with eating, drinking from a cup, and shaving. He noted some slowness in his gait and difficulty getting in and out of a car. His handwriting was shaky and had become smaller over time. His grandfather and uncle had experienced similar tremors; his uncle had been diagnosed with essential tremor. The patient had not received any treatment for this. Notable in the patient's past medical history were hyper-tension and gastroesophageal reflux disease. His medications included atenolol 25 mg QD for hypertension and metoclopramide 10 mg BID for gastroesophageal reflux. The latter condition was also managed with diet. The patient is allergic to penicillin. His patient's blood pressure was 104/67 and pulse was 68. The physical and neurological exam revealed mild masking of facial features with reduction in eye blink. The patient had a mild tremor involving his head and jaw, but no vocal tremor. There was a postural and intentional tremor involving the right greater than left upper extremity and the right foot, noted only while sitting. There was a mild resting tremor involving the right hand, most

pronounced with distraction. The patient had mildly increased muscle tone in the right upper extremity and bradykinetic rapid alternating movements. Finger taps, opening and closing hands, and heel taps were reduced in amplitude and speed, most notably in the right hand. Gait had a slightly stooped posture with a normal stance and stride, without arm swing. Pull test was negative. A writing sample (fig. 5) demonstrates notable tremor. There were no abnormal hand or arm postures during handwriting.

Fig. 5. Handwriting Sample and Spiral Drawing

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part VI. The Basal Ganglia. 2013. Pp. 982–998.

2. Lanciego J.L., Luquin N., Obeso J.A. Functional Neuroanatomy of the Basal Ganglia, s Cold Spring Harb Perspect Med, 2012, doi: 10.1101/cshperspect.a009621

3. URL: https://www.kenhub.com/en/library/anatomy/basal-ganglia

Case 9. Movement Disorders II

Kenny is a seemingly normal teenager, except for one thing: he experiences uncontrollable bodily and facial movements. At a young age, he started having “fits” of facial grimacing, frequent blinking, and lip puckering.

By the third grade, these were accompanied by various vocalizations; he would growl, snort, and grunt at odd times, or hum tunelessly for up to an hour. This was distracting both to his teacher and his class mates, and fairly distressing for both Kenny and his parents.

Kenny exhibited other odd behaviors. He would spin himself around and around (beginning slowly and then increasing in speed) until he was so dizzy he couldn’t stand. Often, he could not sit still for very long; at unexpected times he would throw himself out of his chair or off a bench for no apparent reason. He also had overriding compulsions to touch objects, including parts of his own body, over and over again. Along with these impulses, Kenny also continuously wrung and washed his hands. As he aged, he learned to resist these desires for a brief period of time, but often he just couldn’t help himself. Oddly enough, these desires seemed to increase whenever he was under stress, which, unfortunately, was frequently.

Not only did Kenny like to spin himself, he also was strangely attracted to spinning things. On more than one occasion he had run straight into a revolving door as he was trying to dodge in and out of it. He was musically talented, and was known in his high school jazz band for his strangely (and wildly) creative improvisations on the drums.

Much to Kenny's and his parents' relief, the movements, including the spinning, began to decrease in both severity and frequency when he entered adolescence. He would still jerk occasionally and shout at unexpected times, but things had improved. However, his compulsions to touch items and wash his hands remained unchecked.

At several points during his childhood, Kenny's doctors tried various pharmacological interventions. Clonidine, haldol, and pimozide had all been tried with varying success, but had side effects that worried both Kenny's parents and his doctors. Buspirone seemed to help with the hand wringing and hand washing, but not with the twitches and vocalizations. His doctors had also tried exposure therapy, which seemed to be the most effective in further reducing at least some of his strange movements.

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part VI. The Basal Ganglia. 2013. Pp. 991–998.

2. Shaw Z.A., Coffey J.B. Tics and Tourette Syndrome, Psychiatr Clin North Am. 2014. Sep; 37(3):269-86. doi: 10.1016/j.psc.2014.05.001

3. Tourette Association of America. URL: https://tourette.org

Case 10. Language. Louis and Gerald

Patient I. Mark is a right-handed man in his mid-50s who has recently suffered from a cerebrovascular accident (CVA). This has left him with a right-sided hemiparesis (weakness) and significant language issues. In particular, Louis's right arm and hand were too weak to grasp anything.

During the first week after his CVA, Louis was unable to utter more than single words. This was incredibly frustrating for him, but he was able to communicate using Scrabble tiles (he could spell out nongrammatical and misspelled sentences of three or four words). He appeared to understand what was being said to him, and his communications did answer inquiries, although they were very sparse and lacking in "smoothness" (he often sounded like Tarzan when he spoke).

