

Please check the examination details below before entering your candidate information

Candidate surname

Other names

Centre Number

Candidate Number

**Pearson Edexcel International Advanced Level**

**Monday 5 June 2023**

Morning (Time: 1 hour 45 minutes)

Paper  
reference

**WBI15/01**

**Biology**

**International Advanced Level**

**UNIT 5: Respiration, Internal Environment,  
Coordination and Gene Technology**

**You must have:**

Scientific article (enclosed), scientific calculator, ruler, HB pencil

Total Marks

## Instructions

- Use **black** ink or ball-point pen.
- **Fill in the boxes** at the top of this page with your name, centre number and candidate number.
- Answer **all** questions.
- Answer the questions in the spaces provided  
– *there may be more space than you need.*
- **Show all your working out** in calculations and **include units** where appropriate.

## Information

- The total mark for this paper is 90.
- The marks for **each** question are shown in brackets  
– *use this as a guide as to how much time to spend on each question.*
- In questions marked with an **asterisk** (\*), marks will be awarded for your ability to structure your answer logically, showing how the points that you make are related or follow on from each other where appropriate.

## Advice

- Read each question carefully before you start to answer it.
- Try to answer every question.
- Check your answers if you have time at the end.

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Answer ALL questions. Write your answers in the spaces provided.

Some questions must be answered with a cross in a box ☒. If you change your mind about an answer, put a line through the box ☒ and then mark your new answer with a cross ☒.

1 The human eye responds to different light intensities.

(a) The table shows the mean pupil diameter in different light intensities.

Light intensity	Pupil diameter / mm
bright light	3.35
normal room light	3.86
darkness	6.41

Calculate the percentage increase in the mean diameter of the pupil when a person moves from bright light into darkness.

(1)

Answer .....%

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(b) During the fight or flight response the pupils of a person increase in diameter.

(i) Which is the name of the hormone involved in the fight or flight response?

(1)

- A adrenaline
- B antidiuretic hormone
- C thromboplastin
- D uracil

(ii) Describe how this change in diameter is brought about by the muscles of the iris.

(3)

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**(Total for Question 1 = 5 marks)**

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2 Many of the metabolic processes taking place in cells require ATP.

(a) The electron transport chain (ETC) is involved in the production of ATP.

(i) Where is the site of the electron transport chain?

(1)

- A** cytoplasm
- B** inner mitochondrial membrane
- C** mitochondrial matrix
- D** outer mitochondrial membrane

(ii) Enzymes are involved in the production of ATP by the electron transport chain.

Which type of molecule is an enzyme?

(1)

- A** carbohydrate
- B** lipid
- C** phospholipid
- D** protein



(iii) Describe the role of reduced NAD in aerobic respiration.

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(b) Carbon monoxide and cyanide affect the production of ATP.

(i) Carbon monoxide binds to the haem group of haemoglobin.

Explain how carbon monoxide will affect the production of ATP.

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(ii) Cyanide stops the transfer of electrons along the electron transport chain.

Explain why cyanide does not affect the production of ATP from anaerobic respiration.

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3 The ventilation rate of animals will depend on many factors.

(a) State **two** lung conditions that affect the ventilation rate of a human.

(2)

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(b) The table shows the mean resting ventilation rate of five species of animal.

Animal	Body mass / kg	Resting ventilation rate / breaths per second
Talapoin monkey	1.3	$0.54 \pm 0.09$
Ring-tailed lemur	2.9	$0.53 \pm 0.04$
Crested porcupine	20.0	$0.30 \pm 0.03$
Siberian tiger	134.0	$0.27 \pm 0.06$
Hippopotamus	2210.0	$0.12 \pm 0.03$

(i) Comment on the relationship between the mean resting ventilation rate and the body mass of animals.

(3)

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(ii) The tidal volume for a resting talapoin monkey was found to be  $40 \text{ cm}^3$ .

