Principles of and Medical Treatment for Depression

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Abstract
It is not well known that depression is a result of a combination of three symptoms, which is an issue with respect to current treatment of depression. Specifically, it is not well known that the tension and contraction of the muscles that are in direct contact with the skull play a major role in depression. Therefore, these factors should be taken into account when developing a comprehensive treatment for depression.

Introduction
1 The current state of depression In the past, depression was considered an “illnesses of the heart/mind” or “heart/mind catching a cold.” The definition of depression is now vastly different [1] . It is currently considered to be a “disorder of the brain.” Lack of serotonin in the brain is considered to be the main cause of this “disorder of the brain.” Although not completely wrong, this definition is somewhat simplistic, and therefore, we are not able to completely cure depression [2] . In addition, besides drug treatment, other proposals that have been made, including “cognitive therapy,” “interpersonal therapy,” “diet therapy,” and “exercise” [3] .

2 Depression: treatment history Depression is said to have originated in ancient Greece; however, there is no clearly established principle of depression [4] . In other words, mankind has been unable to provide an in-depth clarification of depression for the past 3700 years. In 1935, a surgical procedure, lobotomy, performed in Portugal drew a lot of attention worldwide because it brought about a temporary improvement among patients. However, this procedure was observed to result in serious adverse effects; therefore, it is no longer performed in Japan after 1975 [5] [6] . Osamu Dazai, Natsume Soseki, and Ryunosuke Akutagawa are a few people who were suspected to have depression [7] .

Objective
Current major problems with depression despite treatments such as medication and cognitive therapy include: 1) Patients who go into remission but are not fully cured 2) Patients who quickly relapse right after returning to work, etc. 3) Patients who must live with the acceptance the fact that they have depression No radical solution has been found yet for these issues.
Our objective is to find a solution.
(Fig. 1) 3 regions of the head

| “A”  | Pink     | Cerebrum, brainstem and so on. |
| “B”  | Green    | Cranial nerve, cerebellum and so on. |
| “C”  | Yellow   | Epicranial muscles, galea aponeurotica, mastication muscle, cranial meninx and so on |

(Fig. 2) 3 symptoms of the head region

1. Decrease/depletion in serotonin levels
2. Excess/accumulation of histamine
3. Abnormal tension, contraction, and fixation of muscles including the epicranial muscles
**Fig. 3** Effectiveness of the test drug(s) towards the immobility time during forced swim

![Graph showing immobility time comparison between different groups](image)

**Mean ± SD**

**n = 10**

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**Table 1: Determination of significant difference**

<table>
<thead>
<tr>
<th>Study group</th>
<th>P value</th>
<th>Significant difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control group vs. imipramine 5 mg/kg group</td>
<td>7.42E-05</td>
<td>Present</td>
</tr>
<tr>
<td>Vehicle control group vs. reagent S-1 group (300 mg/kg)</td>
<td>0.0060</td>
<td>Present</td>
</tr>
<tr>
<td>Vehicle control group vs. reagent H-1 group (250 mg/kg)</td>
<td>0.0004</td>
<td>Present</td>
</tr>
<tr>
<td>Vehicle control group vs. reagent K-1 group (150 mg/kg)</td>
<td>0.0005</td>
<td>Present</td>
</tr>
</tbody>
</table>
Results & Discussion

Results

The immobility periods of the mice were measured and mean values were compared between the vehicle control group and each of the groups who were administered with the test drug. Compared with the vehicle control group, all treated groups showed a significant decrease in the immobility time. The experiment yielded the following observations: positive control group ($P = 7.42E-05$), reagent S-1 group ($P = 0.0060$), reagent H-1 group ($P = 0.0004$), and reagent K-1 group ($P = 0.0050$) (Fig. 3 and Table 1).

This experiment shows that imipramine, the positive control substance, yielded a significant reduction in the immobility time. Therefore, this experiment was considered to have been established as an anti-depression test model. Moreover, S-1, H-1, and K-1 were observed to significantly decrease the immobility time.

