Application of digital therapeutics (DTx) for temporomandibular disorder (TMD) patients

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Abstract
Due to the pandemic situation of the Covid-19 virus, our daily life has changed a lot [1]. Many changes have also taken place in the fields of medicine and dentistry. The most prominent field is the field of digital medicine, and the field of digital therapeutics (DTx) has developed rapidly along with the technology of other fields [2,3]. In the case of digital therapeutics, it is evaluated that it can be remarkably applied in the field that requires behavioral control or the field that requires the approach of mental health medicine. In addition, studies are being carried out notably in high blood pressure, diabetes, heart-related diseases, addiction, dementia, and ADHD that require management as an chronic disease. However, in the field of dentistry, there are not many fields where digital therapeutics are applied prominently, but application to temporomandibular disorder can be devised [4], and the reason for this can be discussed in this article.

Keywords
Covid-19; Dentistry; Mental health; Addiction.

Introduction
Digital therapy is an Evidence-based therapy, and the most important feature is that it is software-based. It aims to prevent, manage, and treat medical disorders. The easiest explanation is that the patient uses software to self-manage his/her symptoms to relieve symptoms and improve quality of life [5]. In addition, digital therapeutics are still evolving more effectively with the development of various technologies. In addition to the spread of smartphones, for example, Artificial Intelligence (AI), Internet of Things (IoT), Virtual Reality (VR), and Augmented Reality (AR) [6,7]. The core concept of digital therapeutics is self-managing and is based on cognitive behavioral therapy. This method can work effectively in many chronic, high-recurring diseases that require behavioral control. For example, it can be effective in drug addiction, alcoholism, or smoking cessation treatment [8]. In fact, the first digital treatment to receive USFDA
approval is a drug addiction treatment (reSET®, Pear Therapeutics Inc., Boston, USA). Since then, research and development in many diseases has been made. For example, high blood pressure, diabetes, Alzheimer’s disease, insomnia, depression, etc. are being developed [9-18].

However, the use of digital therapeutics in dentistry, not medicine, is currently insignificant. It is safe to say that there is currently little research and development of digital therapeutics in the field of dental or dentistry other than teledentistry. In this review, the application of digital therapeutics to patients with temporomandibular disorder will be considered.

**Temporomandibular disorder and Digital therapeutics (DTx)**

Temporomandibular disorder refers to pain and functional limitation occurring in the maxillofacial region. According to a relatively recent study, it is reported that about 5-15% of the total adult population suffers from it [19]. Interestingly, there is also a study result that TMD occurs more frequently in modern people [20]. A recent systematic review and meta-analysis in 2021 concluded that the prevalence of TMD was 31% for adults and 11% for children and adolescence [21]. The etiology of TMD is known to be multifactoral, and the exact mechanism has not been elucidated. However, it is known that physical factors and psychological factors contribute together [22-24]. In practice, skeletomuscular problems can lead to problems with internal derangement of TMJ. This can lead to pain and other symptoms and, in severe cases, osteoarthritis. The presence of skeletomuscular anomalies does not result in the same degree of symptoms and pain. We should therefore pay attention to biopsychosocial factors, and there have been many studies on this point [23,25]. High levels of depression and anxiety were significantly associated with the development of symptoms of TMD. In addition, in patients with existing TMD symptoms, stress became a factor that accelerated and worsened symptoms. In addition, there is a study reporting that depression and stress were increased along with symptoms related to TMD during social lockdown and personal isolation due to COVID-19 [26,27].

There are many difficulties in accurately classifying and treating TMD itself. Recently, there have been many studies to classify these TMDs. As a result, the Diagnostic Criteria for Temporomandibular Disorder (DC/TMD) is the most widely known and accepted for classification and standardization of TMD. In DC/TMD, classification and diagnosis are made through two axes. Axis-I focuses on biological based factors of joints and musculature. On the other hand, Axis-II focuses on psychosocial & behavioral factors [28]. Clinicians treating TMD must record these assessment items. Clinicians also need to determine if the patient has any habits (smoking, drinking, bruxism or clenching etc). It is also necessary to understand the psychological history.

The answer to the question of how and how important psychosocial factors affect TMD is that they are very important factors. Evidence from many studies has demonstrated that psychosocial factors develop and aggravate the state of chronic pain, and that this tendency is also seen in patients with TMD [29-31]. It is also important to note that psychosocial and cognitive behavioral interventions in these patients with acute TMD are sufficiently effective in preventing the transition to chronic TMD [32]. The start of treatment and management of TMD patients begins with understanding the importance of education and
self-management, not drug treatment and the use of splint devices. Many clinicians give patients an anatomical schematic or explanation of the mechanism of TMD. It also explains and recommends self-management methods in daily life. For example, sleep hygiene, avoiding parafunctional habits, and abstaining from caffeine and alcohol [33].