The minute ventilation is the volume of gas inhaled or exhaled from the lungs in one minute.

Calculate the respiratory minute ventilation for a resting talapoin monkey.

Give your answer in  $\text{dm}^3$  to **two** significant figures.

(2)

.....  $\text{dm}^3$

(c) An increase in activity level results in a change in the ventilation rate.

Describe why this change occurs and how it is controlled.

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4 Movement in mammals results from interactions between muscles, tendons, ligaments and bones.

(a) How many of the following statements about tendons are correct?

(1)

- tendons act as extensors
- tendons are myogenic
- tendons connect muscles to bones

- A** 0
- B** 1
- C** 2
- D** 3

(b) The photograph shows part of a skeletal muscle fibre as seen using an electron microscope.



P Q RS T U

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(i) Which pair of letters represents the length of one sarcomere?

- A** P to T
- B** P to U
- C** Q to T
- D** R to S

(ii) Calculate the magnification of this image.

Give your answer in standard form.

(2)

Answer .....

(iii) Describe how the structure of a fast twitch muscle fibre differs from a slow twitch muscle fibre.

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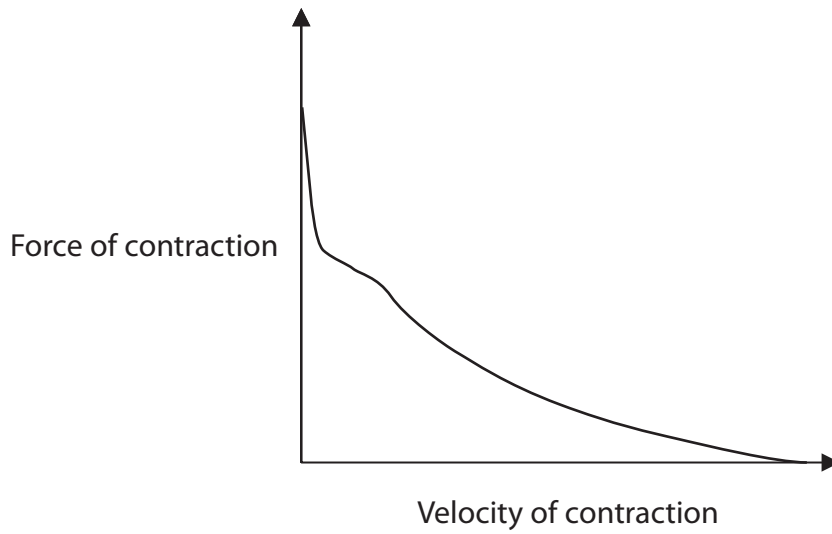
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(c) The graph shows the relationship between the force of muscle contraction and the velocity of muscle contraction.



The greater the number of cross bridges formed between actin and myosin the greater the force of contraction of a muscle.

Explain the relationship between the force and the velocity of contraction of a muscle.

(3)

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5 The kidney is an organ that is involved in osmoregulation and the production of urine.

(a) (i) Which substances are filtered from the blood in the Bowman's (renal) capsule of a healthy individual?

(1)

- A glucose and prothrombin
- B glucose and urea
- C glycogen and urea
- D urea and prothrombin

(ii) Which part of the Bowman's (renal) capsule prevents plasma proteins from being filtered out of the bloodstream?

(1)

- A basement membrane
- B smooth muscle of the capillaries
- C epithelial cells of the collecting duct
- D epithelial cells of the loop of Henlé

(iii) Which transport mechanism is responsible for the uptake of glucose into the cells of the proximal tubule?

(1)

- A endocytosis
- B exocytosis
- C osmosis
- D sodium co-transport



(b) Describe how the loop of Henlé acts as a countercurrent multiplier.

