Lecture 8
Brain and nervous system
Thiamine lack
Wernicke's encephalopathy
Lack of niacin
Pellagra
Uremic coma
Diabetic coma
Dehydration
Na K Ca
Electrolyte imbalance
Poisoning
Poison

Cerebrovascular accident
Orthostatic fainting
Shock
D I C
Thiamine lack
Wernicke's encephalopathy

Low CBF
Adams-Stokes syndrome
Cardiac infarction
Anemia
Lung disease
Excessive injection of Insulin
Insulinoma
Hepatic coma
Low blood of sugar
Low O2

Cerebral cortex
Thalamus
Hypothalamus

Metabolic acidosis

Prostaglandin D2
(prostaglandin D2)
Prostaglandin E2
(prostaglandin E2)

Sleep center
Pituitary gland
Mesencephalic reticular formation
Medullary reticular formation

Arousal center
(A back hypothalamus)

Cerebral cortex
Thalamus
Hypothalamus

Diabetic coma
Metabolic acidosis

Dehydration
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Na K Ca

Adams-Stokes syndrome
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Cerebral cortex
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Prostaglandin D2
(prostaglandin D2)
Prostaglandin E2
(prostaglandin E2)

Sleep center
Pituitary gland
Mesencephalic reticular formation
Medullary reticular formation

Arousal center
(A back hypothalamus)
## Frequency difference of Japan-U.S. of serotonin transportation body gene multi type

<table>
<thead>
<tr>
<th>Type</th>
<th>%</th>
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<tbody>
<tr>
<td>LS type</td>
<td>30.1</td>
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<tr>
<td>SS type</td>
<td>68.2</td>
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<tr>
<td>LL type</td>
<td>1.7</td>
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<tr>
<td>LS type</td>
<td>48.9</td>
</tr>
<tr>
<td>SS type</td>
<td></td>
</tr>
</tbody>
</table>

The Japanese educates kindly and severely to the group and the individual because the character to which it is the same as mild others and relieves it.

The education, the resource, and the target of composure are given and it teaches to an independent, independent student of the United States freely.

Teacher, please shut up!
More objective than the psychological test.

When the fearful expression is seen, the amygdaloid nucleus (right picture red) that shows feelings of likes and dislikes acts. It reacts to the Japanese and the amygdaloid nucleus reacts to a lot of S/S types that are sensitively.

Inherited difference of emotion by functional, magnetic resonance image method

Serotonin transporter

S type

L type

DRD4
(Dopamine D4 receptor)

State of excitation always

7R/7R

Stability orientation

Tendency for something new. Curious

48 bp tandem repeat
2R
3R
4R
5R
6R
7R

R. P. Ebstein et al. 1996
5-HTTLPR
(5-hydroxytryptamine transporter linked polymorphic region)

promoter

5-HTTLPR

Long type

S
hort type

Aggressive, Independent

Sensitive, Nervous

L is transcript revitalization ten times S

Receptor

Serotonin

Lesch KP et al. 1996

By 「The mind has been understood here」
Kosuke Oki
The mad cow disease is discovered from cannibals' Kuru disease.

Cannibals in New Guinea → Sheep

Sheep → The cow was made to eat sheep's scrap meat

The cow → Eating the hamburger steak with which the nerve mixes


Milk is safe

Nobel Prize in Medicine in 1997

The agents responsible for mad cow disease is a protein of not the microorganism but Prion. It acts on the Prion in normal person's brain and it changes it into no To Prion.

Nobel Prize in Medicine in 1997

It is Japan that in the world with a lot of dementias and bedridden.