Factors influencing pain include the patient’s own beliefs, surrounding environment, family relationships, and interpersonal relationships, which affect the onset, development, and persistence of pain. In this sense, the axis-II classification of DC/TMD shows the importance of psychosocial aspect. This allows us to understand the factors that are variously related to the patient’s depression, anxiety, and parafunctional behaviors, as well as the aspects that make judgments about pain or symptoms. However, allowing this approach to treat TMD can make it seem like the dental clinician has given up on the patient and has entered the final stage. These impressions can in turn negatively affect the patient and aggravate the disease [33]. Therefore, it is necessary to approach, evaluate, and explain to the patient the Axis-II part from the initial treatment stage of TMD. This will be very important in suppressing the chronicity of TMD and reducing the recurrence rate.

Digital therapeutics have advantages in many ways, but the advantage is that they can aid in this self-management and amplify the therapeutic effect resulting from the patient’s self-evaluation and continuous cognition. As mentioned in the previous paragraph, this aspect of TMD treatment is very important. Therefore, among dental treatment or oral maxillofacial treatment, digital therapeutic seems to be very effective, especially for TMD.

In the past, Turner and colleagues have studied cognitive behavioral therapy for TMD using a daily electronic device. This study was conducted in 2005 and before the development of smartphones. It is thought that the size and performance of the device would have been much more inconvenient than it is now. In the study, after TMD treatment at the clinic, it was divided into a group that performed self-management and a group that performed pain-management using an electronic device. Check lists include pain, interference, jaw limitation, negative mood, and pain-related belief. As a result, in the group that proceeded with the cognitive behavioral approach, there was more improvement, and the improvement effect was significant in the psychological aspect. This study has proven that the cognitive behavioral approach based on self-monitoring through the device daily in TMD patients helps normalize the symptoms of TMD and jaw limitation and influences the psychological aspect [36].

However, the study discussed that a long-term follow-up is needed in the future and a high degree of patient participation is needed. In addition, it was expected that the device would be changed to be simple and convenient for users to solve it.

Now, about 20 years later, with the development of smartphone-based electric devices and technologies, digital therapeutics are expected to be effective and as a basis for sufficiently applying to TMD.

According to a review by Minervini et al [34], after covid-19, the incidence of TMD was higher due to emotional stress, and when ‘Teledentistry’ was applied, it was found to be effective as an adjunct to existing
treatment. In addition, Salazar-Fernandez and colleagues [35] positively evaluated teledentistry and its effectiveness in patients with TMD.

In addition, with the development of Internet of Things (IOT) technology and Artificial Intelligence (AI), digital therapeutics are expected to become more sophisticated.

### Table 1: Change in Clinical Parameters from Baseline (Day of Hospital Admission) Pre and Post Use of First and Second CytoSorb® Device.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Instrument</th>
<th>No. of items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain intensity</td>
<td>Graded Chronic Pain Scale (GCPS)</td>
<td>3</td>
</tr>
<tr>
<td>Pain location</td>
<td>Pain drawing</td>
<td>1</td>
</tr>
<tr>
<td>Physical function</td>
<td>Graded Chronic Pain Scale (GCPS)</td>
<td>4</td>
</tr>
<tr>
<td>Limitation</td>
<td>Jaw-function limitation Scale-short form (JFLS)</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Jaw-function limitation Scale-long form (JFLS)</td>
<td>20</td>
</tr>
<tr>
<td>Distress</td>
<td>Patient Health Questionnaire-4 (PHQ-4)</td>
<td>4</td>
</tr>
<tr>
<td>Depression</td>
<td>Patient Health Questionnaire-9 (PHQ-9)</td>
<td>9</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Generalized Anxiety Disorder- 7 (GAD-7)</td>
<td>7</td>
</tr>
<tr>
<td>Physical symptoms</td>
<td>Patient Health Questionnaire-15 (PHQ-15)</td>
<td>15</td>
</tr>
<tr>
<td>Parafunction</td>
<td>Oral Behaviors checklist (OBC)</td>
<td>21</td>
</tr>
</tbody>
</table>

**Conclusion**

Digital therapeutics are expected to cause a paradigm shift that will change the medical world in the future. Although a lot of development and research is still needed, evidence-based studies have been published that prove a good effect in various diseases. Digital therapeutics can be effectively used in areas where behavior correction, self-monitoring, cognitive behavioral treatment, etc. must be applied or needed.
In the field of dentistry or oral and maxillofacial region, there are patients with TMD that require this type of treatment. Psychosocial factors have been proven to be major factors in the cause and development of TMD. Clinicians need not only symptomatic treatment but also psychosocial and habitual approaches and active treatment. However, this aspect tends to be overlooked and difficult to access by most clinicians. However, with the introduction of digital therapeutics, intervention in the DC/TMD axis-II region in TMD patients is expected to become easier, and the development of the underlying technologies is also expected to help make application easier and simpler for patients. In the future, digital therapeutics have great potential to be used in the TMD field. Expectations for effectiveness can be evaluated positively when referring to previous and recent studies.

References


