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EDITORS
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CONTENTS

Chapter 1

LAPAROSCOPIC VERTICAL SLEEVE GASTRECTOMY; TECHNIQUE, COMPLICATION & OUTCOMES

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INTRODUCTION:

Bariatric surgery has been seen as the most effective way to lose weight and improve weight-related comorbidities. Vertical sleeve gastrectomy (VSG) constitutes most of the bariatric surgical procedures performed in the USA today (1).

VSG was first defined in 1988 as the restrictive component of the biliopancreatic divergence-duedonalswitch procedure (2). The American Society for Metabolic and Bariatric Surgery (ASMBS) accepted VSG as a viable primary bariatric procedure in 2012; after serious complications have been seen in patients after Duodenal switch operations, especially in super obese individuals, and the VSG procedure was found to be effective both in terms of weight loss and improvement of the comorbidities (3,4).

It has been observed that the morbidity and mortality rates are lower, as VSG is easier to perform and the operation time is shorter (5). The VSG has become increasingly popular among surgeons due to its technical and surgical advantages. The absence of performing a gastrointestinal-anastomosis facilitated the procedure in terms of its learning curve (6). Complication rates vary between 0.7% and 4% in different series, and there was no significant difference from other obesity procedures in the literature. Re-operation and staple line leak are still considered to be the two most important complications of VSG (7).

PERIOD BEFORE SURGICAL DECISION:

Every individual applying for any type of bariatric intervention is evaluated by a multidisciplinary team. They are categorized using the World Health Organization's Body Mass Index (BMI) classification (Table 1) (8). All non-surgical methods are tried first. Individuals who cannot achieve adequate results with medical treatment, diet and physical activity and whose BMI is either 40 or more alone or patients those BMI between 35 and 40 with weight-related comorbidities (Diabetus Mellitus, Hypertension, sleep apnea syndrome, Metabolic syndrome…) are considered candidates for bariatric surgery (9). The multidisciplinary team (endocrine diseases specialist, psychiatry specialist, general surgery specialist and anesthesiologist) decides whether the patients have any obstacle to have this surgery. For patients who are determined to be suitable for surgery, the appropriate surgical procedure is decided according to their clinical (reflux symptoms, comorbidities …), laboratory and gastroscopy findings.

BMI	Nutritionalstatus
Below18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Pre-obesity
30.0–34.9	Obesityclass I
35.0–39.9	Obesityclass II
Above 40	Obesityclass III

Table 1:Nutritional status WHO

SURGICAL TECHNIQUE : How we do it?

In order to prevent the venous thrombo-embolism; before the operation the patient is dressed with anti-embolism stockings and an intermittent compression device is also used. The patient is placed in a supine position, legs extended (french position) and a reverse trendelenburg positioning is used. For the surgery 5 ports are used; one 10 mm for the camera, one 12 mm for the stapler, two 5 mm for the auxiliary tools, and one 5 mm for the left lobe retraction of the liver. The layout of the ports is shown in Figure 1.
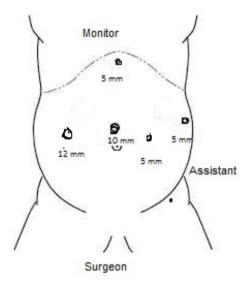

Figure 1: Port positions.

A camera with a size of 10 mm and an angle of 30 degrees is used for laparoscopy. The gastric great curvature is devascularized with vessel-sealing devices, starting from the antrum from a distance of 4 cm from the pylorus distally, and in such a way that the gastric fundus is completely released and the left crus is exposed proximally. Devascularization is done as close to the stomach as possible, and great emphasis is placed on the good sealing of the gastric breves vessels especially at the level of the spleen. The assistant assists during devascularization of the greater curvature of the stomach by lateralizing the omentum. Posterior gastro-pancreatic adhesions are separated. Care is taken to avoid any pancreatic injury during this stage. After the stomach is completely freed from the omentum , 34-40 F bougie is advanced to a distance of 4 cm from the pylorus. The volume of the stomach that will remain is determined with the help of the bougie and the stomach is divided by stapling with a 60 mm stapler starting from the distal of the bougie. Good positioning of the bougie and the first two staples are of great importance in terms of the risk of stenosis and twist that may occur in the remnant stomach afterwards. Care is taken not to divide the incisura angularis too close. In order to minimize the risk of bleeding that may be seen from the staple lines; black tristaplers are used for the antrum region and the purple staples for the proximal gastric parts. In addition, stapling is performed by lateralizing the anterior and posterior surfaces of the stomach equally so that the staple line is straight. Metallic clips are placed on possible leak sites reinforcing the stapler line if needed. In order to strengthen the stapler line and reduce the possibility of possible leakage; the omentum is fixed to the stapler line with an absorbable suture. The bougie is pulled to the proximal part of the remnant stomach with the help of an anesthetist. Test was done for any possible leakage from the stapler line with a mixture of 100 cc 0.9% NaCl and methylene blue. The resected stomach remnant is removed from the 12 mm port site. A drain is placed in the gastro-splenic space for any drainage or possible hemorrhage. The surgery is then terminated.

POSTOPERATIVE PERIOD:

The pain and the nausea are controlled during the hospital stay, especially for the first 24 hours after the surgery. In order to minimize possible post-operative nausea, care is taken not to use opioids during the surgery (10). Nausea is tried to be minimized by giving antiemetic drugs to the patients after the surgery. Early mobilization; which is one of the important points of the Enhanced Recovery After Surgery (ERAS) protocol, is known to be effective both in reducing postoperative pain in patients and in accelerating the initiation of the bowel movements (11). In our clinic, we recommend mobilization for bariatric surgery patients after the 4th postoperative hour. Patients' vital signs such as blood pressure, pulse, fever

and saturation are also followed up during their stay in the hospital. Changes in vital signs can be a warning sign in terms of any leakage and bleeding. Because the Functional Residual Capacity (FRC) is decreased in the obese individuals; atelectasis is common in the postoperative period (12). In our clinic, lung exercises are recommended to patients in the postoperative period to prevent atelectasis. In the postoperative period, daily hemogram and C-reactive protein (CRP) follow-up are performed. If the patient is fine in terms of clinical and vital signs; on the postoperative day 1, liquid diet is started. Again, if there are no signs of bleeding (low hemoglobin, hemorrhage in the drain, hypotension or tachycardia) on the postoperative 1st day, a Low Molecular Weight Heparin (LMWH) prophylaxis is started for the prevention of any thrombo-embolism. Patients who do not have any postoperative complications and that can tolerate a liquid diet are discharged within 48-72 hours postoperatively.

THE EFFECT OF SLEEVE GASTRECTOMY ON WEIGHT LOSS AND COMORBIDITIES

In December 2012, the Fourth International Consensus Summit on SG (4ICSSG) was held in New York with the participation of 130 obesity surgeons from all around the world. The aim was to share their experiences and to create a more homogeneous technique for VSG. As a result of the surveys conducted at this meeting and from the data's gathered from the follow-up of these surgeons; % Excess Weight Lose from VSG was observed to be, % 59.3% in the 1st year, 59.0% in the 2nd year, 54.7% in the 3rd year, 52.3% in the 4th and 5th years, and %50.6 in the 6th year in those operated patients (13). Bohdjalian et al. also in their study found that the 5-year %EWL was 54.8 ± 6.9 (14). It is known that the most frequently applied bariatric surgical procedures in the world are sleeve gastrectomy (SG) and roux-n-y gastric bypass (RNYGB) surgeries. In a recent randomized controlled study involving 217 patients undergoing SG or RYGB; although the data tended to be in favor of RYGB (61.1% for SG, 68.3% for RYGB) no statistically significant difference was found in terms of %EWL at 5 years among them (15). It is known that one of the most important condition seen in long-term follow-up of patients after getting a sleeve gastrectomy is weight regain. In a study evaluating weight regain after SG, weight regain was seen in 61 (87.1%) patients in the postoperative follow up. The mean regained weight was 8.1 ± 4.8 kg at 24 months postoperatively (16).

In their study Vasileios et al. regarding the obesity-related comorbidities demonstrated that the improvement of the comorbidities were observed in; 66.7% of type 2 Diabetes Mellitus (DM) patients, 57.1% of hypertension (HT) patients, and 74.1% of patients with sleep apnea at 5 years after surgery (17). In another study conducted by Flavius et al. which was evaluating

the effect of SG on comorbidities reported improvements of; 80% in DM, 42.5% in HT and 70.1% in snoring during sleep. Also in the same study, it was found that having this surgery and losing weight contributed to the improvement in; the self-confidence 83%, the social life 34%, the family life 27% and the sexual life 45% of these patients (16).

The curative effect of LSG on comorbidities was demonstrated to be less than that of the RYGB or bilio-pancreatic divergence surgeries. But when the weight loss and its sustainability were compared; it was seen that there was no significant difference in the short term (6th year) follow ups, but there were significant differences in the favor of bypass procedures in terms of both EWL and Total Weight Loss (TWL) in 11 years and above. However, the study reveals that LSG provides an excess weight loss of 62.5% in 11 years. It was also observed that about 1 in 4 patients; in their follow ups, required a revision surgery for the weight regaining. Although disturbing GERD symptoms can be seen, patient satisfaction has been found to be good after the surgery (17,18).

Glomb et al. (19) examined the long-term metabolic effects of SG, and there was a significant reduction in %EWL between patients with 1 and 3 years of follow-up and the patients with 1 and 5 years of follow-up (-4.8%, P = .007; and -16.3%, respectively, P < .001). It was found that the decrease in %EWL between 3 and 5 year follow-ups were not statistically significant (19).

Changes in high-density lipoprotein (HDL) cholesterol and triglyceride levels were significant when compared with the preoperative levels (P<.001). The decrease in low-density lipoprotein (LDL) cholesterol was found to be significant at first year (P=.04) and 3 years (P=.04); but the effect was not statistically significant at 5 years postoperative. The proportion of patients who stopped using drugs for T2DM was 64.5% at 1 year, 48.3% at 3 years, and 55.5% at 5 years. Complete remission of diabetes was observed at the rate of 50.7%, 38.2%, and 20.0%, respectively, in the 1st, 3rd, and 5th years, and remission of hypertension was observed at a rate of 46.3%, 48.0%, and 45.5%, respectively after the surgery (19).

LIMITATIONS OF SLEEVE GASTRECTOMY

Gustavo et al. (18) compared the long-term results of bariatric surgical procedures. In this study, Gastroesophageal Reflux Disease (GERD) occurred in 9 of 42 sleeve gastrectomy patients and 7 of these patients had to use Proton Pump Inhibitor (PPI), 1 patient had hiatoplasty and 1 patient was revised to RNYGB procedure for the GERD treatment. SG not only creates a new GERD, but also increases the symptoms in obese patients

already having a GERD. Therefore, for the bariatric surgery candidates with GERD; bypass procedures should be preferred rather than the SG procedure. When the excess weight and total weight loss and its short and long-term results are evaluated after having sleeve gastrectomy; similar results were obtained with other procedures in the short term, while weight regain is seen more common in SG in the long term follow ups (18).

COMPLICATIONS:

STRICTURE:

Dysphagia, nausea and vomiting, inability to consume solid food , reflux symptoms especially during the transition period to solid food after SG should bring to mind the possibility of stricture. It is especially seen at the incisura angularis level (junction of corpus and antrum) (Figure 2).

Figure 2: Stricture at the Junction of corpus and antrum.

The clinic is variable and depends on how soon after the operation the signs of obstruction appear; however, the symptoms are mostly the same. Sometimes, leakage due to stenosis can also be seen. With the appearance of these symptoms after the sleeve surgery, the diagnosis can be done with barium radiography and endoscopy. Although endoscopic dilation is preferred primarily in the approach to patients diagnosed with stenosis; strictureoplasty, revision to RNYGB surgery or even sometimes

total gastrectomy can be done in severe cases. Stenosis can be prevented by keeping a safe distance between the incisura angularis and the gastric edge where the stapler is applied. Routine use of a 36 F bougie; to keep this appropriate safe distance and to prevent the stricture is recommended. During the stapler resection of the stomach the staple line should be kept straight. The stomach should be lying flat and smooth while using the stapler; the anterior and posterior walls of the stomach should be even, to keep the stapler line symmetrical preventing any possible twist. Excessive resection of the posterior stomach wall with the stapler may cause stenosis-like symptoms by causing twist of the remnant sleeve in the postoperative period. If this happens the surgical treatment is the last approach, but it should be known that it should not be avoided if necessary (20).

LEAK

Leakage is known to be the most dangerous and feared complication after SG. Its incidence is 1-2%. The most common location of the fistula was found to be near the His angle, and secondly, in the antrum at the beginning of the gastric stapler line. Postoperative tachycardia ($\geq$ 100 beats/min), hyperthermia ($\geq$ 38C), peritonitis (diffuse abdominal tenderness), pulmonary symptoms (cough and sputum production), and intra-abdominal abscess (localized abdominal tenderness) suggest a leak state.

Rebibo et al. divides gastric leaks into two groups; according to their clinical experience, as early-onset Gastric Leak (GL) (between 1 and 7 days postoperatively) and delayed-onset GL (postoperative day 8 and later).The most appropriate method for diagnosis is oral contrast-enhanced abdominal computed tomography (CT) and/or upper gastrointestinal endoscopy. The treatment approach after diagnosis should be multidisciplinary and this team consists of surgeon, radiologist, intensive care specialist and gastroenterologist (21, 22).

Bashah et al. determined the approach according to the number and size of the fistula opening diagnosed after the surgery (recommends endoscopic stent for single fistula or multiple fistulas larger than 5mm, and recommends endoscopic clip or double pigtail for single fistula smaller than 5mm) (22). Giuliani et al. stated that Double Pigtail Stent (DPS) should be the standard treatment approach in fistulas seen after SG. It has been stated that DPS is better than other methods with its low complication rate and well tolerated by patients. DPS placed in the fistula tract endoscopically also provides internal drainage feature. The ideal duration of treatment is suggested to be 6 weeks. However, it is known to be less effective in cases of large leaks (23).

Ferraz et al. recommends endoscopic stenting as the first approach

for leaks after SG. The proposed stent is a 150 mm long, silicone inner and outer polyurethane coated stent, which was recommended to be placed 5 cm above the gastro-esophageal junction. The mean duration of stent treatment was 4 weeks. Surgery is the last option in cases that cannot be controlled by non-surgical methods. The surgical approach (laparoscopy or laparotomy) is determined according to the clinical condition of the patients. Peritoneal cleaning and cavity drainage are aimed with surgery (24).

Endoscopic approaches are the first and most well-known approach in the management of post-SG leaks. DPS and covered stent applications are known to be the most widely used techniques. DPS is thought to be an advantageous method by providing effective granulation as well as drainage of the collection. Other methods are over-the-scope clip (OVESCO), adhesives, internal VAC (e-VAC) and septotomy, which are used less frequently. Covered stent use is recommended as the initial treatment for 1 cm and larger defects. Pigtail drain can be placed after 15 days of treatment. Important steps in the leak management after the SG is; using broad-spectrum antibiotics, endoscopic methods, simultaneous drainage if there is an accompanying intra-abdominal abscess and nutritional support. Surgical option (laparoscopy or laparotomy) may be the appropriate method in large leaks and progressive cases deteriorating the general status of the patients (25).