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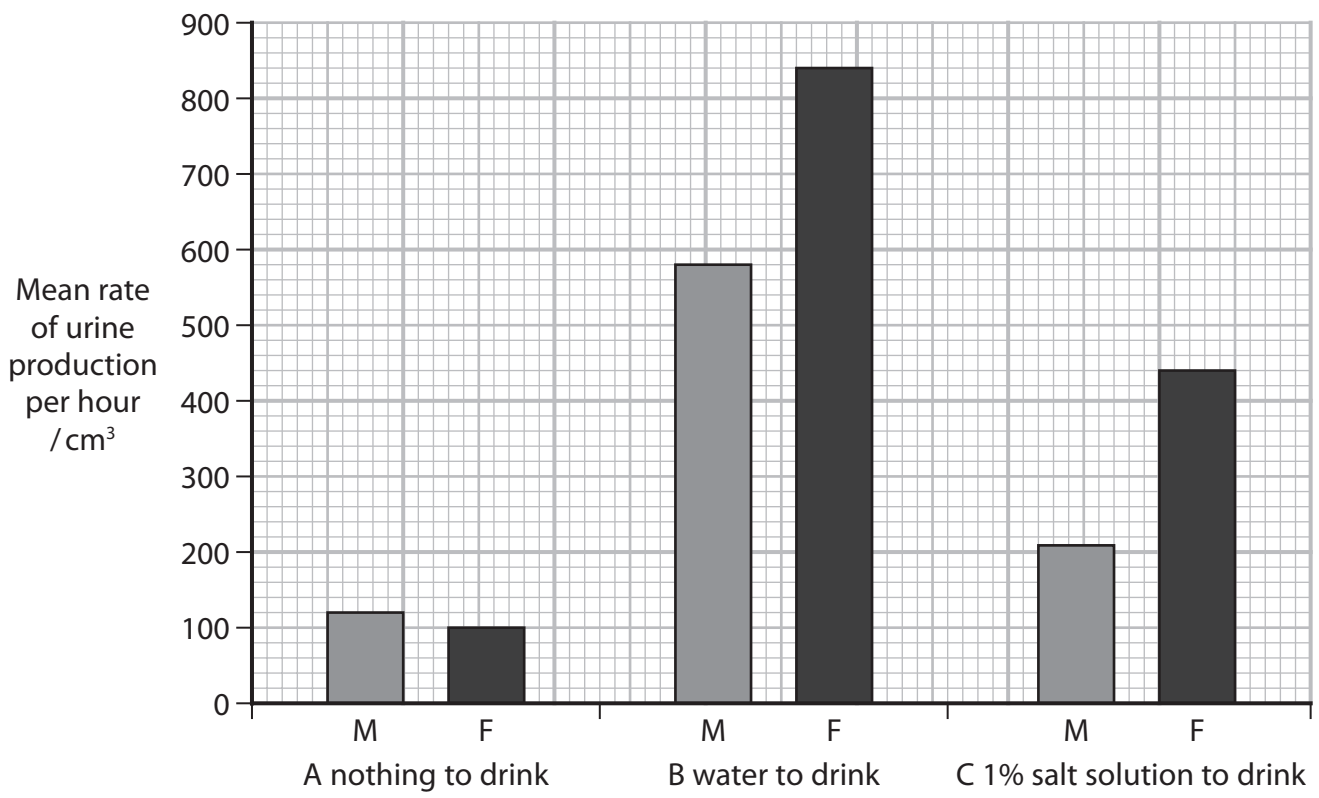
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(c) In an investigation, one group of people was given nothing to drink, a second group was given water and the third group was given 1% salt solution to drink.

The mean rate of urine production was recorded for the males and females in each group.

The graph shows the results of this investigation.



(i) Calculate the ratio of the mean rate of urine production for the females in the three groups.

Express your answer as nothing to drink:water to drink:salt solution to drink.

Give your answer to one significant figure.

(2)

Answer .....





(ii) Describe **two** conclusions that can be drawn from the results of this investigation.

(2)

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(iii) Explain the effect on the mean urine output of the group drinking water.