Over the next few weeks, his speech improved slightly although it was still clearly very difficult for him. He was able to articulate short sentences with few function words, but his prosody was lacking. When Mark spoke, he sounded like a robot (lacking in emotional tone) no matter what he said. He could, however, repeat simple sentences spoken to him.

Patient II. James is a 60-year-old right-handed man who has suffered a medial cerebral artery infarction that initially resulted in a severe expressive aphasia and right-sided hemiparesis (weakness). After one year of speech therapy, his articulation improved, although it was still somewhat labored. In addition to this, he was severely impaired in his ability to name objects. When confronted with pictures, he was only able to name 47 out of 114 pictures. However, he was significantly better at reading words and sentences aloud. He showed no signs of paraphasia (inappropriate word substitutions), and his writing was only mildly impaired.

Here is an example of a conversation between James and his doctor:

Doctor [holding up a coffee cup]: Can you tell me what this is?

James: Oh, you know … isn't that funny, oh I know, it's one of those things, … geez … it's something that you hold, right? … Uhmm … it holds stuff …

Doctor [now showing a pencil]: How about this?

James: Um … ok … I know what that is … isn't it something you use to … you know … oh darn it … you use it to write, I think … It's one of those things that … Ugh! … I must be getting old.

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part IX. Language, Thought, Affect, and Learning. 2013. Pp. 1353–1373; 5th ed. McGraw-Hill, New York.

2. The Brain from Top to Bottom: From Tought to Language. Broca's Area, Wernicke's Area, and Other Language-Processing Areas in the Brain. URL: http://thebrain.mcgill.ca/

Case 11. Addiction and withdrawal

You and your roommates have decided to go to a fraternity party on Saturday night. You arrive at the fraternity house and see another classmate, Jenn, from your psychology class. You go over to say hello and see what she thought of the first exam, but Jenn seems to be acting very strangely. She starts describing fantastic colors made by the lights and how the dance floor is a beautiful sea of diamonds. You take a look around and realize the lights are nothing special, while the floor is definitely made of wood. You take another look at Jenn; her pupils are dilated and she keeps hugging everyone. When she comes over to hug you and tell you how much she's missed you since yesterday, you observe that Jenn is sweating and clenching her teeth. Additionally, you can feel her heartbeat when she makes contact with you. What drug has Jenn taken?

Table 4

Major classes of Addictive drugs. Fill in the table

Class of drugs	Molecular target (Receptors)	Drug examples
…	…	…

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part VII. The Unconscious and Conscious Processing of Neural Information, Homeostasis, Motivation, and Addictive States. 2013. Pp. 1101–1113.

2. The web-site of the National Institute on Drug Abuse. URL: https://www.drugabuse.gov/

Case 12. Learning and memory

A new drug for restoring memory functions in patients with severe dementia has been designed in the research group, where you have just started your internship. Your supervisor asked you to design experiments and test the drug, first, *in vitro* and then, *in vivo.* You chose hippocampal neuronal cell culture for the in vitro experiment to access synaptogenesis of neurons, treated by new drug. Before the next meeting with your supervisor, you have to choose read-out parameters for the experiment and be able to convince your supervisor why they are crucial.

You still have to decide which animal model to choose for behavioral testing since you are not sure whether working memory, short-term and long-term memory processing are the same in humans and animals.

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part IX. Language, Thought, Affect, and Learning, Learning and memory, Homeostasis,

Motivation, and Addictive States. 2013. Pp. 1441–1459; Cellular Mechanisms of Implicit Memory Storage and the Biological Basis of Individuality. Pp.1461–1485.

Case 13. Cognition

You wonder how much animals understand what they really do, and if they really can think. But very fast you focus on how that is in humans: what kind of mental action or process is active to acquire knowledge and understand our own thinking, experiences and perceptions and to control motoric activity. What is thinking anyway? How do the chemical and electrical signals produced by neurons in the brain give rise to cognitive processes, such as perception, memory, understanding, insight, and reasoning? Which regions in the brain are involved with cognition and how do they work together? By the way what is cognition really? And is there a specific topography of functional related areas regarding cognition? What is the difference to this respect between the primary, secondary and tertiary cortex? What information reaches our consciousness mind, what remains unconscious and why? Do we use also unconscious information to feed cognition?

Literature:

1. Kandel E.R., Schwartz J.H., Jessell T.M. Principles of Neural Science. Part IV. The Neural Basis of Cognition. 2013. Pp. 338, 392–410; 5th ed. McGraw-Hill, New York.

2. Robbins T.W. Cognition: The Ultimate Brain Function, Neuropsychopharmacology Reviews (2011) 36, 1–2; doi:10.1038/npp.2010.171

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