BLEEDING

Bleeding after SG is one of the most important complications and it is most commonly seen from the stapler line. Postoperative bleeding can be diagnosed by imaging, clinically and laboratory findings. Bleeding is considered positive when patients have active bleeding on a CT scan, a decrease in hemoglobin of at least 2 units, a need for blood transfusion, or a reoperation to control the bleeding. This situation can be minimized by strengthening the stapler line. In order to strengthen the stapler line, partial or complete suturing of the omentum to the stapler line and also some support materials can be used. For postoperative bleeding patients undergo hemogram and vital signs follow-up and also blood transfusions if needed. It is recommended to consider reoperation as another option in cases that cannot be controlled conservatively (26, 27).

CONCLUSION

SG is an important procedure in the treatment of morbid obesity with its sufficient weight loss, effectiveness in improvement in comorbidities and ease of the application and is among the most widely used bariatric surgery methods worldwide. Possible complications can be minimized

with the standardization of the surgical technique and experience. Today, its application is increasingly accepted as an effective and a safe procedure.
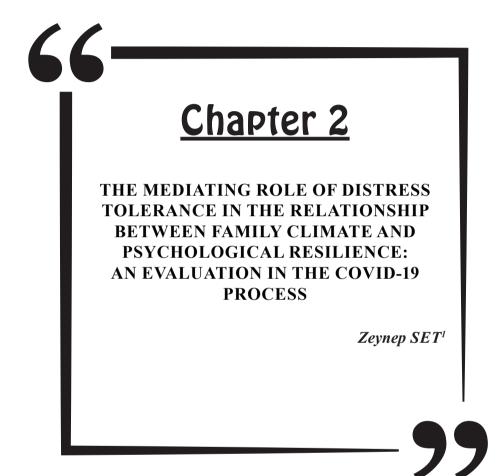
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Chapter 2

THE MEDIATING ROLE OF DISTRESS TOLERANCE IN THE RELATIONSHIP BETWEEN FAMILY CLIMATE AND PSYCHOLOGICAL RESILIENCE: AN EVALUATION IN THE COVID-19 PROCESS

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Introduction

The coronavirus (COVID-19) first appeared in the Chinese province of Wuhan and quickly spread to the rest of the world (Zhou et al., 2020). The COVID-19 pandemic is a public health problem with serious multifaceted consequences for people's lives and mental health. With many new cases and deaths every day, the epidemic creates anxiety and uncertainty in the society. Many people struggle to recover from COVID-19 or mourn their loved ones without access to important cultural rituals. Social isolation methods such as closing schools, staying at home voluntarily, and reducing physical interactions between people are one of the most effective protection methods against the virus (Gu, Jiang, Zhao, & Zheng, 2020; Tian et al., 2020). Sudden and impactful changes in daily life are likely to affect people's psychological health. Stress and anxiety can be experienced in unpredictable and threatening situations such as the coronavirus pandemic. However, our stress system has evolved to respond in adaptive ways to different situations and enables us to cope with difficulties (Kloet, Joels, & Holsboer, 2005). Most people are trying to adapt to the coronavirus reality. Despite this, not everyone can cope with stress in the same way and cannot adapt to the new situation. Although it is possible for individuals exposed to difficult experiences to develop psychological health problems, many people can maintain their functionality (Bonanno, 2004). The ability to maintain psychological resilience is considered important in the face of the uncertain effects of the pandemic.

Psychological Resilience

Resilience is defined as an individual's ability to cope with stress despite being exposed to a serious stressor that may contribute to various physical, behavioral, emotional and cognitive symptoms (Bonanno, 2004). Another meaning used is the ability to show positive adaptation despite adversity (Luthar, 2006). The capacity to adapt and cope with distressing situations is effective for individuals and societies to adapt to the new situation in a timely and effective manner (Rodriguez-Llanes, Vos, & Guha-Sapir, 2013). Individuals with high psychological resilience can be protected from stressful situations with the interaction of their individual, family and social resources (Friborg, Hjemdal, Rosenvinge, & Martinussen, 2003).

Family Climate

It is thought that the family is the closest system with which the individual interacts and has an impact on lifelong development (Bowlby, 1969; Bronfrenner, 1989). According to Bowlby's attachment theory, the bond between children and their primary caregivers is important for emotional, social and cognitive development (Bowlby, 1969; Bowlby, 1973). According to the family systems theory, the family is an open system

in communication with the environment and thus can continue to function when faced with difficult experiences. The psychological atmosphere of a family is defined as the "family climate" and consists of components such as family organization, the quality of the relationship between individuals and their social interactions (van Stejin, Oerlemans, van Aken, Buitelaar, & Rommelse, 2015). Emotional and cognitive harmony within the family ensures that family members stay together in times of crisis and facilitates their adaptation to difficult situations (Björnberg & Nicholson, 2007). No study has been found that directly investigates the relationship between family climate and resilience. In the current study, it is thought that positive family climate will increase psychological resilience and affect the reactions given during the pandemic process.

Distress Tolerance

The capacity to tolerate distress, on the other hand, refers to an individual's perceived or real ability to withstand negative psychological situations (Brown, Lejuez, Kahler, Strong, & Zvolensky, 2005). For this reason, it is thought that the capacity to tolerate distress will affect the evaluation of negative emotional states and their results. In fact, individuals with a low distress tolerance seem to be more likely to overreact to stressful situations because they think their anxiety symptoms are uncontrollable. These individuals also have difficulties coping with distress. They try to avoid stressful situations by using strategies that aim to quickly eliminate negative emotional states (Simons & Gaber, 2005). Contrary to this situation, individuals with high psychological resilience have the belief that they can change situations under difficult conditions, strive for this cause, and can return to their former state when adversities pass (Seçkin & Hasanoğlu, 2016). In this context, it is thought that psychological resilience will increase the ability to tolerate distress. Family climate is of great importance on individuals' attitudes, judgments and behaviors towards the difficulties they encounter in life (van Stejin et al., 2015). Therefore, it is thought that the improvement of the family climate during the pandemic process will increase the capacity to withstand adversity. The purpose of this study is to evaluate the mediating role of distress tolerance in the relationship between family climate and resilience during the COVID-19 process.

Method

Design

This research is designed according to the relational screening model, which aims to evaluate the mediating effect of the capacity to tolerate distress in the relationship between family climate and psychological resilience levels of individuals over the age of 18 during the current

COVID-19 epidemic. The following model was determined to be tested within the scope of this study. The hypotheses determined in the hypothesis model are:

1. Improvement of family climate increases the level of psychological resilience.

2. Improvement of family climate increases the level of tolerance of distress.

3. Increasing the level of distress tolerance increases the level of psychological resilience.

4. The capacity to tolerate distress has a mediating effect on the relationship between family climate and resilience.

Figure 1. Hypothesis Model, RIF: Family Climate Scale Relatedness in Family Sub-Dimension Total; INTA: Family Climate Scale Intergenerational Authority Sub-Dimension Total; COGC: Family Climate Scale Cognitive Cohesion Sub-Dimension Total; APP: Distress Tolerance Scale Appraisal Sub-Dimension Total; TOL: Distress Tolerance Scale Tolerance Sub-Dimension Total; ABS: Distress Tolerance Scale Absorption Sub-Dimension Total; REG: Distress Tolerance Scale Regulation Sub-Dimension Total; BRS1-6: Single Item Scores on Brief Resilience Scale

Participants

The lower limit for the sample size of the study was calculated as 189 with the G*Power 3.1.9.2 package program [f^2=0.15, α=.05, number of predictive variables:13 observed variables]. The study group of the research consists of 221 people. 63 (28.5%) of the individuals in the study group were male, 158 (71.5%) were female, and their ages ranged from 18 to 62. Information on other demographic characteristics of the participants is given in Table 1.

Considering the demographic characteristics of the participants, 42.5% of them were in the 18-25 age range; 76.9% of them were university graduates; 52.5% did not work; 62.9% of them have regular income; 52.5% of them were married or had a partner; 50.2% of them spent most of their life in the big city; 72.4% of them are in the middle income level; 36.2% of them have a good relationship quality with their spouse/partner; It was determined that 20.4% had a good relationship quality with their child.

Table 1

Demographic and Pandemic-related Information

Demographic Information		n	%	Demographic Information		n	%
Age	18-25	94	42.5	Level of Income	Very Low	7	3.2
	26-35	53	24		Low	19	8.6
	36-50	56	25.3		Middle	160	72.4
	51-62	18	8.1		High	30	13.6
Education	Primary School	2	0.9		Very High	5	2.3
	Middle School	4	1.8	Quality of Spouse-Partner Relationship	None	78	35.3
	High School	13	5.9		Bad	7	3.2
	College	12	5.4		Good	80	36.2
	University	170	76.9		Very Good	56	25.3
	Graduate	20	9	Quality of Relationship with Child	None	133	60.2
Employment	Unem-ployed	116	52.5		Bad	2	0.9
	Employed	105	47.5		Good	41	18.6
Regular Income	No	82	37.1		Very Good	45	20.4
	Yes	139	62.9	**Total**		**221**	**100**
Marital Status	Married/ Has a Partner	116	52.5				
	Single	105	47.5				
Spent Most of The Life in	Village/ Town	14	6.3				
	Province	45	20.4				
	City	51	23.1				
	Big City	111	50.2				

Instruments

Family Climate Scale

It was developed by Björnberg and Nicholson (2007) to examine the characteristics of individuals related to family climate, and Gönül, Baş and Acar (2018) adapted the scale into Turkish. The scale consists of 34 items in total and is a 5-point Likert-type scale that includes statements such as "Strongly Disagree", "Disagree", "Undecided", "Agree", "Strongly

Agree". Family Climate Scale consists of three sub-dimensions: relatedness in family, intergenerational authority, and cognitive cohesion. High scores indicate that the dimension is more important and experienced in the family, while low scores indicate that the dimension is not given much importance and experienced in the family. The Cronbach Alpha internal consistency reliability coefficient of the scale was found to be .91, and it was found to be.90 for the current study.

Distress Tolerance Scale

It is a self-report measurement tool that evaluates individuals' levels of tolerating distress. The scale has a 5-point Likert-type rating as (1) I totally agree (2) I agree (3) I am undecided (4) I disagree and (5) I totally disagree. The scale has a total of 15 items and four sub-dimensions: tolerance, absorption, appraisal, and regulation. The Turkish adaptation of the scale was carried out by Akın et al. (2015). Internal consistency reliability coefficients were found as .72, .78, .82 and .74 for the subscales, respectively. The Cronbach Alpha reliability coefficient of the scale for this study was calculated as .91.

The Brief Resilience Scale

The scale was developed by Smith et al. (2008) to measure the psychological resilience of individuals. The scale is a 5-point Likert-type, 6-item, one-dimensional measurement tool. High scores on the scale indicate high psychological resilience. The Turkish adaptation of the scale was carried out by Dogan (2015). The internal consistency reliability coefficient of the scale was found to vary between .80 and .91. The test-retest reliability coefficient was found to be between .62 and .69. The Cronbach Alpha coefficient of the scale for this study was calculated as .86.

Procedure

It has been observed that it takes 10-15 minutes to answer the data collection kit prepared by the researcher to collect the data of the research. Research data is collected via Google Forms, and each participant was allowed to attend the study once. Data collection link was shared on Facebook, Instagram, and Twitter, then volunteers participated. There was no time restriction for filling the form.

Statistical Analysis

The hypothetical model planned to be tested in the research was tested with the IBM Spss Amos 21 package program. The fit of the model to the data was evaluated with the goodness of fit values. Acceptable limits for goodness of fit value were determined ≤5 for Chi-Square/df, ≥.90 for CFI, NNFI, and GFI; and ≤.08 for RMSEA and SRMR (Cokluk, Şekercioğlu,

& Büyüköztürk, 2012). We used two steps model test procedure in this study. Namely, measurement model was tested first then structural model was considered. Before the structural equation modeling [SEM] analysis, normal distribution was assessed via skewness and kurtosis values. All values were in the normal distribution limits. Thanks to online data collection, there were no missing values. Participants were required to answer all questions.

Results

Descriptive Statistics

Descriptive statistics are given in Table 2. When the values given in Table 2 are examined, the skewness values were observed to vary between .01 and -1.57; and kurtosis values were observed to vary between -.10 and 2.81. Considering these values, it can be stated that the data do not deviate from the normal distribution and therefore are within the limits of the normal distribution (Field, 2005, Tabachnick & Fidell, 2013).

Table 2

Descriptive Statistics

Variables	Min.	Max	$\bar{x}$	SD	Skewness	Kurtosis
FCS- Relatedness in Family Dimension Total	30	105	89.67	14.33	-1.57	2.81
FCS- Intergenerational Authority Dimension Total	7	33	19.45	5.13	0.08	-0.49
FCS- Cognitive Cohesion Dimension Total	6	30	19.61	4.56	-0.31	0.25
DTS- Appraisal Dimension Total	8	30	22.31	5.27	-0.43	-0.67
DTS- Tolerance Dimension Total	3	15	9.99	2.95	-0.24	-0.73
DTS- Absorption Dimension Total	3	15	10.00	3.31	-0.35	-0.59
DTS- Regulation Dimension Total	3	15	8.61	3.04	-0.07	-0.69
BRS1	1	5	3.66	0.96	-0.42	-0.10
BRS2	1	5	3.56	1.16	-0.41	-0.76
BRS3	1	5	3.61	1.11	-0.52	-0.30
BRS4	1	5	3.44	1.22	-0.53	-0.59
BRS5	1	5	3.15	1.06	0.01	-0.55
BRS6	1	5	3.38	1.24	-0.37	-0.88

FCS: Family Climate Scale; DTS: Distress Tolerance Scale; BRS1-6: Brief Resilience Scale Single Items

Correlations Between Observed Variables

Correlations between variables were evaluated with the Pearson Correlation Coefficient. The results obtained are given in Table 3. When the values are examined, it is found that there is no correlation value above .90, which indicates the multicollinearity problem.

Table 3

Correlations Between Observed Variables

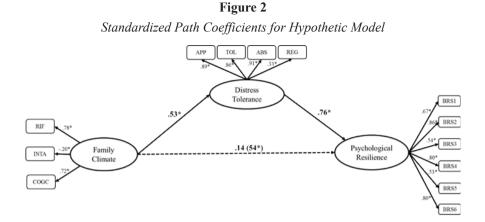|	1	2	3	4	5	6	7	8	9	10	11	12
RIF	-											
INTA	-.18*	-										
COGC	.56*	-.08	-									
APP	.39*	-.16*	.40*	-								
TOL	.32*	-.20*	.32*	.77*	-							
ABS	.31*	-.15*	.38*	.79*	.79*	-						
REG	-.01	.03	-.01	.26*	.33*	.35*	-					
BRS1	.30*	-.03	.18*	.50*	.38*	.47*	-.11	-				
BRS2	.34*	-.11	.27*	.64*	.57*	.67*	.15*	.61*	-			
BRS3	.22*	.02	.28*	.30*	.27*	.30*	-.05	.57*	.45*	-		
BRS4	.37*	-.15*	.29*	.59*	.60*	.62*	.22*	.48*	.68*	.42*	-	
BRS5	.22*	-.07	.19*	.34*	.25*	.36*	-.06	.45*	.50*	.38*	.41*	-
BRS6	.33*	-.19*	.37*	.69*	.62*	.66*	.09	.49*	.66*	.41*	.64*	.36*

*p<.05, RIF: Family Climate Scale Relatedness in Family Sub-Dimension Total; INTA: Family Climate Scale Intergenerational Authority Sub-Dimension Total; COGC: Family Climate Scale Cognitive Cohesion Sub-Dimension Total; APP: Distress Tolerance Scale Appraisal Sub-Dimension Total; TOL: Distress Tolerance Scale Tolerance Sub-Dimension Total; ABS: Distress Tolerance Scale Absorption Sub-Dimension Total; REG: Distress Tolerance Scale Regulation Sub-Dimension Total; BRS1-6: Single Item Scores on Brief Resilience Scale

Model Test

The goodness of fit values obtained after testing the measurement model of the hypothetical model were found to be $\chi2/df$ (197.98/62) = 3.19; RMSEA:.10 (.084-.12); IFI:.91; CFI:.91; and GFI:.88. It was determined that all values were within acceptable limits. In the measurement model, it was found that all factor loads varied between .20 and .91 and were significant at the .01 level.