(2)

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6 The concentration of ions in the blood is controlled by homeostasis.

(a) Explain how ions can cross the cell membrane.

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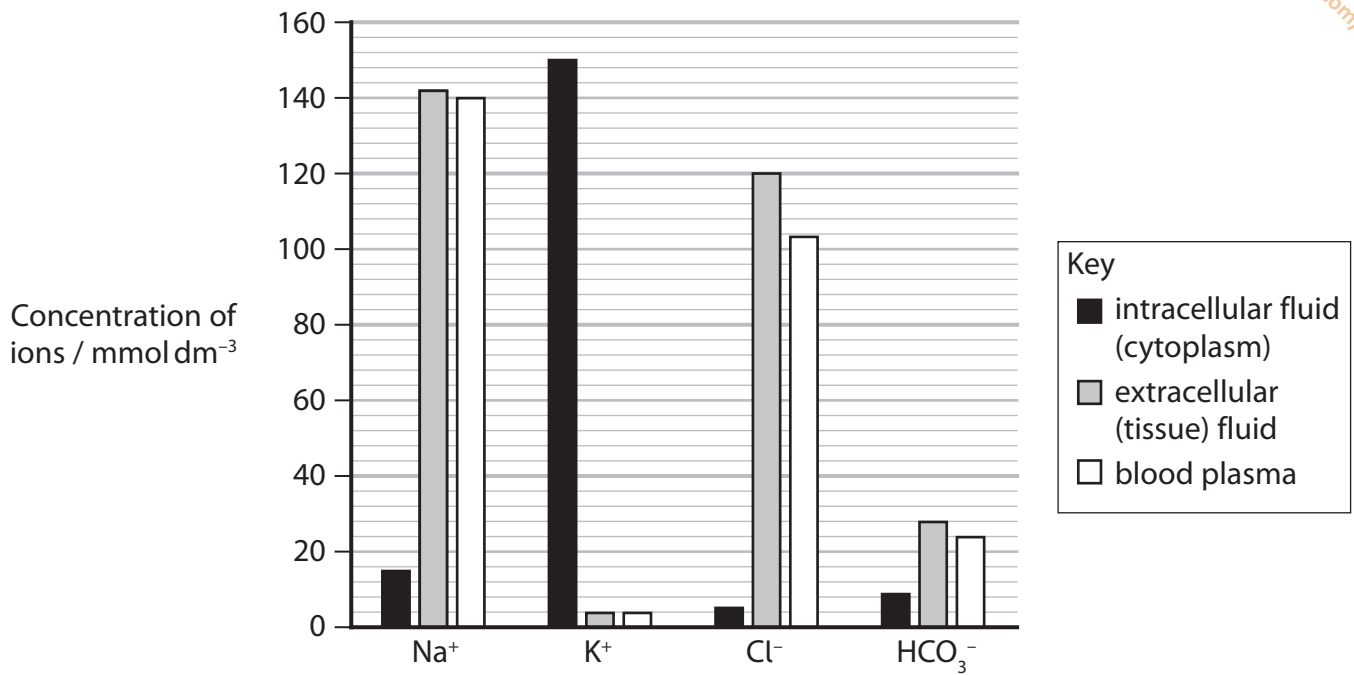
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\*(b) Ions are found within fluids in the human body in different concentrations.

The graph shows the concentration of ions in intracellular fluid (cytoplasm), extracellular (tissue) fluid) and blood plasma.



The ions are used to perform vital functions within the metabolism of the cells.

Discuss how the distribution and concentrations of the ions shown in the graph contribute to their biological roles.

Use the information given in the graph and your own knowledge to support your answer.

(6)

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(Total for Question 6 = 9 marks)



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7 Serotonin is produced by neurones in the brain.

(a) How many of the following statements about serotonin are correct?