The above results suggest that reagents S-1, H-1, and K-1 demonstrated an antidepressant effect.

Reagent name/Weight of the diluting agent used/Name of constituents in pure form/Weight in the pure form

<table>
<thead>
<tr>
<th>Imipramine/5 mg/kg</th>
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</thead>
<tbody>
<tr>
<td>Reagent S-1/300 mg/kg/Sumatriptan/39 mg/kg</td>
</tr>
<tr>
<td>Reagent H-1/250 mg/kg/Diphenhydramine/9 mg/kg</td>
</tr>
<tr>
<td>Reagent K-1/150 mg/kg/Tolperisone hydrochloride/56 mg/kg</td>
</tr>
</tbody>
</table>

Figure Legend

a Fig 1 The three major regions associated with depression
b Fig 2 The three major symptoms associated with depression
c Fig 3 Effectiveness of the test drug(s) towards the immobility time during forced swim
d Table 1 Determination of significant difference
e Table 2 Correlation of the regions and symptoms associated with depression
Discussion

Principles of Depression

Depression is considered to be a disorder of the mind/heart as well as the brain. However, this disorder is more complex and cannot be completely understood easily. Depression is “a disorder that affects the entire neck and head region above the Adam’s apple.” In addition, depression is not simply the presence of one symptom, i.e., “decreased serotonin or lack of serotonin.” If depression had just one symptom, a cure would have been found after conducting several experimental studies. However, a cure cannot be found as easily if there is a combination of 2–3 symptoms. In other words, depression is “an anomaly of 3 major regions” and “a combination of 2–3 symptoms associated with them.” The concept of depression needs to be clarified by addressing these principles.

The three kinds of drugs for the treatment of depression

As per the current standards, only one type of drug is recommended to treat depression; however, this is inadequate. If one type of drug does not yield any effect, simultaneous administration of several drugs at random also tends to be ineffective. In this report, the authors propose a set of three types of drugs to treat depression—this is extremely important. It is apparent that the dose and administration period of the drugs necessary is different for the treatment of each symptom, and consequently, the improvement they bring about will be different. It is better to treat one symptom at a time in a systematic manner.

The following is a list of constituents of the three types of drugs:

Constituents of reagent S-1/Sumatriptan, 5-hydroxytryptamine, almotriptan, eletriptan, naratriptan, and lmitriptan

Constituents of reagent H-1/Diphenhydramine, chlorpheniramine, clemastine, alimemazine, and hydroxyethylpromethazine,

Constituents of reagent K-1/Tolperisone and tizanidine

Conclusions

The three major regions associated with depression (Fig 1):

As mentioned above, depression is “a disorder that affects the entire neck and head region above the Adam’s apple.” This region may be divided into the following three parts: 1. The cerebrum, limbic cortex, brain stem, thalamus, hypothalamus, and pons 2. The cranial nerves (trigeminal, maxillary, mandibular, ophthalmic, and facial nerves and facial muscles), cerebellum, and cervical region 3. The skull bone and regions that come in contact with the interior and exterior parts of the skull bone: cerebral meninx, epicranial muscles (frontalis, occipital, and temporal muscles), galea aponeurotica, mastication muscles, and the entire scalp.

The three major symptoms associated with depression (Fig 2):

The main cause of depression is considered to be a “decrease/depletion in serotonin.” However, this is not the only cause. The following are the three symptoms of depression, which may be independent or interlinked: 1. Decrease/depletion of serotonin; 2. Excess/accumulation of histamine; and 3. Abnormal tension and contraction and fixation of “the nerve of skull bone,” cerebral meninx, epicranial muscles, frontalis muscles, occipital muscles, temporal muscles, galea aponeurotica, and mastication muscles. Correlation of the regions and symptoms associated with depression (Table 2).

Additional Information

Methods and Supplementary Material

Please see https://sciencematters.io/articles/201609000003.

Acknowledgements

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Ethics Statement

This experiment was properly conducted in compliance with the animal experiment provisions of the request destination company.
Citations