After the measurement model test, the structural model test was performed, and the goodness of fit values obtained for the model were $\chi2/df$ (197.98/62) = 3.19; RMSEA:.10 (.084-.12); IFI:.91; CFI:.91; and GFI:.88. It was determined that all values were within acceptable limits.

Figure 2

Standardized Path Coefficients for Hypothetic Model

*p<.05. RIF: Family Climate Scale Relatedness in Family Sub-Dimension Total; INTA: Family Climate Scale Intergenerational Authority Sub-Dimension Total; COGC: Family Climate Scale Cognitive Cohesion Sub-Dimension Total; APP: Distress Tolerance Scale Appraisal Sub-Dimension Total; TOL: Distress Tolerance Scale Tolerance Sub-Dimension Total; ABS: Distress Tolerance Scale Absorption Sub-Dimension Total; REG: Distress Tolerance Scale Regulation Sub-Dimension Total; BRS1-6: Single Item Scores on Brief Resilience Scale

When the standardized path coefficients in the model were examined, it was found that family climate predicted resilience (β =.54, p<.05) and distress tolerance (β =.53, p<.05) at a statistically significant level; also, that tolerating distress predicts resilience (β =.76, p<.05) at a statistically significant level.

While the predictive effect of family climate on resilience is β=.54, p<.05, this effect becomes β=.14, p>.05 and ceases to be statistically significant by including distress tolerance in the model. Accordingly, it can be stated that the capacity to tolerate distress has a full mediating effect on the relationship between family climate and resilience. The significance of this indirect effect was evaluated by the bootstrapping technique (in 1000 samples), it was determined that this indirect effect was significant at the .001 level (99CI: 209-598). In addition, it is seen that family climate and the capacity to tolerate distress together explain about 70% of the resilience variable.

Discussion

In this study, the mediating role of tolerating distress in the relationship between family climate and resilience during the COVID-19 process was evaluated.

The results of the study show that family climate significantly predicts resilience and tolerating distress. The measures taken and the restrictions brought against the rapid contagious effect of COVID-19 have caused many changes in daily life. The restrictions imposed have significantly affected socialization and increased the time spent together by individuals living with their families at home. It is known that social support increases resilience in distressed situations (Netuveli et al., 2008). The studies of Ergül and Yılmaz (2020) during the COVID-19 process show that individuals attach importance to supporting, being compatible and caring for each other in the family (Ergül and Yılmaz, 2020). The results of the study can be interpreted that the improvement of the family climate facilitates the adaptation of individuals to the pandemic process and contributes to psychological resilience, as it increases the sense of unity in the family and the belief that they can cope with difficult situations. Similarly, individuals with balanced family compatibility and communication are thought to have improved decision-making mechanisms and be more functional in difficult situations (Gönül, Baş, & Acar, 2018). In this context, it can be thought that individuals' coping methods will be better in crisis situations and the level of toleration of distress increases because they see anxiety as controllable.

In addition, the results show that tolerating distress significantly predicts resilience. Accordingly, it can be stated that the capacity to tolerate distress has a full mediating effect on the relationship between family climate and resilience. Individuals with high psychological resilience can adapt to stressful situations, cope with difficulties, and perform well despite stress (Hasanoğlu & Seçkin, 2016). Therefore, it is understandable that psychological resilience increases as the level of distress tolerance does.

Pandemic periods are generally defined by feelings of fear and confusion, as there is uncertainty about information reliability, risk of getting sick, and prevention methods (WHO, 2005, Kanadiya and Sallar, 2011). Today, there are additional concerns such as the uncertainty of when the COVID-19 process will end, the lack of adequate medical care for everyone or the insufficient economic resources. For this reason, it is thought that it is important to determine the relevant variables to minimize the harmful effects of psychological stress. Resilience theory focuses on individual, social and contextual variables and positive features that enable coping with distressing situations (Fergus & Zimmerman, 2005). The results of the study suggest that supporting the tolerance of distress will support better coping with this uncertainty prevailing process and will facilitate the adaptation process. The results of the study also show that family climate may be important to strengthen psychological resilience and ensure its sustainability. It is thought that it may be important for the

support activities organized during the COVID-19 process to target the family system together with individual support to increase psychological resilience.

While evaluating the results of the study, current limitations should also be considered. The data of the study is based on online self-report assessments collected during the pandemic. Since the data were collected in a single time period, it is a cross-sectional study, so causality cannot be mentioned. Different methods can be used in future studies. Due to the restrictions in the pandemic process, while communication with other social resources decreased, the time spent at home and with the family increased significantly, increasing the importance of the family as a social resource in this challenging period. Future research should examine other important variables, such as distress tolerance, in the relationship between family climate and resilience or general psychological well-being. In addition, practical applications can be developed both at the family level (e.g., family climate) and at the individual level (e.g., psychological resilience, self-efficacy, self-compassion) during the COVID-19 process. Developing interventions to improve psychological resilience and psychological well-being through family climate and individual coping skills may be an effective tool for individuals that struggle with the disease. The COVID-19 epidemic has shown that humanity can be exposed to many unexpected, sudden and deadly situations. It is recommended that future studies focus more on the healing aspect of family and family climate, especially in all kinds of challenging situations that threaten individuals, and work on different variables, especially in fragmented families. Family climate can have a psychologically detrimental effect on health as well as the supportive one. To create a healthier and more supportive family climate, parental attitudes should be studied within the framework of object relations and attachment theories. In the light of current studies, parenting training can be given to couples through local governments. At this point, creating structured programs based on theories and research data may be another study proposal. In addition to all these, it is recommended to conduct more detailed studies on the ability of individuals to tolerate distress and how this ability can be developed.

Conclusion

Distress tolerance is a full mediator in the relationship between family climate and psychological resilience. It seems that family climate is a supportive and protective factor for individuals, specifically during this COVID-19 pandemic.
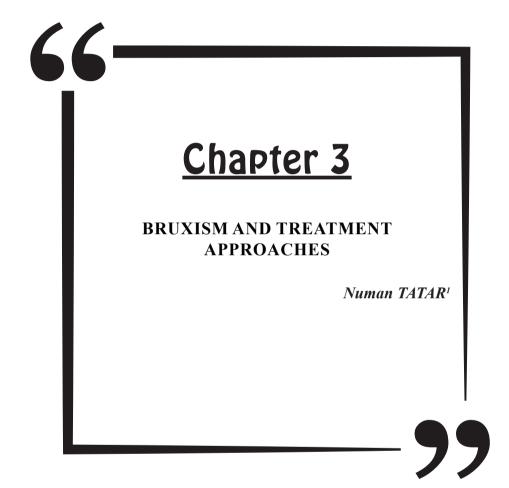
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Chapter 3

BRUXISM AND TREATMENT APPROACHES

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Bruxism is a parafunctional habit that is included in temporomandibular disorders and occurs as a result of overloading stomatognathic structures with clenching and grinding. These changes that occur on the temporomandibular joint are the flattening of the condyles and the loss of convexity of the articular eminence. At the same time, bruxism is the chewing movement of the mandible manifested by severe head and neck pain, limitation of jaw movements, pain and spasm in the chewing muscles, characterized by involuntary, rhythmic and non-functional teeth clenching and grinding, which is usually seen during sleep.(Akamatsu, Minagi, & Sato, 1996; Kataoka et al., 2015; Reddy, Kumar, Sravanthi, Mohsin, & Anuhya, 2014) In individuals with sleep bruxism, the sound of teeth grinding disturbs their sleep partners. This feature is used by dentists in diagnosing sleep bruxism.(BAYINDIR & GÜLDAĞ; Dawson, 1974; Yengin, 2000) In 1990, The International Classification of Sleep Disorders (ICSD) evaluated bruxism among the Parasomnia categories and defined it as a movement disorder with squeezing and squeezing.

Since the forces during functional activities spread to many teeth, teeth and supporting structures are not damaged. The wear of a few teeth seen as a result of parafunctional activities shows that this movement occurs in the eccentric position, the condyle is not in a stable condition, the tension in the chewing muscles increases and pathological conditions occur.

Most people are unaware of the habit of bruxism. In bruxism, the diagnosis can be made more easily if there is sound and clicking in the temporomandibular joint. The teeth and periodontium remain under pressure during chewing. With this habit, the tubercles can be completely eroded and become a flat occlusal surface and its incidence is between 5-20%.(BAYINDIR & GÜLDAĞ; Cosme, Baldisserotto, Canabarro, & Shinkai, 2005)

In the early periods, researchers generally tried to determine the relationship between occlusal interferences and bruxism. In the literature, it is emphasized that there is a direct relationship between occlusal interferences and muscle hyperactivity and incoordination. It has been reported that these occlusal interferences may cause parafunctional jaw movements.(Dawson, 1974)

It has been reported that bruxism may lead to an increase in the volume and strength of the masticatory muscles.(BAYINDIR & GÜLDAĞ; Dawson, 1974; Okeson, 1987) On the other hand, Cosme et al., in their study with young toothed individuals, stated that although they found lower maximal bite force values in individuals with bruxism compared to normal individuals, they did not find a statistical difference.(Cosme et al., 2005)

Etiology of Bruxism:

Among the causes of bruxism:

1. Local,

2. Systemic,

3. Psychological,

4. To the profession; there are related factors.

During bruxism, the bite forces that occur at night are more than the forces that occur in physiological functions during the day, and it is detected by a strain gauge device attached to the right and left molars in the lower jaw.(Akishige, 1992; BAYINDIR & GÜLDAĞ; Clark, 1984; Restrepo, Alvarez, Jaramillo, Velez, & Valencia, 2001)

Local factors:

Local factors are usually associated with mild occlusal discrepancies, mild discomfort, and chronic tension. Bruxism consists of an unconscious effort by the patient to remove a local irritating factor to keep more teeth in contact.

Occlusal incompatibilities can be a direct cause of bruxism. However, if the occlusal relationship is impaired or the presence of early contacts is combined with nervous tension, the possibility of causing bruxism increases even more.

It is accepted that patients with bruxism sleep in such a way that external pressure is applied to the lower jaw. It is stated that side and prone sleeping positions cause bruxism, while unilateral side positions cause joint and muscle pain.

Tooth mobility can also cause or increase bruxism. Usually the food on the teeth, Mobility is observed with plaque retention and subsequent tissue loss. Elimination of centric and protrusive contacts resulting in loss of interface contacts and increased mobility in anterior teeth, and splint therapy are viable options for such patients.

Studies on whether bruxism is associated with obstructive sleep apnea syndrome have emphasized that there is no direct relationship.(Akishige, 1992; BAYINDIR & GÜLDAĞ; Restrepo et al., 2001)

Systemic factors:

The role of most systemic factors is difficult to determine. Digestive system incompatibilities, nutritional deficiencies, allergies or endocrine disorders have all been reported as causative factors. In some cases, hereditary history has also been described.(BAYINDIR & GÜLDAĞ)

Pyschological factors:

Emotional tension causes many nervous habits. One of them is bruxism. Psychological factors are considered the most common cause of bruxism. Various emotional events such as stress, fear, anger, which the person cannot express with psychological problems, may remain hidden in the subconscious. These conditions can cause bruxism in individuals. Bruxism can be a sign of nervous tension in children. This can also occur during obstructions that usually occur during the mixed dentition period. By making occlusal arrangements, the sharp edges are smoothed and polished, and the factors are eliminated. Orthodontic treatment or a bite plate can be applied to protect the opposing teeth until the permanent teeth erupt or the necessary correction is made.(Akishige, 1992; BAYINDIR & GÜLDAĞ; Restrepo et al., 2001)

Occupational factors:

Occupational factors play an important role in the emergence of this disorder. Although it is known that there is no definite cause, bruxism often develops in occupations that are busy with physical activities and in professions that work under stress such as administrators and law enforcement officers. In addition, bruxism has been described in individuals who have the habit of biting various tools such as toothpicks, chewing tobacco and chewing gum.(Akishige, 1992; BAYINDIR & GÜLDAĞ; Restrepo et al., 2001)

Bruxism Diagnosis and Clinical Symptoms:

Bruxism, which can cause craniomandibular disorders, is considered a parafunctional habit.(Kataoka et al., 2015) It is difficult to diagnose bruxism because of its nonspecific pathology.(Holmgren, Sheikholeslam, Riise, & Kopp, 1990)

Localized or generalized radiolucency in the clinical manifestation of bruxism, There may be mobility, migration and bending of the teeth. In addition, depending on the chewing force applied, it may cause destruction of the alveolar bone.

Individuals with bruxism unconsciously grind their teeth while asleep or awake and they squeak. Therefore, the biggest challenge in bruxism is in restorative dentistry.

The most prominent feature of sleep bruxism is; They are rhythmic, chewy-like jaw movements and long-lasting and strong muscle contractions.

As it is known, sleep consists of two main stages: physiological REM sleep and non-REM sleep. Non-Rem sleep first occurs when a person goes to bed at night to sleep. Non-REM sleep, which consists of four stages, is

light in the first stage, gradually deepens, the third and fourth stages are the stages with the highest arousal threshold and it is called slow wave sleep. Non-REM sleep is followed by REM sleep, which occurs approximately 90 minutes later. In some studies investigating bruxism and sleep stages, it is argued that parafunctional activity is more frequently in the REM stage, while another group of researchers report that they are observed in the non-REM stage and especially in the 2nd stage. It has been determined that there is an increase in non-rhythmic, short-intermittent body movements in addition to clenching and grinding their teeth at night in individuals with the habit of bruxism.(Okeson, Phillips, Berry, Cook, & Cabelka, 1991; Restrepo et al., 2001; Saraçoğlu, Veznedaroğlu, Cura, & Akdeniz, 2001; Sjöholm, Polo, & Alihanka, 1992)

In its long-term existence, bruxism may affect the structure of periodontal tissues, causing bone loss, gingival recession and even tooth loss.(Akishige, 1992; BAYINDIR & GÜLDAĞ; Clark, 1984; Dawson, 1974)

Treatment Methods:

There are 3 general approaches to treat bruxism:

Behavioral treatment: The dentist gives explanations and warnings to the patient about his habit. It is tried to prevent the disease by creating awareness in the patient. Specific behavioral therapies can be applied as biofeedback and hypnosis.(BAYINDIR & GÜLDAĞ)

Emotional treatment: Provided with psychological guidance. If the underlying factors of bruxism are caused by an emotional event, neural factors should be corrected for the treatment of the disease. In addition, it has been reported that the use of small doses of tricyclic antidepressants (10-20 mg before bedtime) results in a decrease in teeth clenching and grinding activity due to changing the sleep cycle, and relieving morning muscle pain.(Figure 1) Saracoglu et al. investigated the efficacy of ampitriptyline in the treatment of bruxism, and reported that as a result, they significantly reduced bruxism and related muscle pain.(Saraçoğlu et al., 2001)

Figure 1: tricyclic antidepressants

1. Interceptive treatment: This treatment is divided into 2 in itself:

a. Regulation of occlusion

     i. Occlusal restorations

     ii. Orthodontically

Occlusal corrections play an important role in treatment when there is early contact with or pre-existing with the placement of dental restorations (Figure 2). More common occlusal replacements may also require reconstruction or orthodontic treatment. However, careful analysis should be performed on oral diagnostic models before occlusal correction is performed. If there is uncertainty about the patient's acceptance of this form of treatment and the dentist's experience, occlusal correction should first be done indirectly with the use of a removable appliance.