(1)

- L-dopa can be converted into serotonin in the brain
- Serotonin is a neurotransmitter
- Serotonin is produced by post-synaptic neurones

- A** 0
- B** 1
- C** 2
- D** 3

(b) There are 14 different serotonin receptors found in the human nervous system.

Three different genes are used to produce these receptors.

Explain how three genes can produce 14 different receptors for serotonin.

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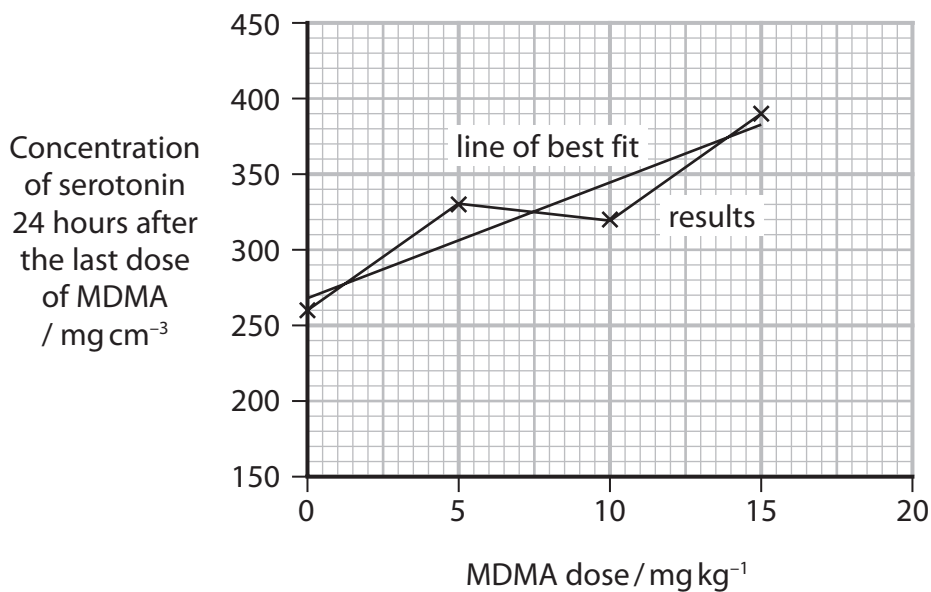
(c) The effect of MDMA (ecstasy) on serotonin concentration in rats was investigated.

Rats were given different concentrations of MDMA by mouth twice daily for a week.

The concentration of serotonin in the cerebrospinal fluid of the rats was analysed 24 hours after the last dose of MDMA.

Cerebrospinal fluid is fluid that surrounds the brain and spinal cord.

The graph shows the effect of MDMA on the concentration of serotonin and a line of best fit is shown on the graph.



(i) Determine the effect of MDMA on the serotonin level in the cerebrospinal fluid.

(2)

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(ii) Predict the concentration of serotonin for a dose of  $17.5 \text{ mg kg}^{-1}$  of MDMA.

Use the line of best fit.

Give your answer in  $\text{g cm}^{-3}$ .

(2)

.....  $\text{g cm}^{-3}$

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8 The scientific document you have studied is adapted from the article 'Microbiota-gut-brain axis and the central nervous system' by Xiqun Zhu, Yong Han, Jing Du, Renzhong Liu, Ketao Jin and Wei Yi in *Oncotarget* (2017).

Use the information from the article and your own knowledge to answer the following questions.

(a) "Gut microorganisms play an important role... affecting human metabolic functions by decomposing the complex polysaccharides in food".

Explain the role of gut microorganisms in decomposing complex polysaccharides (paragraph 2).

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(b) Describe how the vagus nerve is involved in the control of heart rate (paragraph 6).

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(c) "Microorganisms can also enhance the anti-tumor immune effect of drugs by promoting T cell accumulation and transformation."

Explain how microorganisms promote the accumulation of mature T-killer cells that enhance the anti-tumour effects of drugs (paragraph 7).

