Ⅱ期

令和2年度
武蔵野大学大学院　薬科学研究科　薬科学専攻 修士課程　入学試験問題 （1 月 12 日）
［ 英語 ］

【問題１】次の文章を読んで各問に答えよ。

The blood-brain barrier (BBB) regulates the communication between the vasculature and the brain. Aging and neurological disorders have been associated with BBB defects.

A growing body of evidence shows that epileptic activity is frequent but often undiagnosed in patients with Alzheimer's disease (AD) and has major therapeutic implications. Here, we analyzed electroencephalogram (EEG) data from patients with AD and found an EEG signature of transient slowing of the cortical network that we termed paroxysmal slow wave events (PSWEs). The occurrence per minute of the PSWEs was correlated with level of cognitive impairment. Interictal (between seizures) PSWEs were also found in patients with epilepsy, localized to cortical regions displaying blood-brain barrier (BBB) dysfunction, and in three rodent models with BBB pathology: aged mice, young 5x familial AD model, and status epilepticus–induced (a) in young rats. To investigate the potential causative role of BBB dysfunction in network modifications underlying PSWEs, we infused the serum protein albumin directly into the cerebral ventricles of naïve young rats. Infusion of albumin, but not artificial cerebrospinal fluid control, resulted in high incidence of (b). Our results identify PSWEs as an EEG manifestation of nonconvulsive seizures in patients with AD and suggest BBB (c) as an underlying mechanism and as a promising therapeutic target.

（Science Translational Medicine, 4 Dec 2019 Vol. 11 Issue 521）

（出典表記:From Blood-brain barrier dysfunction in aging induces hyperactivation of TGFß signaling and chronic yet reversible neural dysfunction, Science Translational Medicine 04 Dec 2019: Vol. 11, Issue 521. Reprinted with permission from AAAS.）

electroencephalogram (EEG)：脳波、paroxysmal slow wave events (PSWEs)：発作性徐波イベント
status epilepticus：てんかん重積状態、cerebral ventricles：脳室

問1　(a) (b) (c)に入る 1 語を問題文から選んで記しなさい。
問2　げっ歯類での知見に基づき、血液脳関門と特定の疾患との関連性について 200 字程度で説明しなさい。

【問題２】次の文章を読んで各問に答えよ。

２-１．BACKGROUNG

Awareness of, and interest in, genomic data obtained from clinical studies are growing. In particular, genomic research could be used in all phases of drug development to assess genomic correlates of drug response, and to understand mechanisms of disease or drug pharmacology.①The identification of genomic biomarkers underlying variability in drug response may be valuable to optimize patient therapy, design more efficient studies, and inform drug labelling. Furthermore, the generation and interpretation of genomic data, both within and across clinical studies and drug development programs, allow for a better understanding of pharmacological and pathological mechanisms and enable the identification of new drug targets

２-２．COMMUNICATION OF FINDINGS

Research institutions and sponsors who generate genomic data in a study are encouraged to adopt a position and mechanisms regarding return of data to subjects, as appropriate. The position should articulate whether the intended research findings, incidental findings, neither or both will be communicated. Ideally, the position would describe the timing of such communication (during or after the clinical study), by whom (e.g., investigator, physician, genetic counselor), and to whom (subjects, or the primary care giver or legal guardian in case subjects are children or subjects have been diagnosed with dementia). ②When communicating results to subjects, the pertinence of genetic counseling should be evaluated; the impact of results on treatment decisions should be interpreted clinically and discussed with the subject (or the primary care giver or legal guardian). The subject's desire and consent as to whether receiving such information should be respected. In addition, the applied assay and its level of validation should be considered, as this may affect the accuracy and validity of the results.

（ICH-E18 Guideline on Genomic Sampling and Management of Genomic Data より引用）

sponsor：治験依頼者、investigator：治験責任医師、legal guardian：法定後見人

問1 下線部①を和訳しなさい。

問2 下線部②を和訳しなさい。

問3 臨床試験において収集されたゲノムデータを被験者に開示する際の方針として、規定しておくことが理想的であるとされる 3 事項を例示とともに記しなさい。