Figure 2: Occlusal correction with using artucilating paper

It has been reported in the studies that the idea that the problem will be solved by correcting the occlusion by selective molting is completely wrong.(BAYINDIR & GÜLDAĞ)

b. Indirect occlusal correction

According to another group of researchers, sleeping positions should be corrected in addition to dental treatment. It is believed that intraoral treatment will be more successful if patients change their sleeping positions in a way that reduces and relieves bad tooth contact.(BAYINDIR & GÜLDAĞ)

The most suitable sleeping position for patients with bruxism is the supine position. An improved side position is recommended for patients who do not sleep on their back. The head should be supported in line with the spinal cord and the skull should not press against the lower jaw. An anatomical pillow supports this position, while a second pillow supports the elevated shoulder and arm, relieving the pressure on the neck.(BAYINDIR & GÜLDAĞ)

Indirect Occlusal Correction is achieved by the following methods ;

a. Soft vinyl mouth guards,

b. Muscle relaxant splints,

Anterior bite plate appliances(Hamada, Kotani, Kawazoe, & Yamada, 1982; Holmgren et al., 1990; Okeson, 1987; Okeson et al., 1991)

Use of Appliances:

Tooth surfaces are protected by making bite appliances (Figure 3). Musculoskeletal during bruxism forces in the system are regulated. At the same time, the splinting movement that may occur in the teeth can be prevented. One of the advantages of occlusal splints is that they reduce nighttime erosion. Acrylic splints can also wear out, but replacing them is much easier than replacing tooth structures.

Figure 3: Biting appliances for muscle relaxation

In the study, it was observed that the electromyographic activity level was significantly changed in 71 % of the patients with the use of an occlusal splint.(Sheikholeslam, Holmgren, & Riise, 1986) Splints can be obtained by providing occlusal relationship with the models in the closing state, or they are made with hot - cold acrylic on a free lower or upper jaw model or with PVC plates in a pressure modeling device. After the splint is applied to the patient, it is said that he can remove it when he needs to speak, since it will initially cause speech difficulties. 2-3 week checks are made. It is used for 2 months. During this period, the diagnosis and treatment

method is determined, and the patient's permanent treatment is started or the splint usage period is extended. In addition to these splint treatments, alternative treatment methods are also applied by dentists. One of them is Botox applications. Botox (Botulinum toxin) is a toxin obtained from the bacterium Clostridium botulinum. Botox shows its effect by preventing the release of substances that provide conduction in the nerve endings, and by stopping the transmission between the nerves and the organs reached by the nerves. The cessation of nerve conduction ensures that the functions of the organ reached by the nerve are reduced or completely lost. The mechanism of action of Botox is used in many areas of medicine. Botox is administered as an injection and is not a painful procedure, a slight pain may be felt at the time of injection. The masseter muscle contributes to somewhere around 43% of the intrinsic strength of the jaw-closing muscles, the temporalis muscle about 36%, and the medial pterygoid around 21%.(Weijs & Hillen, 1985) Therefore, it is aimed to prevent bruxism by applying Botox to certain parts of the temporal and masseter muscles (Figure 4). When injected into striated muscle, chemical denervation of the muscle occurs within 2–3 days and lasts for 2–3 months. After approximately 3 months, the recovery of muscle function often occurs because of the gradual sprouting of nerve endings and the formation of new neuromuscular junctions.(Jankovic, 2004) When Botox loses its effect, the application can be repeated. When people who are regularly applied botox for 2 years continue the application in the same order, there may be a significant weakening in their muscles and a change in facial expression. For this reason, it is beneficial to make applications at longer intervals after the 2nd year. In their study, Tan and Jankovic reported that the pain and spasms in the masseter muscles decreased, and in some cases completely resolved, in the rate of teeth clenching after BTX-A injections they applied to their patients with severe bruxism.(Tan & Jankovic, 2000) In addition, it has been emphasized that the use of vibratory feedback devices with occlusal appliances inhibits bruxism without causing any sleep disorders. It is reported that biofeedback methods will be developed over time and made available to dentists.(Saraçoğlu et al., 2001)
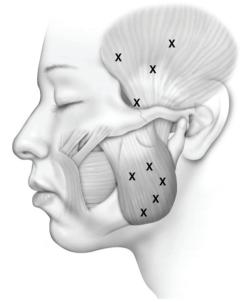
Figure 4: Illustration demonstrating the points of application of botulinum toxin in the masseter and temporal muscles

Another alternative treatment method is hypnosis. Generally, in order to cope with bruxism, it is necessary to eliminate the individual problems and the underlying causes of the person. No one wants to damage their teeth, restorations or dental structures. But this is an involuntary behavior. It simply happens as a habit and long-term emotional problems can magnify the problem. Teaching the method in which the patient can relax herself/himself is the simplest solution. With hypnos, the individual can be controlled and relaxed.(Lavigne, Rompre, & Montplaisir, 1996) Various orofacial pains can be reduced or eliminated with hypnosis. There are studies on this subject.(Abrahamsen, Baad-Hansen, & Svensson, 2008; Golan, 1989; Simon & Lewis, 2000; Stam, McGRATH, & Brooke, 1984)

Conclusion and Recommendations:

Bruxism is a parafunctional habit characterized by non-functional clenching and grinding of the teeth. Bruxism is known to cause temporomandibular joint discomfort. The aim in the treatment of bruxism is to eliminate the cause. Today, besides dental and pharmacological treatment methods, behavioral and cognitive treatment methods have become popular. However, in treating bruxism of a multifactorial nature, A single treatment option may not be sufficient. Therefore, in the treatment of bruxism, current treatment approaches should be included in addition to conventional treatment methods.

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Chapter 4

LANGUAGE DISORDERS AND ARTIFICIAL INTELLIGENCE

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What is Artificial Intelligence

It is hard to imagine life in the 21st century without the existence of intelligent systems. Significant advances in computer science have paved the way to the development of more powerful and elaborate computer systems that are able to fulfill tasks of different complexity. Artificial Intelligence (AI) in the present world takes different forms and is used almost in every aspect of our everyday routine. The examples of AI which have widespread use include speech assistants like Alexa and Siri, autonomous cars, characters in video games, automated translation services, or a recommender in an online commerce site (Reidl, 2019: 33).

The term *"intelligence"* has been defined in various ways depending on the discipline and the way it approaches the term. The term persists to maintain its importance in such fields as computer engineering, philosophy, mathematics, and neuroscience. Whether human intelligence can be measured and what is the right way to do it still remains a question. The "computational" character of intelligence has been widely accepted in the field of information technologies and one of the suitable definitions was proposed by McCarthy, the founder of the term "Artificial Intelligence". According to the researcher, intelligence is *"the computational part of the ability to achieve goals in the world. Varying kinds and degrees of intelligence occur in people, many animals and some machines"* (2007: 2). The more practical character of this debatable concept is highlighted in the definition given by Coppin who interprets intelligence as *"an ability to deal with new situations; the ability to solve problems; to answer questions, to devise plans, and so on"* (2004: 4).

The many-faceted approach to intelligence in general has led to versatile definitions of AI existing in the body of literature. For example, the multidisciplinary character of the term is emphasized in the definition proposed by the European Council *"Artificial intelligence is a set of sciences, theories and techniques (including mathematical logic, statistics, probabilities, computational neurobiology, computer science) that aims to imitate the cognitive abilities of a human being"* (Council of Europe, n.d.). The similarity between human and artificial intelligence is emphasized in the definition given by Reidl: *"Artificial intelligence (AI) is the study and design of algorithms that perform tasks or behaviors that a person could reasonably deem to require intelligence if a human were to do it"* (2019: 33). The most striking similarity among the definitions of AI refers to its resemblance to human intelligence and the ability not only to reproduce and replicate the functions of the latter but one day may be even to surpass some human capabilities.

Another important feature which lies at the basis of AI is the need for constant development and improvement of the machine learning techniques. This point was first highlighted in the manifest titled "A Proposal for the Dartmouth Summer Research Project on Artificial Intelligence" and written by John McCarthy and a group of computer scientists including such renowned figures of computer science as Marvin Minsky and Claude Shannon. "The study is to proceed on the basis of the conjecture that every aspect of learning or any other feature of intelligence can in principle be so precisely described that a machine can be made to simulate it. An attempt will be made to find how to make machines use language, form abstractions and concepts, solve kinds of problems now reserved for humans, and improve themselves" is stated in the paper. The term "Artificial Intelligence" is also attributed to McCarthy and his colleagues.

The Origins of Artificial Intelligence

Although AI is a relatively new discipline and the time of its founding can be traced back to the mid-fifties of the 20th century, a thorough research in the field demonstrates that the origins of AI may be attributed to a much earlier period.

The origins of AI are often associated with the ancient times, the ideas of Greek philosophers and engineers and later to the inventions associated with the Renaissance period (Sakın, Çetiner & Özdemir, 2021). As suggested in the body of literature, the first theory related to logic was proposed by Aristotle (Bibel, 2014: 88; Coppin, 2014: 6; Nilsson, 1988: 10). Although he didn't propose any mechanism that would replace human thinking, he came up with the idea of syllogisms that was aimed at the explanation of deductive reasoning used by computer systems and AI in the future (Park, W.J. & Park, J.B., 2018: 596). However, not only philosophers but also mathematicians later developed the ideas of logical reasoning. Gottfried Wilhelm Leibniz laid the foundations for a formal mathematical language of reasoning. Boolean algebra invented by George Boole in the 19th century is still widely used by computer scientists nowadays. Charles Babbage is credited for the design of the world's first computer – the Analytic Engine (Coppin, 2004: 8).

Despite the existence of some scientific background in the computational field, the rapid development of AI is thought to have started after a paper published by a mathematician and computer scientist Alan Turing in 1950 titled "Computing Machinery and Intelligence". The Turing Test proposed in the paper became widely known as the approach which determines whether computers are able to compete with people in terms of intelligence (Guo, 2015: 4).

The term "Artificial Intelligence" was coined in 1956 and is attributed to John McCarthy, at that time member of Dartmouth College, who with a group of scientists organized a two-month workshop to study AI after issuing "A Proposal for a Project on Artificial Intelligence". Together with Marvin Minsky, Nathaniel Rochester and Claude E. Shannon, McCarthy devoted himself to the study of AI, which was going "to proceed on the basis of the conjecture that every aspect of learning or any other feature of intelligence can in principle be so precisely described that a machine can be made to simulate it" (McCarthy, Minsky, Rochester & Shannon, 2006: 12). The subsequent years saw a great progress in the field of AI with the development of ELIZA, a natural language processing tool, and the General Problem Solver Program. Despite the achieved success, the period between 1970 and 1980 is termed as the "Winter of AI" as the American government spending for the development of AI were substantially decreased. The powerful comeback was not made until 1997 when IBM's Deep Blue program defeated the world's chess champion Gary Kasparov in a chess tournament. Another computer's success in the game was recorded in 2015 when the AlphaGo program developed by Google beat the world's champion in the Chinese board game Go, which is considered even more complex than chess (Haenlein & Kaplan, 2019: 3-4).

With the development of new technologies, the place of AI in the modern world has changed dramatically. The new evolutionary stage of AI is referred to as AI 2.0. As predicted by scientists, AI 2.0 will become an indispensable part of our life and will be capable of reconstructing human knowledge in order to generate solutions for social, industrial and environmental problems. Such functions as recognition, control and prediction in some special fields are already carried out by AI on the level comparable or sometimes exceeding the level of human intelligence (Pan, 2016: 410).

Natural Language Processing

Natural Language Processing (NLP) is a field of research within AI that is concerned with the automated analysis (processing) of natural languages (Meurers, 2019). As it can be understood from the abovementioned, the foundations of NLP were laid at the intersection of AI and linguistics, to be more precise, computational linguistics. The belief that computers one day will be intelligent enough to communicate with humans using natural languages is one of the cornerstones of AI. The term "natural language" refers to human languages (e.g. English, Chinese) in their spoken or written form as opposed to artificial, computer languages (e.g. Java, LISP). The various definitions of NLP emphasize its computational character and while some researchers hold it equal to the term *"computational linguistics"* (Otter, Medina, & Kalita, 2020), others regard it as *"the applied*

side of computational linguistics" (Meurers, 2019). The aims of NLP are *to process* a wide range of written and oral information regardless of its genre or style in the human-like manner and to facilitate communication either between people (as in machine translation) or between humans and computers (e.g. conversational agents) (Hirshberg & Manning, 2015: 261). Liddy defines NLP as *"a theoretically motivated range of computational techniques for analyzing and representing naturally occurring texts at one or more levels of linguistic analysis for the purpose of achieving human-like language processing for a range of tasks or applications"* (2001: 2).

NLP is accomplished on seven major linguistic levels: phonology, morphology, syntax, semantic, discourse and pragmatic. The levels of linguistic analysis utilized by NLP are divided into lower and higher ones. The lower levels deal with morphological, lexical and syntactic information represented in the text. The higher levels focus on the semantic, discourse and pragmatic properties of the analysed text. While the lower levels are more suitable for machine processing as contain less variation and are based on explicit rules, the higher levels represent a bigger challenge for natural translation (Joseph, Hlomani, Letsholo, Kaniwa & Sedimo, 2016: 210). Phonetic, phonemic and prosodic information is decoded on the phonological level. The level of morphology and lexis is responsible for the meaning extraction out of a number of variants with different contextual connotations. Next, the text is prossesed on the syntactic level with the help of parsing that is identifying part of speech, word inflections and syntactical relations between the units. On the semantic level the questions of semantic ambiguity of polysemantic words are resolved. And finally the two higher levels, which represent the most serious challenge for NLP programs, are the discourse analysis and the pragmatic level, which is concerned with adding pragmatic meaning to the context including speaker's intentions, beliefs, plans, and goals (Liddy, 2001: 6-9).

The work in the field of NLP originally started with machine translation around 1950s with experimental automated translation from Russian to English. Computers' limited storage capacity, slow working speed and restricted availability of machines complicated the process; nevertheless, the research of that period contributed to the development of syntactic analysis, laid the foundations of parsing and attracted attention to the problem of word polysemy existing in translation. The early systems of machine translation were far from being successful as they could not achieve meaningful translation. They were based on syntax analysis, and only when the semantic component was added, it became possible to avoid some degree of ambiguity between sentences in different languages (Kumar, 2011: 1-7).