(3)

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(d) Describe how fMRI scans could be used to show the activity of the regions of the brain controlling memory and sensation when probiotics are consumed (paragraph 11).

(2)

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(e) Suggest how changes in diet could affect the composition of the gut flora causing imbalances in the naturally occurring chemicals in the brain (paragraph 10).

(3)

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(f) "Multiple sclerosis (MS) is a... demyelinating disease of the nervous system" (paragraph 14).

Symptoms of MS include poor coordination and loss of vision.

Explain how demyelination could result in these symptoms.

(2)

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(g) Gut microorganisms produce LPS (paragraphs 15 and 17).

White blood cells have receptors for LPS on their cell surface.

Describe the techniques that could be used to identify the LPS receptor gene found in white blood cells.

(3)

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**(Total for Question 8 = 20 marks)**

**TOTAL FOR PAPER = 90 MARKS**



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# Pearson Edexcel International Advanced Level

**Monday 5 June 2023**

Morning (Time: 1 hour 45 minutes)

Paper  
reference

**WBI15/01**

## **Biology**

**International Advanced Level**

**UNIT 5: Respiration, Internal Environment,  
Coordination and Gene Technology**

**Scientific article for use with Question 8**

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## Microbiota-gut-brain axis and the central nervous system

### Gut microorganisms

1. The human gut contains various microorganisms, such as bacteria, fungi, parasites, and viruses, and more than 100 million bacteria reside in human gastrointestinal tract, which is 10-100 times the number of eukaryotic cells in our body. After years of common development with the human body, the gut bacteria have reached a mutually beneficial symbiotic state with the human body.
2. Gut microorganisms play an important role in promoting adult development and homeostasis; for example, they can affect human metabolic functions by decomposing the complex polysaccharides in food. In addition, gut microorganisms can regulate gut movement, the gut barrier system and fat distribution. Gut microorganisms can affect immune function through the development of gut-associated lymphoid tissue and by preventing the colonization of pathogens, and they can affect the energy metabolism and mitochondrial function of the host. The intricate relationship governing host and microorganism interactions suggest that when this relationship is abnormal, the microorganisms may cause the pathogenesis of disease or promote the progression of disease. Therefore, recent research has focused on determining the diversity of these microorganisms to clarify the physiological roles they play and eventually to prevent and treat diseases by controlling the microorganism species.
3. There are three main methods for detecting gut microorganisms: the bacteria culture technique, the traditional molecular biology technique that is independent of culture, and high-throughput sequencing technology. The former is mainly used for stool culture, this method is time-consuming, and the bacterial species obtained are limited. The latter two mainly isolate the bacterial DNA from the stool for the detection, the detection is fast, and the bacterial species are complete.

### Microbiota gut-brain axis

4. The central nervous system (CNS) is closely related to the gastrointestinal tract, and the CNS plays an important role in regulating gut function and homeostasis. In turn, the gut flora may affect the CNS and nerve cells, participate in the regulation of nervous system function, affect the pathogenesis and progression of nervous system-related diseases. Due to the complex relationship between the gut microorganism population and the host, the authors proposed a new concept: the microbiota gut-brain axis. The microbiota gut-brain axis is the focus of recent research on the gut microecology. In addition to studies of the relationship between the gut microecology and neurological function, recent studies have emphasized how this relationship affects human health.
5. The brain and gut can be connected through a variety of pathways, including the enteric nervous system (ENS), vagus nerve, the immune system, or the metabolic processes of gut microorganisms.
6. The vagus nerve of the body can control the function of multiple organs, such as heart rate and gut motility; the vagus nerve can also transmit peripheral immune signals to the CNS. The vagus signal from the gut can trigger an anti-inflammatory response against the sepsis induced by microorganisms. Gut microorganisms can affect brain functions through the vagus nerve; after a vagotomy, the microorganisms will not be able to regulate behaviors.