Checkpoints where the dementia is doubted

**Forgetting that happens with aging**

The name of the actor who reflects in the television cannot be recalled.
It has forgotten to buy one carelessly though it went shopping.
Sentences are being written, the Chinese character cannot be recalled, and it often uses a dictionary

**Forgetting that should be noted**

A personal experience of the previous state is forgotten for a moment.
The same thing is repeated many times in a series of conversation

**Dangerous sign**

Not understanding my age.
Not understanding a familiar interpersonal relationship.
How of dementia symptom to appear

- emotional disorder
- Main symptom
- Excitement
- Impaired orientation
- Not computable
- Confusion
- Delusion
- Not computing
- Easy angry
- Not perception
- Perplexity
- Not writing
- Hallucination
- Creation of talk
- Symptom in surrounding
- Defect of memory
- Other intellectual disabilities
Cause of Dementia

1. Degenerative nervous disease (Alzheimer's disease, etc.)

2. Vascular dementia = Dementia by cerebral infarction and brain hemorrhage

3. Disease can be treated
   Chronic subdural hematoma
   Normal pressure hydrocephalus
   Brain tumor
   False dementia
   Dementia symptom by medicine
## Relation of dangerous rate of lifestyle and cerebrovascular dementia

<table>
<thead>
<tr>
<th></th>
<th>not leisure active</th>
<th>Past of hypertension</th>
<th>not exercise active</th>
<th>Head injury loses senses</th>
<th>Nonparticipation to the medical examination</th>
<th>Risk (odds ratio)</th>
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<tbody>
<tr>
<td>Non factor</td>
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<td></td>
<td></td>
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<td>1factor</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
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<td></td>
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<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>2.7</td>
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<tr>
<td></td>
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<td>−</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>2.5</td>
</tr>
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<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>2.2</td>
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<tr>
<td>2factors</td>
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<td></td>
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<td>5.3～42.2</td>
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<tr>
<td>3factors</td>
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<td></td>
<td></td>
<td>14.5～115.6</td>
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<tr>
<td>4factors</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>42.6～284.9</td>
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<tr>
<td>5factors</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>613.4</td>
</tr>
</tbody>
</table>

To prevent the acknowledgment syndrome, the simple calculation is read aloud early

Brain when easy calculation problem is solved fast

Working of the brain when an easy calculation problem is solved as soon as possible is shown. It is understood that a lot of places of a right and left brain move actively

Brain when complicated calculation is solved

Working of the brain when working on the complicated calculation is shown. The prefrontal region and times of a lower head of a left brain work. A right brain doesn't work

Brain when book is read aloud

Working of the brain when the book is read aloud is shown. More much more places work than reading it silently by a right and left brain. It is understood the faster the reading speed is the prefrontal region, the more to work
Risk of folic acid intake and cerebral infarction
(follow-up survey of 43,732 men and 14 years)

Method of calculating diversity score of food intake

Each food group
“Eat almost every day” 1 point
"Do not eat" is 0 point.
*The maximum becomes ten points.

Relative risk of decrease in higher-order life function of diversity score each crowd of food intake

When various foods are taken, it is not easy to become Dementia


Meat, Seafood, Eggs, Milk, Soybean and processed soy product, Brightly colored vegetable, Sea weed, Potato, Fruit, Oils and fats
1,674 of 68 years old or more is pursued seven years later. 170 people became dementias. 135 people became Alzheimer sooner or later.

### Protective efficacy by fish

<table>
<thead>
<tr>
<th>Rate of appearance</th>
<th>Eat fish (1 time or more everyday)</th>
<th>Eat meat (1 time or more everyday)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 time a week</td>
<td>1 time a week</td>
</tr>
<tr>
<td></td>
<td>2.64</td>
<td>1.75</td>
</tr>
<tr>
<td></td>
<td>Sometimes</td>
<td>Sometimes</td>
</tr>
<tr>
<td></td>
<td>5.29</td>
<td>1.83</td>
</tr>
<tr>
<td></td>
<td>Not at all</td>
<td>Not at all</td>
</tr>
<tr>
<td></td>
<td>6.26</td>
<td>6.26</td>
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</table>
The vegetable and the fruit prevent Alzheimer