One of the most significant advances in the field of NLP is related to the developments in the corpus-based or statistical linguistic data in the 1990s. Machine learning and training over large amounts of data proved to be more effective and led to the appearance of a new approach to language processing, so called data-driven approach. NLP uses a range of machine learning approaches. Basically, machine learning is *"a particular approach to the design of intelligent system in which the system adapts its behavior based on data"* (Reidl, 2019: 33). Thus, machine learning is a set of strategies which machines can be trained to exercise in order to learn specific algorithms on their own. With such technological advances as faster Internet, computers with increased memory capacity, and access to large amounts of text, many of the previously existing machine learning techniques have been either completely replaced by the new ones or significantly enhanced in order to meet the demands of modern society (Otter et al., 2020: 1-2). One of these recent innovations in the field of NLP, particularly in the area of machine translation, is the use of deep learning algorithms through artificial neural networks. With the help of deep learning technologies, the system can first be trained through some representational models and then can translate sentences on its own (Hirshberg & Manning, 2015: 262).

In the course of time NLP has expanded to a large and prospective area of computer science with a variety of applications not only in for the competent but also ordinary users. Generally, in the field of NLP it is possible to differentiate between the "core" and "application" areas which address different aspects of language processing. While core areas deal with more fundamental problems like language modeling and language processing on different levels such as morphological, syntactic and semantic, the application area focuses on finding more practical solutions for various problems related to language procession. NLP has proved to be especially useful for the text and speech-related tasks, which can facilitate much of the research work in different areas of knowledge. (Otter et al., 2020: 1-2). The tasks are carried out with the help of deep learning algorithms and are applicable on different linguistic levels.

On the level of syntax NLP focuses on such basic tasks as part-of-speech tagging and parsing. With the help of part-of-speech tagging it becomes possible to categorize words according to their part of speech, the function widely used in corpus linguistics. Parsing refers to the syntactic analysis of a string of words or sentences to show the syntactic relations within the designated groups of words. Parsing is subdivided into constituency and dependency parsing. As shown in Figure 1.1, while constituency parsing makes an analysis of syntactic structures of a sentence and results in building of a parse tree, dependency parsing is

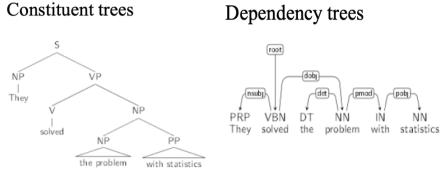concerned with the syntactic dependency relations between the words in a sentence (Torfi et al., 2021: 7-8).

Figure 1.1. Constituent and Dependency Tree Examples (https://www.cs.upc. edu/~horacio/snlp/depparsing-snlp.pdf)

On the semantic level NLP uses deep learning algorithms to complete such tasks as information extraction and retrieval, question-answering and machine translation. While the goal of information extraction is to elicit structured data out of "unstructured" information, for example, online media posts, information retrieval is aimed at the retrieval of targeted information such as text or images from bigger clusters of data. Question-answering is another modern application of NLP. Interactive applications such as Siri, Alexa, Ok Google, used by modern smart-phones are examples of question-answering tasks carried out with the help of deep learning.

The tasks completed with the help of NLP on the level of discourse can be exemplified with text classification and automatic summarization. The main purpose of text classification is to categorize the given texts according to a specific discourse. The purpose of text summarization is to produce a summary of a document or a set of documents.

The abovementioned applications of NLP are concerned with either generation or understanding of the written text. However, NLP can be also used for understanding and generation of speech. Dialogue systems, which include intelligent conversational machines used for automated customer service in various areas, facilitate human-computer interaction in the modern world. Apple's Siri and Amazon's Alexa are among the most prominent examples of dialogue systems used by a great number of people every day (Torfi et al., 2021: 9-16).

The working principles and current applications of Artificial Neural Networks will be discussed in more detail in the next section.

Neural Networks

Artificial Intelligence, machine learning, neural networks and deep

learning are closely related to each other and co-exist in the same system. As it can be seen from the diagram in Figure 1.2. AI is the broadest area that encompasses machine learning, Artificial Neural Networks (ANNs) as part of machine learning and deep learning as an approach within the operation of ANNs. Machine Learning is one of the approaches to the training of AI. Within the field of machine learning computers are taught to solve the problems they encounter by identifying their own strategies on the basis of data fed into the system. In this way the process of learning becomes completely automated. Machine learning algorithms also represent a very demanding task for the experts as the development of those is a multi-step and time-consuming process. Artificial Neural Networks or Neural Networks, as they are frequently referred to, constitute a subfield of machine learning. Such core task of machine learning as data representation, for example, is completed through neural networks.
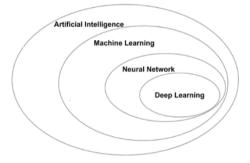

Figure 1.2. *(Adapted from https://livebook.manning.com/book/deep-learning-with-javascript/chapter-1/v-8/12)*

Neural networks take their origins from the biological system of neurons existing in the human and animal brain. The connections within the real biological brain and the layers, which are neurons comprised of, were loosely adapted to the artificial systems of learning and led to the development of networks functioning within the field of machine learning and AI. Deep Learning, in its turn, is recognized as one of the techniques of Machine Learning which is realized through deep, multilayered neural networks as opposed to shallow networks. The methods of Deep Learning are currently applied in face detection, speech recognition, natural language processing, and robotics (Arel, 2010). In the next two sections we are going to take a closer look at biological neural networks and their artificial counterparts.

Artificial Neural Networks

Throughout the history of humankind people have always been fascinated by the working principles of the brain as a human organ with

the most complex structure. Human brain comprises around 100 billion neurons, which are regarded as the most important brain cells and are connected to each other through myriads of junctions called synapses. The main function of neurons is to maintain the processes of learning and memorizing. Learning is usually carried out either by adjusting existing synapses or by creating new synoptical connections. Advances in neuroscience in general and the findings concerning the functions of neocortex, which is basically a set of layers in the human cerebral cortex, led to the idea of creation of artificial networks. The biological model of neural connections within a human brain proposed by Nobel laureates David H. Hubel & Torsten Wiesel inspired the modeling of ANNs (Ongsulee, 2017).

Although ANNs were developed to simulate real neuron activity, in fact they bear very far resemblance with their biological counterparts. If biological and artificial network are compared, the figures speak for themselves. Cerebral cortex contains about 10^{11} neurons. Each neuron is attached to 1000-10.000 other neurons involved in $10^{14} – 10^{15}$ connections. In contrast, ANNs consist of around 1000-10.000 neurons and each of them has from five to 100 links with other neurons (Basheer & Hajmeer, 2000: 7). Thus, ANNs are trying to imitate the architecture of the real neural network yet are unable to function with the same productivity and complexity (Ahire, 15-17).

Basic Architecture of Artificial Neural Networks

The most common structure of an ANN is comprised of artificial neurons similar to neurons in biological organisms. The neurons are grouped into several layers which include: the input, the hidden layer and the output layer.
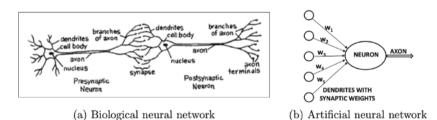

(a) Biological neural network   (b) Artificial neural network

Figure 1.3. *Biological and Artificial Neural Networks (Aggarwal, 2018: 1)*

The input layer corresponds to the dendrites in the biological neural network. The next, middle layer, defined as the hidden layer, represents the cell body of a neuron. The third layer, the output was developed by the analogy with the synaptic outputs in the human brain (Smartsheet, 2018).

Similar to the neurons in the human brain, artificial neurons are also connected to each other through a complex network of algorithms. Every connection has a weight which is processed accordingly by the neuron.

In the so called "model generalization" approach, the training data with picture representations may be fed into the neural network as the input and pictures with labels may be given as the output. For example, if an ANN is trained with various representations of apples, it will eventually be able to recognize an apple in a new image. Thus, the system is trained to generalize the properties of images and apply them to the ones it has never seen before. Scientists predict that in the foreseeable future the number of ANNs trained by computers might be comparable to the number of neurons in the human brain (Aggarwal, 2018: 20-21).

ANNs through machine learning techniques are trained to recognize the data previously fed into the system, in other words, they are trained to perform the tasks of pattern recognition. Pattern recognition is the most fundamental purpose of machine learning since it originated from the idea that machines must be supplied with artificial intelligence to learn through experience (Chen, Challita, Walid, Yin & Debbah, 7). In humans pattern recognition is a process performed through learning, to be more precise, it is a mechanism done through trial and errors. For example, a child learns to walk by first crawling, then standing up, making steps, then falling and standing up again. In this way the walking behavior is successfully trained and modelled in the child's brain. Machine learning is also a process that resembles the way a teacher would teach children to recognize shapes, colors and letters. Thus, the system is able to work with the new data it hasn't seen before using the previous patterns. The difference is that human brain processes new information and carries out pattern recognition tasks much faster and much more effectively than any computer system. However, writing an algorithm that would train the AI systems to perform pattern recognition tasks is a time-consuming and sophisticated job related to the procession of vast quantity of data (Aggarwal, 2018: 17–19).

The two most common patterns of learning in neural network algorithms include supervised and unsupervised learning. These two models of learning differ from each other in the way data is fed into the system. In the supervised learning neural networks data is given in the form of input and specified output, or target. The specified output indicates what the neural network's result should look like. The weights are adjusted in the way to guide the system to the correct output with minimal errors. These sets of data are memorized and system is expected to recall the given patterns of data and apply it correctly in the future. A crucial feature of the training set is its representativity, it must represent the training model correctly (Zou, Han, & So, 2008: 19). In contrast, unsupervised neural networks do not use target training sets. The neural network is expected to discover the intrinsic pattern in the data in order to use it in the future (MacKay,2005:471).

(a) Supervised Machine Learning

(b) Unsupervised Machine Learning

Figure 1.4. *Supervised and Unsupervised Machine Learning Algorithms*

Applications of ANNs

ANNs and their architecture have significantly changed since the 1980s leading to the expansion of their use in various industrial fields. The classic applications of ANNs include pattern and image recognition, control and classification. However, the state-of-the art functions of ANNs allow them to be applied for more complicated tasks in such spheres as robotics, aviation, medicine, and business (Shumann & Gupta, 2010: 2).

Due to expanding amounts of data generated by computers, there is now a growing need for automated procession and classififcation of this data accross various areas of human activity. Since ANNs are one of the machine learning frameworks capable of processing data in a manner similar to human brain, the use ANNs algorithms has become pervasive in many sectors such as health care, marketing and sales, finance and communication. The main tasks executed by ANNs can be roughly divided into four groups: classification of data, prediction, clustering of data and associating the familiar patterns of data with the new ones (Abiodun, Jantan, Omolara, Dada, Mohamed, & Arshad, 2018). The performance of these tasks is crucial for many industries. In aerospace ANNs are used in aircraft control systems and auto-piloting. Manufacturing makes use of ANNs in relation to product design and analysis, planning and management. The area of telecommunication applies ANNs for network control, pattern recognition (semantic parsing, speech recognition, spell check), and translation of spoken languages. Automotive industry, health care and marketing are just some other examples of areas that successfully implement ANN algorithms in their work. In the recent time ANNs have also started to being used in wireless communication and networking. The

level of interaction between people and mobile devices has significantly increased and ANNs are perfect instruments to store and analyze human behavior for wireless communication (Chan et al., 7–9). Thus, it becomes clear that the application of ANNs is ubiquitous in the world of modern technology.

Artificial Intelligence in Language Research

Artificial intelligence, which has been rapidly progressing from its very start, in the present day world is extensively used in different areas including speech assistants, autonomous vehicles, and robotic applications, to name a few. Undoubtedly, one of the areas where artificial intelligence has been applied quite a lot recently is the health care system. The areas of application of artificial intelligence in the health care can be roughly divided into two major groups. While the first one is concerned with administrative areas such as general health management, cost quality management and documentation processes, the other one covers such areas of medical practice as early diagnosis, treatment, robotic surgeries, radiological image analysis and test results follow-up (Akalın & Veranyurt, 2020: 5). If we are to determine the problems within health care that artificial intelligence focuses on, the following should be mentioned: diagnosis of diseases, classification of diseases, detection of diseases, processing of medical images, prediction of diseases, development of medical support systems, diagnosis of diseases, determination of the degree of risk of diseases, prognosis follow-up of diseases, monitoring of diseases, public health, health services management and specifying physician's diagnosis (Hoşgör & Güngördü, 2022:401-402).

Natural language processing (NLP) has been widely used in the healthcare research and practice. With the help of NLP-based dictation systems the verbal expressions of doctors, nurses or patients can be decoded and answered by the artificial intelligence systems (Bresnick, 2018 & Marr, 2018). Technological developments of artificial intelligence at the liguistic level have led to the rise of various applications in the healthcare sector. An artificial intelligence tool "Woebot" offers verbal support to patients with different psychological disorders by analyzing their emotional status and using various therapeutical methods. For problem analysis Artificial intelligence uses the system of Natural language processing. Upon the analysis of verbal responses of speakers, artificial intelligence predicts the follow-up dialogues based on the expression patterns. "Joyable", which has the feature of a chat robot, helps people with negative feelings and thoughts to get rid of these negativities. During its interviews with people the robot guides them on the way to positive feelings and emotions. "Wysa" is an artificial intelligence service with emotional intellect. The bot uses cognitive behavioral therapy techniques to get in touch with

people and offers its users individual development practices based on the personality analysis. Another chatbot with utilizing a cognitive behavioral therapy method is called "Sanvello". While having similar features to other chatbots, it also produces character and psyhco analysis based on the written text, audio or video material obtained from its users. The bot also enables people to communicate with each other due to its interactive features.

In line with the widespread use of artificial intelligence in the healthcare services, the artificial intellignece systems have also been used in multidisciplinary studies.

Neuroscience, the study of human brain, overlapping neurolinguistcs, which includes language research, also plays a critical role in this context. Neurolinguistic research analyses language components according to their localization in the brain and also focuses on language disorders that occur as a result of neurological conditions (Tanrıdağ, 2020: 145). Advancements in the healthcare system brought by the widespread use of artificial intelligence have also led to the improvements in the linguistic research in this area. In particular, the application called "TikTalk" developed by an Israeli company is one of the significant exemples in this field. This practical application designed to use by language pathologists during therapy is an artificial intelligence system, which analyses speaker's pronunciation and aims at detecting linguistic errors in children with language and speech disorders by making them pronounce words while playing a game. Thus, the application both enables a language therapist to track the language performance of a speaker after the session and gives a child an opportinuty to unergo therapy in an enjoyable way away from his family.

Conclusion and Recommendations

One of the most outstanding features of human beings is their superior language ability. Due to this ability people are able to understand, perceive and think critically. Perhaps, the most significant feature that distinguishes artificial intelligence from other inventions of the new technological era is that it also develops a superior language skill typical of humans. Artificial intelligence with its presence almost in every field today has been progressing by imitating human brain through such subfields as machine learning, artificial neural networks, deep learning, natural language processing and text mining. Specifically, the advances in the field of Natural Language Processing have equipped artificial intelligence beings with human-like abilities to understand, perceive, interpret and give appropriate feedback. In this respect, it is of critical importantce to use it effectively in research areas focused on language disorders such as

neurolinguistics and language pathology. Watson for Health, Deep Mind, Aidoc, CardioLogs and IoT-based remote monitoring systems are actively used in the early diagnosis and treatment of diseases (Büyükgöze & Dereli, 2019; Gomez Pinilla, 2013; Shin, 2019; Darshan & Anandakumar, 2015). Similarly, integrating artificial intelligence into language disorders research will facilitate the work of physicians and language pathologists in detecting the symptoms of language disorders, supporting the correct diagnosis based on the symptoms, and play an effective role in the implementation of the necessary treatment or therapy.