7. Because gut microorganisms can directly affect the immune system, immune activation may be the pathway for transmitting microbial actions to the CNS. Microorganisms can also enhance the anti-tumor immune effect of drugs by promoting T cell accumulation and transformation, and microorganisms are very important for the immune function of organisms. The immune system plays an important role in maintaining health by maintaining gut homeostasis.
8. Microorganisms can also cause neurophysiological changes in the host by producing chemical substances that bind to the receptors inside and outside of the gut.
9. In addition, studies have shown that the microbiota may affect the CNS by altering adult hippocampal neurogenesis (AHN). The adult hippocampus and lateral ventricle have the function of generating new neurons. AHN has a role in learning and memory and can have affect on the pathogenesis of many neurological disorder-related diseases and symptoms, such as epilepsy, depression, Alzheimer's disease (AD), and Parkinson's disease (PD).

### **Microorganisms and brain function**

10. The impact of microorganisms on behavior and cognition has been increasingly recognized. Microbial signals can regulate important functions of healthy human bodies, and growing evidence has demonstrated that many diseases are due to disturbances of gut microorganisms. Early studies in animals showed that the introduction of single, unique flora could lead to the development of anxiety-like behavior, and this change was accompanied by the activation of neurons in the brain that relied on the gut information transmitted to the brain via the vagus nerve.
11. The change in gut microorganisms found in sterile animals or with the use of probiotics, antibiotics, and colonization with fecal microorganisms can influence the cognitive function of the host. For example, supplementation with probiotics for a week prior to infection can not only prevent the microorganism disturbance caused by the infection but also prevent the changes in cognitive behavior caused by stress. Liang et al. found that probiotics could significantly improve the cognitive dysfunction induced by chronic restraint stress. In a human experiment, fMRI tests found that the activities in the brain regions that control brain memory and the processing of sensation were altered after female volunteers consumed fermented milk that contained probiotics. The above various studies found that the stability of the equilibrium state of normal microorganisms in the gut was closely related to brain development and function.

### **Microbiota-gut-brain axis and neuropsychological disorders**

12. Schizophrenia is a neuropsychological disorder, and whole-genome analysis suggests that immunity-related genes may be changed in schizophrenia patients. Microorganisms and intestinal mucosal cells can regulate the changes in chemical factors, such as the proinflammatory interleukin-8 (IL-8) and IL-1 or the anti-inflammatory IL-10 and transforming growth factor  $\beta$  (TGF $\beta$ ). The serum levels of proinflammatory cytokines in schizophrenia patients are higher than those of normal controls, and the levels of serum inflammatory markers are positively correlated with the clinical symptoms of schizophrenia patients.

13. Gut bacteria can also produce harmful substances that damage the intestinal epithelial barrier, causing neurotoxic bacterial products and proteins to enter the circulatory system. Severance et al. found that the concentration of antibodies against *Saccharomyces cerevisiae* was higher in the body of schizophrenia patients, and this genus was a marker of gut inflammation. An increase in the levels of circulating pathogen antigen can cause the host to respond to its own tissues and cells through a form of molecular induction, and this response is the central process of autoimmune diseases. Compared with the normal population, schizophrenia patients have a higher probability of developing autoimmune disorders, and specific brain regions of schizophrenia patients, such as the hippocampus, amygdala, and frontal cortex, have higher levels of autoimmune antibodies.

### **Microbiota-gut-brain axis and neurodegenerative diseases**

14. Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the nervous system, and its etiology is still unclear. MS is associated with a significant increase in the number of cells that have immune response to the patients' own nervous system because gut microorganisms play an important role in the development of the autoimmune system and are associated with a variety of autoimmune and metabolic diseases. Therefore, it is speculated that gut symbiotic microorganisms play an important role in the susceptibility to MS.