<table>
<thead>
<tr>
<th>Location</th>
<th>Period</th>
<th>Age Range</th>
<th>Follow-Up Period</th>
<th>Intakes of Vitamin E &amp; C</th>
<th>Intakes of Vitamin E</th>
<th>Intakes of Vitamin C</th>
<th>Intakes of Vitamin E &amp; C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicago</td>
<td>1993-2000.</td>
<td>815 of 65 years old or more</td>
<td>Average 3.9 years</td>
<td>Low from few crowds</td>
<td>70%</td>
<td>Low from few crowds</td>
<td>43%</td>
</tr>
<tr>
<td>Rotterdam</td>
<td>1993-2000.</td>
<td>5395 of 55 years old or more</td>
<td>Average 6 years</td>
<td>Low from few crowds</td>
<td>43%</td>
<td>Low from few crowds</td>
<td>43%</td>
</tr>
</tbody>
</table>

It is the effect none even if it takes it as supplement.
Food that prevents Dementia (1995→2002)

![Graph showing the amount of increase and decrease in consumption of different foods from 1995 to 2002. The categories are brightly colored vegetables, beans, seafood, and potato.]

As for the content of the folic acid, in the analysis table, availability is different.

**Structure of folic acids**

Folic acid (Pteroylpolyglutamic acid)

- Mono-glutamic acid type folic acid
- Polyglutamic acid type folic acid

Folic acid in multivitamin and enriched food

Folic acid in natural food

(Monoglutamic folic acid: polyglutamic folic acid = 1:2)

Pteridine

Aminobenzoic acid

Mono-glutamic acid type folic acid or

Polyglutamic acid type folic acid (n=2~11)
The number of homo cysteines increases due to folic acid shortage
From the folic acid to the reaction of DNA methylation

• ① Transportation body small intestines and → Fomiltetorahidoro folic acid → Metenil tet rahydrofolic acid → Metirentetorahidoro folic acid of folic acid

• ② Metirentetorahidoro folic acid + NADH→ methylenetetrahydrofolate reductase → Meltet etorahidoro folic acid + NAD

• ③ homo cysteine + Metiltetorahidoro folic acid → methionine synthetase → methionine + tetrahydrofolic acid

• ④ Methylate + of C methionine + ATP→ S adenosylmethionine → DNACpG island S adenosyl homo cysteine. The activity leaf acid lack after DNA methyl transferase (five kinds) generates the egg is measured due to 14C methyllic radical uniting decrease to DNA.
Digestion, absorption of folic acid, and resolution of Porigltamil radical

Starch, Protein, Folic acid

Protein

Folic acid

amylase

Protease

Folic acids

Mono-glutamic acid type folic acid

Polyglutamic folic acid

RFC-1:1 reduction folic acid transportation body multi type

Small intestines epithelial cell

Blood

5-methylenetetrahydrofolate
This folic acid reinforced plan and eating folic acid amounts in the United States (DFEs)

- Obligated synthetic folic acids of the grain processed foods such as bread and cereals (every 100g) to be strengthened in the United States in 1998 140mg

- Eating folic acid this amount $= \text{Folic acid under meal} + 1.7 \times \text{Amount of synthetic folic acid}$

<table>
<thead>
<tr>
<th>Folic acid in food that exists naturally</th>
<th>$\rightarrow$ Absorption factor of 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic folic acid in enriched food</td>
<td>$\rightarrow$ Absorption factor of 85%</td>
</tr>
</tbody>
</table>

The correction coefficient of this 1.7 originates in the ratio in which the presumption availability of a synthetic folic acid in food is divided by the presumption average availability of eating sericulture

$\left( 85 \div 50 = 1.7 \right)$
When the folic acid is insufficient, it becomes an acknowledgment syndrome

- Rise of homo cysteine in blood
- Dementia
- Cerebral infarction
- Cardiac infarction

Don’t like vegetables
Constitution (gene)

It is not worrying if it notes it for a moment because this gene polymorphism is a small difference of the gene between normal people.
Even if the folic acid, VB6, and the VB12 intake are fulfilled, the density of the person of the TT type of the serum total homocysteine is high.