Specifically, the development of artificial intelligence systems in integration with such branches as Neurology, Otorhinolaryngology and Psychiatry/Psychology will facilitate neurolinguists and language pathologists in language disorders research. Neurolinguists will be able to deepen their brain research due to artificial intelligence, and language pathologists will be able to personilaze their therapy thanks to the applications developed. In addition, in the future it will be possible to reduce the workload of speech and language therapists, to easily monitor the progress of patients, to receive instant feedback, to ensure that the family takes a more active part in therapy, to detect language disorders in schools early and to make necessary guidance and interventions due to the instant screening systems.

Despite a large number of patients with speech and language disorders in Turkey and around the world, the insufficient number of speech and language therapists also prevents patients from accessing high-quality, low-price and equally accessible therapy. The development of therapy robots integrated into advanced cloud systems that will facilitate the work of language pathologists is extremely important both for language and speech therapists and for patients with speech and language disorders who for some reasons cannot get in touch with therapists or have the need for more qualified support, is of utmost importance.

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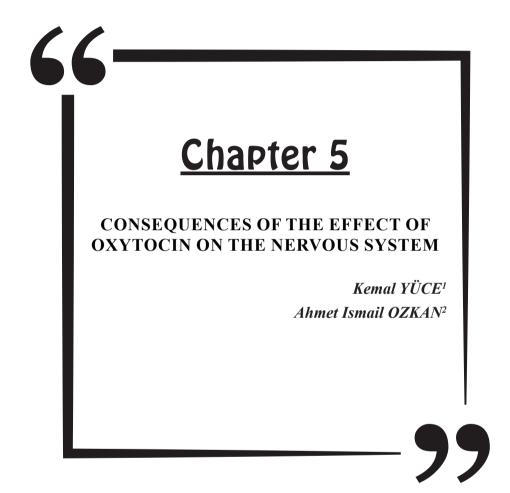
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Chapter 5

CONSEQUENCES OF THE EFFECT OF OXYTOCIN ON THE NERVOUS SYSTEM

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Introduction

The neuropeptide oxytocin (OXT), which is involved in social approach, social awareness, and bonding, is crucial in the regulation of complex social behavior and consciousness. Social issues like autism, social anxiety disorder (SAD), and borderline personality disorder (BPD) are linked to the OXT system. In the supraoptic and paraventricular nuclei of the hypothalamus, magnocellular neurons produce OXT, which is then carried by axonal extensions to the posterior lobe of the pituitary. Secretory vesicles are also stored here and released into the peripheral circulation. OXT is secreted outside from the axonal terminals as well as from the dendrites into the extracellular spaces. This not only causes local effects, but also allows it to affect distant areas of the brain. Because OXT can be transported by diffusion to relatively distant parts of the brain. However, smaller parvocellular neurons in the OXT -producing paraventricular nuclei extend to other areas of the brain. Thus, OXT is transported from the parvocellular neurons of the hypothalamus to different parts of the brain. Hippocampus, amygdala, suprachiasmatic nucleus, striatum, brainstem and bed nucleus of stria terminalis are among the brain regions where OXT is transported. It acts as a neurotransmitter or neuromodulator by acting on nerve conduction in these places (Heinrichs, Chen, & Domes, 2012). OXT is deposited with neurophysin 1 at axon terminals. Neurophysin 1 dimerizes with oxytocin and is involved in the proper packaging, targeting, and storage of oxytocin. When OXT is released from the granules, it leaves the neurophysin and free OXT enters the plasma. OXT does not bind to plasma proteins. OXT is degraded by enzymes in the gastrointestinal tract, but is rapidly absorbed when administered buccally or intranasally (Roby, 2019). OXT encourages interpersonal relationships between two or more people and motivates, mediates, and rewards the cognitive and behavioral processes that underlie the emergence of a stable social group and its dynamics. These connections can be beneficial (producing neurologic reward, lowering anxiety, and indicating consequences that improve wellbeing) or harmful (increasing anxiety and distress and thus revealing a problematic, debilitating social situation) (Crespi, 2016).

Oxytocin acts as both a hormone and a neurotransmitter in the brain. The golgi transports prooxytocin to secretory sites at axon terminals and somatodendritic areas from the cell bodies of hypothalamic neurons in the paraventricular and supraoptic nuclei. The somatodendritic regions secrete oxytocin, which diffuses throughout the hypothalamus and adjacent brain areas. Brain oxytocin travels to brain regions involved in social behavior and binds to its receptors there. Annexin A1 (ANXA1) controls the transport of oxytocin vesicles between the cell body and the axon in a manner sensitive to protein kinase C (PKC) and protein

kinase A (PKA) (Makani et al., 2013). Oxytocin is then released from the axon terminal in the posterior pituitary gland into the bloodstream. Magnocellular neurons in the supraoptic nucleus (SON), which are involved in controlling the release of vasopressin and oxytocin from the posterior pituitary, receive inputs from the brainstem. Some neurons that project directly to the SON from the nucleus tractus solitarius (NTS) in the brainstem are specifically activated at birth. A significant number of these are noradrenergic and control the release of oxytocin during childbirth. Intracerebroventricular somatostatin increased neuron firing rates of SON oxytocin and vasopressin. Studies have shown that somatostatin neurons in NTS are activated during birth, and somatostatin has a direct inhibitory effect on oxytocin neurons (Meddle, Bull, Leng, Russell, & Ludwig, 2010). Parvocellular oxytocin neurons extend to the midbrain, brain stem, and spinal cord and are involved in the regulation of food intake, respiration, erection, copulation, cardiovascular reactions, gastric reflexes, and pain perception. Parvocellular oxytocin synapses with magnocellular oxytocin neurons in SON. Parvocellular oxytocin neurons control the activity of magnocellular oxytocin in the PVN (Grinevich & Ludwig, 2021). The blood-brain barrier's endothelial cells have receptors for advanced glycation end products (RAGE), which carry oxytocin from the peripheral blood to the brain (Yamamoto & Higashida, 2020).

Oxytocin and stress

In the hippocampus, oxytocin treatment greatly improved the corticosterone stress response, decreased the expression of glucocorticoid receptors, and raised the expression of mineralocorticoid receptors. Co-administration of high-dose corticosterone with norepinephrine resulted in hippocampal oxytocin receptor and release of plasma oxytocin. Oxytocin takes an active role as a neurobiological response in the stress response to the odors of predators. Therefore, oxytocin is recommended as a viable therapy for the management of illnesses associated with anxiety (Cohen et al., 2010). The hypothalamus's oxytocin neurons are triggered by both stressful stimuli and food consumption. Oxytocin influences behavioral and neuroendocrine stress responses. Additionally, oxytocin participates in the interactions between stress and food intake and supports proactive, adaptive coping mechanisms (Onaka & Takayanagi, 2019). In response to stressful situations such as fear and exposure to a new environment, the pituitary gland releases oxytocin. The medulla oblongata's noradrenergic projections are thought to control this response. Prolactin-releasing peptide is present in some of these noradrenergic neurons. Prolactin-releasing peptide and noradrenaline stimulate the release of oxytocin into the circulation. Stress stimulus activates prolactin-releasing peptide-containing noradrenergic neurons in the medulla oblongata. Prolactin-

releasing peptide/neuradrenergic extensions, extending from the hypothalamus are likely to regulate oxytocin in response to stress stimuli (Onaka, 2004). Stressors cause both peripheral and central release of oxytocin in laboratory rodents. Mice genetically deficient in oxytocin not only exhibited more anxiety-related behaviors, they also released more corticosterone. These findings showed that central oxytocin was anxiolytic and relieved stress in female mice (Amico, Mantella, Vollmer, & Li, 2004).

The suppression of corticotropin-releasing hormone (CRH) neurons, which control the activation of the hypothalamic-pituitary-adrenal axis in the paraventricular nucleus of the hypothalamus (PVN), is the cause of the reduction of stress brought on by oxytocin. The activation of the hypothalamic-pituitary adrenal axis is regulated by CRH neurons in PVN of the hypothalamus. After NaCl injection, oxytocin-producing neurons are stimulated in the rat PVN, a subgroup of parvocellular neurons develops an oxytocin receptor (Oxtr)-dependent inhibitory tone, and stress-related rises in plasma corticosterone levels cease (Pati et al., 2020). The levels of stress-stimulated plasma ACTH, hypothalamic corticotropin releasing factor (CRF) hnRNA (30 minutes), CRF mRNA, and pituitary pro-opiomelanocortin mRNA (4 hours) were all lowered when oxytocin was administered intracerebroventricularly. This occurred in parallel with the increased stimulus caused by the elevation of plasma estradiol (Ochedalski, Subburaju, Wynn, & Aguilera, 2007).

Oxytocin and social behaviors

The different therapeutic roles of OXT include psychiatric disorders such as anxiety, depression, schizophrenia and autism (Imanieh, Bagheri, Alizadeh, & Ashkani-Esfahani, 2014). In terms of OXT effects, although it generally shows heterogeneity between individuals, it controls human social-emotional behavior and associated brain functions. Mutual cooperation was enhanced by intranasal OXT administration in men but tended to be decreased in women. Only those with the rs53576 GG genotype showed an OXT-related sex impact; people with the rs53576 AA/AG genotype did not (Feng et al., 2015). Aggressive antisocial behavior is the most common reason for adolescent referral to mental health clinics. The OXTR single nucleotide polymorphisms (SNPs) rs6770632 and rs1042778 have been reported to be associated with excessive, persistent, and widespread aggressive behavior in women and men, respectively (Malik, Zai, Abu, Nowrouzi, & Beitchman, 2012). The central nervous system is impacted by oxytocin, which is also engaged in a number of social and non-social behaviours. In both male and female rats, significant positive relationships between hypothalamic OXT and estrogen receptor alpha (ER-α) mRNA expression were observed, and both sexes' hypothalamic OXT mRNA expression increased during development (Matsuzaki et al.,

2015). OXT can be therapeutic in disorders of social communication and interaction, promote attention to objects, and facilitate directed gaze (Le et al., 2021). Oxytocin is a key mediator of social contact, collaboration, and maintenance in social animals like monkeys. Oxytocin has been found to play a role in both grooming and fur scrubbing behaviors. Overall, these findings demonstrate that oxytocin plays a key role in the actions of capuchin monkeys that sustain and strengthen social bonds (Benitez, Sosnowski, Tomeo, & Brosnan, 2018). Oxytocin is important for behaviors such as anxiety, learning, nutrition, and pain perception, as well as for social memory, bonding, sexuality, maternal behavior, and aggression. In addition, there are studies that state that oxytocin is important in creating a sense of trust in humans (Lee, Macbeth, Pagani, & Young, 2009; Leng, Meddle, & Douglas, 2008). Compared to community mothers, clinical mothers interacted with their children in more intrusive and depressive manner. In mothers without mental illness, neuropeptide oxytocin has been linked to more ideal interpersonal behaviors. Baby interference was reduced in mothers hasing increased oxytocin levels. In clinical mothers, higher oxytocin levels were linked to less depressive behaviors (Samuel et al., 2015). In the period leading up to motherhood, endogenous oxytocin has an important role in regulating happy mood, reducing responsiveness to stress, and promoting healthy maternal behaviours (including breastfeeding) (Bell, Erickson, & Carter, 2014). In addition, in mothers who lost their baby, brain oxytocin and corticotropin releasing factor play a role in the formation of maternal behaviors and stress responses in the grieving mother (Demarchi, Pawluski, & Bosch, 2021). Clinical studies have also demonstrated that oxytocin enhances social contact in autistic people (Cherepanov et al., 2017).

Conversely, there are studies that state that oxytocin administration can reveal antisocial behaviors and also the behaviors induced by oxytocin are related to the context of the situation (Piva & Chang, 2018). Aggression and fear behaviors are regulated by the neuropeptides vasopressin and oxytocin. Studies on both animals and people demonstrate the importance of the amygdala in regulating fear and anxiety. Threat stimuli are recognized by the amygdala, which then links them to protective responses. This is achieved through projections linking the brainstem and the hypothalamus regions that control fear responses to the central amygdala. Vasopressin and oxytocin have been found to counter-regulate stimuli entering the amygdala, and oxytocin is involved in controlling the fear state (Debiec, 2005). Plasma levels of oxytocin were significantly lower in patients with borderline personality disorder (BPD) compared to controls. Additionally, the BPD group's oxytocin receptor protein expression was noticeably reduced. Plasma oxytocin levels and the Zuckerman-Kuhlman Personality

Questionnaire (ZKPQ) activity index score were found to be positively correlated. The ZKPQ sociability index score was inversely linked with oxytocin receptor protein expression (Carrasco et al., 2020). Apart from these, it should be noted that there are studies stating that oxytocin is associated with lying behavior (Sindermann, Luo, Becker, Kendrick, & Montag, 2020).

Oxytocin and the reproductive system

Several neurotransmitters, including oxytocin, increase or inhibit the activity of GnRH neurons throughout the reproductive cycle. However, it has been discovered that in a subset of GnRH neurons, oxytocin can directly regulate neuronal activity. In addition, it has been stated that both the neuronal activity of oxytocin and the expression of oxytocin receptors on GnRH cells are not affected by estrogen (Caligioni, Oliver, Jamur, & Franci, 2007). Kisspeptin expression rises in rat periventricular nucleus neurons that project to the oxytocin system in late pregnancy. In anesthetized pregnant rats, kisspeptin administered supraoptically increased the action potential firing rate of oxytocin neurons. This increased firing rate was linked to an increase in oxytocin neuron excitability. Kisspeptin application to hypothalamic sections did not change either the activity of supraoptic nucleus neurons or the strength of synaptic impulses to supraoptic nucleus neurons, but it may activate oxytocin neurons in late pregnancy by momentarily raising oxytocin neuron excitability after each action potential (Abbasi et al., 2022).

Oxytocin and schizophrenia

The effects of the hypothalamic neuropeptide oxytocin on women are unknown, despite the fact that it has been discovered to aid mentalization in men with schizophrenia. In addition, higher anti-dopaminergic drug dosage in male patients with schizophrenia was also associated with a reduced response to oxytocin (Bradley, Tai, Hankin, & Woolley, 2021). Intranasal Oxt administration reduced some heterogeneous symptoms associated with schizophrenia (Rich & Caldwell, 2015). Daily intranasal oxytocin therapy for 2–8 weeks was reported to dramatically lessen psychotic symptoms in schizophrenia. The patients used in the study also showed improvement in social cognition or neurocognition after treatment, although they did not respond to antipsychotic treatment (Pedersen, 2014). It is thought that the oxytocin system may become dysfunctional in patients with schizophrenia. Findings from animal studies have demonstrated a particular efficacy of oxytocin in treatment-resistant schizophrenia patients. Clinical data on trans-nasal OXT therapy in schizophrenic patients do not conclusively demonstrate an overall therapeutic effect on psychopathology, but have found positive effects on higher integrated social cognitive performance,

such as empathy and mentalization (Luckhaus, Juckel, & Hurlemann, 2019). In schizophrenia, abnormal eye gazing is typical and is associated with functional impairment. Visual attention to social stimuli is regulated by the hypothalamic neurotransmitter oxytocin. Intranasal oxytocin increased eye gazing in men with schizophrenia, which is consistent with the results that oxytocin optimizes the processing of social inputs (Bradley et al., 2019). Schizophrenia patients scan less and focus less with their eyes. Oxytocin regulates eye gaze while exploring the environment. Oxytocin increased focus count and dispersion while decreasing average focusing time. It was found that acute intranasal administration of oxytocin may have the potential to increase visual attention in schizophrenia (Porffy et al., 2020). Endogenous oxytocin levels are reported to be related to positive symptoms of schizophrenia and lower scores on positive symptoms are observed in patients with higher serum oxytocin levels. In patients with schizophrenia, lower levels of endogenous oxytocin were linked to more severe positive symptoms. However, it should not be forgotten that there are researchers who state that the opposite is true. Patients with schizophrenia showed a substantial negative connection between oxytocin levels in their cerebrospinal fluid and plasma. Endogenous oxytocin levels were found to be inversely correlated with negative schizophrenia symptoms (Goh, Chen, & Lane, 2021).