15. Proinflammatory factors associated with chronic bowel diseases can induce intracranial inflammation, lead to the death of dopaminergic neurons, and eventually cause the development of PD. The inflammatory changes observed in PD patients and PD animal models are associated with increased gut permeability. LPS is a gut-derived proinflammatory bacterial endotoxin that can cause changes in the substantia nigra, and it can act as a PD-promoting substance. Similarly, Keshavarzian A et al. used high-throughput sequencing technology to examine the stool samples from 38 PD patients and 34 healthy individuals, and they found that the LPS synthesis gene was significantly higher in PD patients than in normal controls.

16. AD is a degenerative disease of the CNS, its onset is recessive, and its disease course is chronically progressive. The pathological markers of AD include extracellular  $\beta$ -amyloid ( $A\beta$ ) senile plaques and intracellular neurofibrillary tangles. The number and maturation of microglial cells in sterile mice are abnormal, resulting in damage to the immune system and ultimately leading to the development of neurological diseases, such as AD. Cognitive behavior impairment is a characteristic of AD patients, and the influence of gut microorganisms on cognitive behavioral capability has demonstrated the role of gut microorganisms in the pathogenesis of AD.

17. The integrity of the BBB is important for brain function and development. The inflammation caused by the changes in gut microorganisms will lead to changes in BBB integrity, which in turn affects brain function. Under normal conditions, LPS cannot enter the bloodstream due to the tight junction between intestinal epithelial cells. However, when the tight junction of cells is disrupted and the permeability is increased, LPS can enter the bloodstream and induce inflammatory response. Studies found that the plasma LPS concentration in AD patients is three times that of normal patients. Furthermore, intraperitoneal injection of LPS into mice can cause an  $A\beta$ -protein increase in hippocampus, cognitive defects, and memory impairment. The increase of the inflow and the decrease in the outflow of the  $A\beta$  protein in AD patients cause the aggregation of the  $A\beta$  protein in AD patients, and this finding suggests a decrease in the capacity to clear the  $A\beta$  protein and an increase in BBB permeability in AD patients. The increased concentration of plasma LPS in AD patients implies an impairment of the gut barrier function and increased gut inflammation and permeability, which further suggests that gut microbiota may participate in the pathophysiological process of AD.



18. Gut microorganisms can also affect brain functions through the synthesis of various substances. Serotonin is very important for cognitive function, 95% of serotonin is synthesized in the gut, and gut microorganisms play an important role in serotonin synthesis. The gut serotonin level in sterile mice was 60% lower than the normal value. The use of serotonin reuptake inhibitors can reduce A $\beta$ -protein levels in the brain, indicating that serotonin can reduce the formation of A $\beta$  plaques, thereby reducing the risk of AD. In sterile mice, BDNF was significantly reduced, and this change was accompanied by cognitive function changes. Similarly, in AD patients, the BDNF levels in the brain and in the serum were significantly reduced. The A $\beta$  production and clearance in the CNS is a dynamic change, and some bacteria and fungi can secrete amyloid, resulting in an increase of amyloid levels in the CNS that disrupts the dynamic balance of the A $\beta$  protein, which leads to A $\beta$ -protein aggregation in the brain and a high AD risk. Therefore, an imbalance in gut microbiota may promote the development of AD by affecting intestinal function and the synthesis and secretion of substances.

### Summary

19. The interactive relationship between the brain and the gut includes neurology, metabolism, hormones, immunity, and other aspects, and changes in any component may lead to a functional change in the two interactive systems. The normal ecological balance of gut microorganisms plays an important role in the maintenance of this relationship. Microorganisms affect the development and function of the CNS through the microbiota-gut-brain axis. The mechanisms of many CNS diseases are still unclear, and the discovery of this complex relationship, the microbiota gut-brain axis, has provided a new research direction for the study of CNS diseases that do not have a clear pathogenic mechanism.

*Adapted from: 'Microbiota-gut-brain axis and the central nervous system' by Xiqun Zhu, Yong Han, Jing Du, Renzhong Liu, Ketao Jin and Wei Yi in Oncotarget (2017).*

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