**p < 0.01, *p < 0.05**

![Graph showing homocysteine levels with CC, CT, and TT genotypes.]
As for the diabetic, folic acid shortage becomes the patient of a multi type with the risk in the limitation food with a lot of acknowledgment syndromes (Alzheimer's disease and apoplexy).

The cerebral infarction increases by a factor of 5.5-7.5 when the homocysteine is high

Unnoticed Cerebral infarction

Cerebral infarction that notices symptoms

** Discovery frequency of cerebral infarction

Araki A. et al. “Association between plasma homocysteine concentrations and asymptomatic cerebral infarction or leukoaraiosis in elderly diabetic patients” Geriatrics and Gerontology International. 3(1), 2003, 15–23
The intelligence decrease begins before the syndrome of acknowledgment when the homo cysteine is high

Achievement test 1  MMSE

Achievement test 2

![Bar chart showing scores for Achievement test 1 and Achievement test 2 with different amounts of homocysteine (nmol/ml)]

Density of serum folic acid according to acknowledgment syndrome senior citizen’s MTHFR C677T gene polymorphism and the total density of serum homocysteine (Dementia senior perwon at Yokufu-Kai)

* p<0.005 (vs. TT)
The person of the TT type also takes the folic acid of 400 μg every day, it is safe

**Gene polymorphism and folic acid blood level**

Cerebral infarction and dementia's worries are a little if 400 μg intakes of the folic acid in case of the type as well as the CC type and the CT type

Density of folic acid in blood

Preliminary examination
Number of 300

Load examination
Number of 100

AOKA, KATO, SAITO, YASUDA, KAGAWA
Acknowledgment level point after density of senior citizen of plasma folic acid and three stages and three years of folic acid intake
Prevention of acknowledgment syndrome of start

Elderly person: 321 (60-74)

Density of plasma folic acid
Folic acid intake amount/day

The density of the serum folic acid falls sharply and the intelligence of the level 80 years old per four Nano mg/ml falls sharply.

Mini mental test score

Serum folic acid
(ng/ml)

Intelligence test of 471 of 87 years old on average. The correlation of MMSE and the density of the serum folic acid is extremely significant:

\[ r = 0.36 (p < 0.0001) \]

The folic acid of 140 \( \mu \)g for every 100g is compulsorily added to bread and cereals in 1998 and it makes significant progress in the United States. A nursing necessary senior citizen decrease Great decrease in cardiac infarction. The deformed child of the nerve also : to 1/8. The folic acid recommendation amount has increased to about twice that of Japan, too.
It increases the serum folic acid because of US citizen's food folic acid strengthening
US citizen's food: decreasing the homo cysteine because of the folic acid strengthening.
Role of folic acid and Food that contains a lot of folic acids

**Functions of folic acids**
- The risk of embryo's nerve tube hypoplasia is decreased
- Arteriosclerosis prevention
- Alzheimer type dementia prevention

**Main supply source of folic acids**
(Mami FUKUSHIMA, Yasuo KAGAWA et al)

1. Spinach: 210μg
2. Roasted laver: 1900μg
3. Green tea: 16μg
4. Extracted material: 210μg
5. Broccoli: 78μg
6. Cabbage: 43μg
7. Egg: 200μg

**Necessary amount of folic acids** (a day)
- 200μg for non-pregnant adults
- 400μg for pregnant women

The Ministry of Health, Labour and Welfare (5th ed Food composition table)
1. The lack of the folic acid intake is measured with the homocysteine.

2. The constitution with the folic acid is an insufficient easily is judged by the inheritance.

Meal investigation (questionnaire) and guidance

Cooking practice and physical exercise

After half a year, inspecting again the homocysteine

It improves it judging the lifestyle that becomes an acknowledgment syndrome easily.

The acknowledgment syndrome and the cerebral infarction can be prevented regardless of the constitution.
The density of the serum folic acid rose according to gene multi type.

<table>
<thead>
<tr>
<th>Gene Type</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
<td>p&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>p&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>p&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

n=27 n=27 n=11
The acknowledgment syndrome can be prevented by the folic acid, the balance food, the exercise, and the brain activity.