Effect of oxytocin on autism

In developing countries, 1% of children have autism. Autism's severe language and social communication deficiencies, as well as the sensory, autonomic, motor, behavioral, and cognitive abnormalities, may be explained by the dysfunctional oxytocin system in infancy (Quattrocki & Friston, 2014). The main symptoms in autism are: speech and communication abnormalities, social dysfunctions, repetitive behaviors and limited interests (Bartz & Hollander, 2008). Oxytocin administration is recommended as an effective drug for some of the main effects of autism, especially in the area of social functioning (Huang, Huang, Ebstein, & Yu, 2021). One of the animal models of autism, Magel2[tm1.1 Mus] mice, was found to have a deficit in social memory. Peripheral oxytocin administered to these animals in infancy improved social behavior until adulthood. The quantity of somatostatin interneurons and oxytocin receptors increased along with the GABAergic activity of CA3-pyramidal cells in both the DG and CA2/CA3 areas. In this mouse model of oxytocin, a delay in GABAergic development was revealed in the offspring. It was stated that this delay occurred due to the phosphorylation change of KCC2. First of all, subcutaneous administration of oxytocin in mutant newborns was found to restore hippocampal changes and social memory in adulthood (Bertoni et al., 2021). In a study, subjects who received oxytocin and

probiotic combination therapy showed significant improvements in their the Clinical Global Impression (CGI) ratings as well as improvements in their Aberrant Behavior Checklist (ABC) and the Social Responsiveness Scale (SRS) compared to those who received a placebo. The combination's prosocial cognition response was highly correlated with the abundance of the *Eubacterium hallii* group (Kong et al., 2021).

Cntnap2 mutant mice are an experimental animal model for autism spectrum disorder. Mutant mice showed an overall decrease in brain oxytocin levels and a reduction in the number of oxytocin immunoreactive neurons in the paraventricular nucleus of the hypothalamus. Melanocortin receptor 4 agonist administration, which triggers endogenous oxytocin release, also quickly reversed the social deficiencies brought on by an oxytocin antagonist. It was found that acute oxytocin neuropeptide treatment to these animals improved their social deficiencies. In these mice, early postnatal treatment with oxytocin was shown to lead to more permanent behavioral improvement in PVN and restoration of oxytocin immunoreactivity (Penagarikano et al., 2015). The heterogeneity of the condition is the primary obstacle to creating effective treatments for autism spectrum disorders. Many genetic mutations pose a high risk for autism, and each mutation is the cause of only a small proportion of autism cases. Synaptic proteins, translation rearrangements, and chromatin modifications can form subsets of risk genes. One of these genes is neuroligin 1. An autism-related mutation in the synaptic adhesion molecule neuroligin-3 (Nlgn3) disrupted oxytocin transmission in dopaminergic neurons and impaired social novelty reactions in mice. Treatment of Nlgn3KO mice with a MAP-kinase inhibitor restored oxytocin and social novelty responses (Hornberg et al., 2020; Penagarikano, 2017).
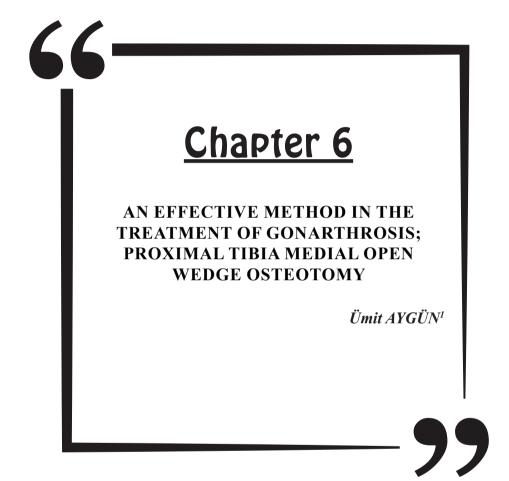
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Chapter 6

AN EFFECTIVE METHOD IN THE TREATMENT OF GONARTHROSIS; PROXIMAL TIBIA MEDIAL OPEN WEDGE OSTEOTOMY

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INTRODUCTION

With the prolongation of human life and the increase in health problems such as obesity, the incidence of degenerative joint diseases, which we call arthritis or arthrosis, is also increasing in our developing age. Undoubtedly, the knee joint is the most common joint that we see osteoarthritis. Today, proximal tibial osteotomies (PTO), a biological treatment method, are widely used in patients with an active lifestyle and pathology requiring intervention for degeneration in the knees, to avoid non-biological methods such as prosthetic surgery and to delay the need for this surgery as much as possible (ROSSI et al., 2011:19, VAN DEN BEMPT et al., 2016:23). These osteotomies are preferred especially in arthritic changes affecting only one compartment of the knee, and in cases with joint alignment disorder in active patients around 50 years of age. In this section, medial open wedge osteotomy (MOWO), one of the PTOs performed in patients with medial osteoarthritis of the knee joint (gonarthrosis), is described. In addition, it has been tried to provide an overview of high tibial osteotomies (HTO).

Knee biomechanics and HTO

Osteoarthritis is a destructive process that occurs as a result of the deterioration of the relationship between the loads on the joint and the structures that oppose it. Knee osteoarthritis is seen in middle and advanced ages and in its etiology; age, gender, inflammatory diseases, metabolic diseases, neuropathy, trauma, avascular necrosis, hereditary and developmental factors play a role. Osteochondral injuries, meniscus pathologies, tibial or femoral deformities, and ligament problems accelerate the development of gonarthrosis in young individuals (HUSSAIN et al., 2016:61, DELL'ISOLA A et al., 2016:17.). Understanding the loads on the knee joint is the most critical step in understanding HTO.

In the coronal plane, body weight passes through the S3 vertebra and is projected onto the hip, thigh, knee, and ankle. While we are on both feet, the load on the knees is evenly distributed, which corresponds to approximately 43% of our body weight for each knee (LIU et al., 2019:8363128, AMIS, 2013:21). When we stand on one leg, the load on the knee corresponds to 93% of the body weight. The effects of this load on the coronal and sagittal planes of the knee are different. With the decrease in the lateral forces of the knee, the increase in body weight, that is, the load on the inner part, the vector passing through the center of the knee shifts towards the inside. We can also see this effect in conditions such as limb inequality and scoliosis **(Figure 1.)**
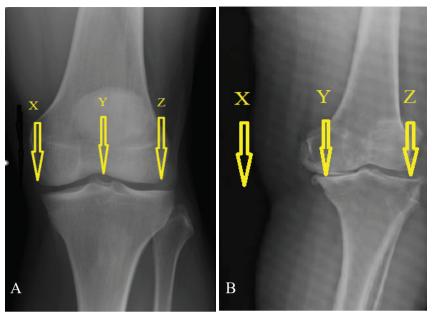
Figure 1. *A) Loads on the normal knee joint B) Shift of the Y vector into the medial joint space with arthritic changes*

In the lower extremity, there is normally 5-7° valgus in the knee joint. In gonarthrosis, which is generally considered as a mechanical problem, most of the body weight passes medially (TIPTON et al., 2015:38). In malalignment, osteoarthritis develops due to the change in the distribution of the load on the knee. Osteotomy appears as an effective treatment method for varus or valgus alignment disorders of the knee. It shows its effect by changing the load distribution in active individuals with isolated medial or lateral compartment pathology and by reducing the load on that area of damage to the cartilage (GARDINER and RICHMOND, 2013:21). In medial osteoarthritis, which is more common, HTO plays a role in reducing pain and slowing arthritic changes. With this treatment, patients do not have to change their activity levels as much as after knee arthroplasty. For this reason, HTO is a preferred treatment method in patients who need high activity levels (ROSSI et al., 2011:19, HUSSAIN et al., 2016:61).

Normally, as the vector passing through the center of the knee shifts to the medial, an increase in compressive forces occurs in this region. Thus, an increase in density occurs in the tibial plateau in the subchondral bone and in the femoral condyle. Due to cartilage damage, narrowing and varus deformity occur in the medial knee over time. It has been shown that this density decreases after HTO (SEO et al., 2020:33). In another study, it was shown that increased medial bone involvement in the scintigraphy improved after osteotomy (GOSHIMA et al., 2019:24, BAE et al., 2021:16).

With the increase in lateral forces in the knee and the lateral shift of the vector passing through the center of the knee, the same damage occurs in the lateral knee and a valgus posture occurs in the knee (VAN DEN BEMPT et al., 2016:23).

The distance of the force generated by the body center of gravity from the knee center creates the adduction moment. This moment, which is divided into two as extrinsic and intrinsic, is important in the development of medial gonarthrosis. The extrinsic adduction moment distance, which is defined as the distance from the center of gravity of the body to the center of the knee with a normal axis, is more important in the development of medial gonarthrosis. Conditions such as coxa vara, wide pelvis, and short femur lead to the development of arthritis in the inner part of the knee by increasing the extrinsic varus distance (MOGHTADAEI et al., 2017:9, 12, WHATLING GM et al., 2020:28). In the study, it was found that during gait analysis, patients with high adduction moment had worse functional results than those with low adduction. It has been emphasized that more corrections can be made in knees with high adduction moments (FANTINI et al., 2020:27, WHELTON et al., 2017:43).

In gonarthrosis, which is generally seen with lower extremity malalignment, drawing the body weight vector to the middle of the tibial spine and making it perpendicular to the transverse line drawn from the tibial plateau constitute the basis of biomechanical treatment in knee osteoarthritis. Maintaining the normal alignment between the tibia and femur and bringing it to the appropriate angle is not sufficient for the body weight vector to pass through the center of the knee. In varus knees, there is usually a decrease in the forces acting on the outside of the knee. To overcome this, additional corrections are necessary. In varus knees, performing the osteotomy from the femur makes the forces acting on the lateral part of the knee more oblique, so that the body-weight vector acts inclined even if it passes through the center of the knee. This causes the femur to slide medially on the tibia. For this reason, correction in varus knees is made from the upper end of the tibia (GOMOLL , 2011:39, PENG et al., 2021:13).

In which situations should HTO be done or not?

Today, there are many treatment options available as treatment methods in gonarthrosis. Patient education, systemic and local drug therapy, physical therapy and rehabilitation, surgical treatment (arthroscopy, osteotomy, arthrodesis, arthroplasty) form the basis of these. Factors such as the age and activity level of the patient, the degree of gonarthrosis, and alignment problems should be considered in surgical treatment (MICHAEL et al., 2010:107, RICHMOND, 2008:34).

HTO is generally applied to young individuals with malalignment and degenerative changes in a single compartment of the knee. Especially due to varus malalignment, the medial compartment is most frequently affected (OLLIVIER et al., 2021:29, MCNAMARA et al., 2013:21). Patients with appropriate indications for this treatment; able to adapt to treatment, active, under 65 years of age, with activity-related pain, <5° flexion contracture, flexion >120°, 5°-15° varus alignment, osteoarthritis less than grade 3 (Ahlback classification), intact lateral and those with patellafemoral compartment and without joint laxity and instability (SANTOSO and WU, 2017:12, SABZEVARI et al., 2016:4).

Those with extensive knee degeneration, tibiafemoral subluxation, advanced osteoporosis, <90° joint range of motion, >15° varus deformity, vascular problems, inflammatory arthritis, history of lateral meniscectomy, and advanced medial compartment arthrosis are absolute contraindications for HTO (SCHLUMBERGER et al., 2021:29, SCHUSTER and RICHTER, 2021:37). Body weight >90kg, physiological age >65, severe patellafemoral complaints, and patella alta-infera conditions constitute relative contraindications (DOWD et al., 2006:13, BONASIAet al., 2014:7).

In this treatment, the patient and the physician should be in harmony, and the patient should be informed about the purpose of the surgery, possible complications, and the rehabilitation process. The indication should be reconsidered in patients who are thought to be unable to adapt.

Preoperative planning

First of all, it should be ensured that the patient's expectations from this surgery are realistic. The advantages and disadvantages of surgery, risks, pain may not disappear completely, but may develop again over time should be explained. It should be mentioned in detail about the rehabilitation process and it should be said that this surgery does not change the anatomy, but aims to relieve the pain with the new deformity it creates. Ultimately, HTO is a saving procedure that gives the patient a painless period of time.

Deformities that need to be corrected before surgery and other pathologies that contribute to the symptoms in the knee should be identified. The dynamic deformity that occurs during walking and the pushing of the knee to the outside during loading should be examined. Varus thrust, which indicates that the damage in the joint is advanced, is a condition that shows that all reaction forces are concentrated on the medial side and causes the damage to progress rapidly. Since this condition is often accompanied by conditions such as flexion contracture, lateral subluxation, and tricompartmental arthrosis, such patients are not suitable for HTO. The reason for this situation, which is generally encountered

in deformities exceeding >15°, is loosening of the lateral ligament due to cartilage loss and cartilage-bone loss developing on the medial side of the knee (LEE and BYUN, 2012:24, ROBIN and NEYRET, 2017:1).

If laxity on the medial side of the knee with gonarthrosis is not taken into account during surgery, it often results in inadequate correction of the osteotomy. The medial joint space, which is opened by the valgus force applied during surgery, does not open due to the adduction moment that is effective in normal walking and the varus type gait continues (KIM et al., 2019:20).

Damage to the medial meniscus, especially with anterior cruciate ligament injury and loosening, may cause arthrosis on the inner side of the knee. In this case, it should be distinguished whether the patient's complaint is caused by pain or laxity. If the patient only complains of pain and does not show signs of instability, HTO alone can be performed. However, in cases accompanied by instability, HTO should be performed with anterior cruciate ligament reconstruction (KLEK and DHAWAN, 2019:12). Height and leg length of patients, rotational problems associated with angular deformity are important. Especially short patients need more correction angles than taller patients (LOIA et al., 2016:4).

Radiological examination

The purposes of the radiographs taken before the operation are evaluating whether the patient is suitable for HTO and the surgical planning. What is expected in the examination is to show a shift in the mechanical alignment of the lower extremity and joint involvement of osteoarthritis in a single compartment. It is generally seen that the knee is varus and medial compartment is involved (LEE et al., 2017:25, SILVA et al., 2015:45). There is not a standard method in radiographic imaging, but many options have been defined.

-Routine anteroposterior, lateral and axial radiographs

-Anteroposterior or posterior-anterior radiographs taken with the knees under load in flexion

-Valgus-varus stress radiographs taken with the knee joint at 20° flexion

- X-ray showing the entire lower extremity while standing (orthorontgenogram-axis)

In these radiographs, the knee should be in a suitable rotation posture, and it should be kept in mind that the accompanying flexion contracture may also affect the position and the degree of correction (SHON et al., 2017:29, OTSUKI et al., 2020:32).

Mechanical and anatomical axis

The line connecting the hip, knee and ankle centers forms the mechanical axis of the lower extremity. There is approximately 5-7° valgus angle difference between the mechanical axis and the anatomical axis **(Figure 2.)**. Since the anatomical axis is affected by deformities of the bone, the use of mechanical axis is more preferred in deformity correction (KAMADA et al., 2019:27). In theory, correction is made where the deformity is the most. In general, correction from the tibia in varus knees and from the femur in valgus knees is preferred. In general, those whose varus angulation of > 15° and valgus angulation of >10° are not considered suitable for HTO due to complications (OGAWA et al., 2020:28). In this type of surgery, sagittal and axial deformities should be corrected, if any. While normal radiographs are sufficient to evaluate the sagittal plane, computed tomography may be required for the axial plane. Magnetic resonance imaging (MRI) may be necessary for the evaluation of cartilage and bone involvement, bone marrow changes, and cruciate ligaments in other compartments. We request MRI for our patients for whom we planned HTO in our clinic **(Figure 3.)**.
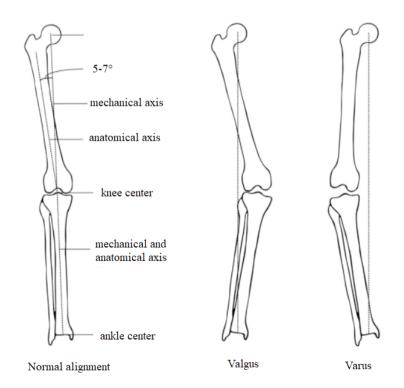

Figure 2. *Mechanical axis of the lower extremity in normal, valgus and varus alignment*

Figure 3. *Knee MRI of the patient who will undergo HTO A) lateral view B) anterior-posterior view*

Many methods have been described for determining the degree of correction. The approach of correcting 3-5° more than the deviation in the mechanical axis has now left the understanding of overcorrection according to the phenomenon. Fujisawa point; is the shift of the new mechanical axis to the medial 1/3 of the lateral compartment (LEE et al., 2020:27). Noyes/ Dugdale point; It is the amount of angle correction between the two axes formed by the center of the femoral head, the point that corresponds to the lateral 62% of the tibial plateau, and the midpoint of the talus roof in the axis graph (RIBEIRO et al., 2013:37). Miniaci et al. described the amount of correction by allowing the mechanical axis to pass 30-40% of the width of the lateral tibial plateau. Here, the head of the fibula became the other marking point (YOON et al., 201628) **(Figure 4.)**.
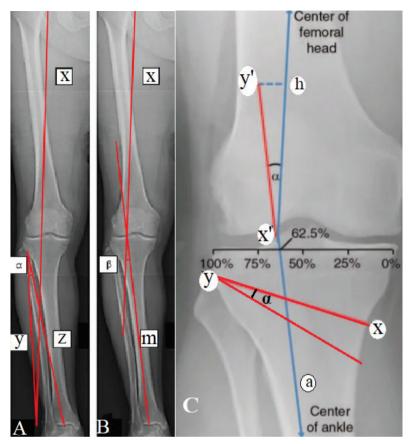
Figure 4. *A) Miniaci's method B) Dugdale's method C) Noyes point; α or β osteotomy correction degree*

Proximal tibia MOWO

Many PTOs were performed based on radiological evaluation alone, even in patients with advanced osteoarthritis in the past. Internal fixation was not usually applied to these patients, and they were left immobilized with a long-term plaster cast after surgery. Today, intra-knee structures including the contralateral compartment are completely evaluated with the help of arthroscopy before osteotomy, detected pathologies can be intervened in the same session, and PTO can be abandoned if necessary. Thanks to the internal or external fixations applied during the surgery, plaster applications are abandoned and the rehabilitation process is started quickly.(LIU and LI, 2013:26, SPAHN et al., 2012:150).

Patients who are considered to undergo osteotomy should be separated from patients who have undergone total knee replacement due to severe arthrosis. An alternative to this surgery may be unicompartmental knee arthroplasty, and its purpose is to provide the patient with a pain-free

comfortable life until total knee arthroplasty, which may be required in the future (CAO et al., 2018:33, FU et al., 2013:28).

One of the PTO methods is MOWO. In this technique, distraction can be applied acutely to correct the deformity and fixation can be done by plate-screw methods. External fixators can be used for fixation when distraction is desired to be done gradually. This is called distraction osteogenesis, callus distraction, or hemicallotasis. Osteotomies can be performed obliquely or transversely straight in the mediolateral plane (monoplanar), retrotubercle osteotomy in which the tibial tubercle is left in the proximal fragment, or V-shaped bi-planned supra-tubercle osteotomy in which the tibial tubercle is left in the distal fragment (KIM et al., 2021:37, JO et al., 2019:27) **(Figure 5.)**.

Figure 5. *A) Monoplanar B) Bi-planar retro-tubercul C) Bi-planar supra-tubercle osteotomies*

Valgus corrective osteotomy of the proximal tibia can be performed from the lateral as closed wedge osteotomy, dome osteotomy or MOWO (BILGEN et al., 2007:35, LAPRADE et al., 2012:28, DUIVENVOORDEN et al., 2014:96). Following Debeyre's description of the medial open wedge

osteotomy proximal to the tibial tubercle, this method was popularized by Hernigou et al. (HERNIGOU et al., 1987:69). Goutallier et al. used a support plate for fixation by supporting the distraction space with cement (GOUTALLIER et al., 1992:78). Many plates in design are used for fixation, such as the Puddu plate, TomoFix plate, support plate, C-plate, T-plate, and wedged plate (GOLOVAKHA et al., 2014:15, CHEN et al., 2019:14).

Two-dimensional improvement in sagittal and coronal plane deformities can be achieved with the MOWO method (MADRY et al., 2017:25, TANAKA et al., 2019:27). Open wedge osteotomies have the advantage of preserving bone stock, as well as the advantage of correcting the deformity close to its source. In the medial open wedge method, there is no need for muscle separation, no shortening of the limbs, no need for fibular osteotomy, no damage to the tibiofibular joint. Thus, fibular nerve damage is minimal (ITOU et al., 2020:28, OZCAN et al., 2017:25). During osteotomy, the lateral cortex is left intact to take advantage of the hinge feature (JO et al., 2018:26). Bone stock is preserved for total knee arthroplasty that may be required over time (HAN et al., 2016:24). Joint stability is ensured by adjusting the tibial inclination, and if there is damage to the anterior and posterior cruciate ligaments, these ligaments can be repaired in the same session (KIM et al., 2018:25, WEILER et al., 2021:34). It plays a stretching role in medial collateral ligament laxity. Autograft taken from the iliac wing alone may cause morbidity (PAPE et al., 2006:14, SATO et al., 2019:20).

External fixators used in the hemicallotasis method may cause complications such as pain, nail infection, hematoma, chronic osteomyelitis, inflammation, reflex sympathetic dystrophy, septic arthritis, deep vein thrombosis ,and loss of correction (OH et al., 2011:16, BAUMS et al., 2005:108). The fixator may not be tolerated by some patients. Those with metaphyseal location may put future total knee arthroplasty at risk (JACOBI et al., 2010:18, PRESTON et al., 2014:472).

The aim of knee osteotomies is to create the mechanical axis of the extremity and to transfer the excessive load from the medial compartment to the lateral compartment. The alignment of the extremity is best done by evaluating the mechanical axis in orthoroentgenographs showing the entire lower extremity. The line drawn from the center of the femoral head to the ankle mortis should normally pass through the center of the knee (ROSSI et al., 2011:19, VAN DEN BEMPT et al., 2016:23) **(Figure 2.)**. Normally, the anatomical axis formed by the combination of the midpoints of the femoral diaphysis meet the mechanical axis at the knee center and there is a physiological valgus angle of approximately 5° between them (KIM et al., 2016:44). Since deformities due to bony or ligament laxity will

be lower than expected on inpatient radiographs, adequate correction may not be achieved with osteotomy. For this reason, many authors recommend standing graphy. Joint compliance angles are evaluated on radiographs taken on one or both feet, and the difference between them indicates ligament laxity (OGINO et al., 2020:21). In cases of ligament laxity, varus or valgus stress radiographs are taken and the degree of laxity is subtracted from the total degree of valgus correction to avoid overcorrection (BODE et al., 2017:25). Routine orthorontgenography is used to evaluate the degree of correction in our clinic.

Surgical technique

In our clinic, we apply the following steps in corrective osteotomy in one plane (monoplanar), which is the most applied in MOWO;

The patient is prepared in such a way that grafts are taken from the ipsilateral iliac wing under spinal or general anesthesia. With arthroscopic intervention, intra-knee pathologies such as degenerated meniscus, irregular cartilage areas, free bodies are intervened, and microfracture is performed if necessary. In cases of suspected anterior cruciate ligament injury before surgery, preparation should have been made. For post-arthroscopy osteotomy, we make an oblique incision of approximately 5-7 cm below the knee joint level, keeping the knee joint in semiflexion and revealing the proximal tibia medial between the medial patellar tendon and the lower border of the tibia. The periosteum is cut in an inverted L shape with the short leg facing back. The superficial fibers of the medial lateral ligament are cut and the periosteum is stripped up to the attachment of the pes anserinus. The osteotomy line is determined by Kirschner wires, starting from 3-4 cm distal to the medial joint space, and passing through the proximal part of the attachment of the patellar tendon to the tibial tubercle, reaching 1-1.5 cm distal to the lateral joint surface and 1 cm medial to the lateral tibial cortex, superolaterally. After checking the suitability in the scope, the medial and anterior cortex is cut under the wires with a cutting motor, and the posterior cortex is cut with an osteotome within the specified limits. In order to take advantage of the hinge feature, care is taken not to break the lateral cortex. The cut bone surfaces are carefully distracted both with osteotomes and manually. Generally before distraction, we send two wires to the tibial plateau, parallel to the articular surface, against the risk of fracture in the lateral tibial plateau. Hernigou's chart was used to correlate the width of the tibia at the osteotomy level with the desired degree of correction (HERNIGOU, 2002:9, HERNIGOU and MA, 2001:8) **(Figure 6.)**. After the necessary opening is provided, our clinical preference is to provide fixation by placing the plate. Bone grafts taken from the iliac wing are then filled into the osteotomy site **(Figure 7.)**. After the tourniquet is opened, we suture only the long leg

of the periosteum and approximate the superficial fibers of the medial lateral ligament. We place a penrose drain on the iliac wing and osteotomy site to be removed the next day. It has been shown that if the fibers of the inner lateral ligament are sutured, it will create a compressive effect, thus affecting the desired correction (SEITZ et al., 2019:27, SEO et al., 2016:44).

β	4	5	6	7	8	9	10	11	12	13	14	15	(16)	17	18	19
M																
50	3	4	5	6	7	8	9	10	10	11	12	13	14	15	16	16
55	4	5	6	7	8	9	10	10	11	12	13	14	15	16	17	18
60	4	5	6	7	8	9	10	11	12	14	15	16	17	18	19	20
(65)	5	6	7	8	9	10	11	12	14	15	16	17	(18)	19	20	21
70	5	6	7	8	10	11	12	13	15	16	17	18	20	21	22	23
75	5	6	8	9	10	12	13	14	16	17	18	20	21	22	24	25
80	6	7	8	10	11	13	14	15	17	18	19	21	22	24	25	26

Figure 6. *M; length of the osteotomy β; desired correction angle. The intersection of the two will give the opening wedge distance. The red circle is an example.*

Figure 7. *A) axis B) anterior-posterior C) lateral radiographs of the patient who underwent HTO on the left knee*

We do not perform fibular osteotomy in our clinic. Thus, the fibula and the proximal tibiafibular joint are not affected, and fibular nerve damage is kept at a minimal level (JEONG et al., 2019:98, DUIVENVOORDEN et al., 2017:25). In a series of 93 cases in which MOWO was applied, peroneal nerve paralysis was found in one knee, which completely healed (HERNIGOU et al., 1987:69). In addition to hydroxyapatite wedges to fill

the osteotomy space, it has been shown that a 2 cm resection was made from the middle part of the fibula diaphysis (KOSHINO et al., 2003:85). Nakamura et al. (2014:96) stated that they performed fibulectomy to protect the peroneal nerve in cases with hemicallotasis requiring correction by >15° and to prevent the deterioration of the tibiafular joint relationship with the proximal displacement of the fibular head.

Two-plan osteotomy in which the tibial tubercle is left in the proximal fragment – Retrotubercle osteotomy

Various proximal tibial osteotomy techniques have been described for patients with patellafemoral problems with damage to the medial compartment. The aim here is to reduce patella-femoral pressure by preventing patellar tendon shortening and tension in the tendon. Since it did not change the tubercle height, patellar height and Q angle in closed wedge osteotomy, retrotubercle osteotomy was introduced later by Murphy (1994:25). It has been shown that the osteotomy technique, in which the tibial tubercle is left in the proximal fragment, is applied in the medial open wedge osteotomy to prevent patella infera formation (HOPWOOD et al., 2016:21, GHINELLI et al., 2021:31) **(Figure 5.)**.

Two-plan osteotomy in which the tibial tubercle is left in the distal fragment – Supratubercle osteotomy

It is a two-plan osteotomy in which the tibial tubercle is left in the distal fragment instead of a straight oblique osteotomy. In this technique, the tibial osteotomy starts more distally and progresses 1.5 cm distal to the lateral joint corner. Usually, bone graft is not used, but it can be used for openings >15 mm. It has been reported that problems such as loss of correction and nonunion observed after Puddu plate application do not develop in this method (KIM et al., 2021:37, STOFFEL et al., 2004:19) **(Figure 5.)**.

In our clinic, we apply a bicortical graft taken from the ipsilateral iliac bone to the osteotomy site. We apply this method because of the pain in the donor area in tricortical grafts. It has been suggested to fill the space formed after distraction with a graft of corticospongious structure (da CUNHA LUCIANO et al., 2015:45). Some researchers reported that it was not necessary to use grafts in distractions ≤7.5 mm (FRANCO et al., 2002:1), some in corrections <12° (SPAHN, 2004:124), and some in osteotomies that were opened by 15 mm (STAUBLI et al., 2003:34, TURKMEN et al., 2014:24). As a result of autograft removal, pain, hematoma, sepsis or difficulties in dressing may be experienced in the area taken (CHAE et al., 2008:15).

In our clinic, we start our patients with low molecular weight heparin

after surgery and tell them to use it for three weeks after discharge on the 4th day. Afterwards, they continue to use the oral antiaggregant for two months. On the second day of the surgery, we start passive knee movements on the CPM device as tolerated by pulling the drains and putting on the angle adjustable knee brace. We mobilize without pressing with crutches. We explain how to continue knee exercises at home after discharge. In general, we see that the knee movements reach around 100° on average in the 2nd week they come to take the sutures. We find this value to be lower in patients with complications such as plateau fractures. We start to give full load in the 2nd month.

Complications that may develop in HTO surgery; intraoperative - lateral tibial plateau fracture, lateral tibial cortex fracture, vessel-nerve injury, postoperative - compartment syndrome, pseudoarthrosis, wound healing problems, pulmonary embolism, deep vein thrombosis, delayed union, infection (MILLER et al., 2009:25, WOODACRE et al., 2016:23).

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