An assessment of sensory sensitivity in women suffering from depression using transcutaneous electrical nerve stimulation

Joanna Witkoś [Corresp., 1], Agnieszka Fusińska-Korpik [1], Magdalena Hartman-Petrycka [2], Agnieszka Nowak [3]

[1] Medicine and Health Science, Andrzej Frycz Modrzewski Krakow University, Kraków, Poland

[2] Department of Basic Biomedical Science, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, Katowice, Poland

[3] Józef Babiński Clinical Hospital in Krakow, Psychiatric Ward, Kraków, Poland

Corresponding Author: Joanna Witkoś
Email address: jwitkos@afm.edu.pl

Beckground. Perception is the result of experiences arising from the mental interpretation of the phenomena occurring, therefore it depends not only on physiology or biology, but is also psychically conditioned**.** The aim of this study was to answer the question: do women who suffer from depression experience an electrical stimulus applied during electrotherapy treatments in the same way as women who are mentally healthy? **Methods**. Depression group - 44 women, who were inpatients treated for depression at the Psychiatric Ward in the Clinical Hospital and control group - 41 women, matched by the age, height and weight, with no mental illness. Measures: threshold for sensing current, type of sensation evoked, hedonic rating. **Results**. Median sensing threshold of electric current (depression vs. control: 7.75mA vs. 8.35mA; no significant), type of sensation evoked (depression vs. control: tingling 90.9% vs. 92.7%, no significant), hedonic rating (depression vs. control: unpleasant 11.4% vs. 2.4%; p=0.003), hedonic rating (mildly ill vs. moderately ill vs. markedly ill: unpleasant 5.3% vs. 6.3% vs. 33.3%; p=0.066). **Conclusions**. Women suffer from depression exhibit a similar threshold of sensitivity to an electrical stimulus as mentally healthy women, however the hedonic rating of the stimulus acting on the skin in the group of clinically depressed women was more negative than in the mentally healthy subjects. The stimulus was described as 'unpleasant' for many of the mentally unhealthy women. The most negative sensations related to the electrical stimulus were experienced by women with the highest severity of mental illness according to The Clinical Global Impression - Severity Scale.

1   An assessment of sensory sensitivity in women suffering from depression using transcutaneous

2   electrical nerve stimulation

4   Joanna Witkoś[1], Agnieszka Fusińska-Korpik[1], Magdalena Hartman-Petrycka[2], Agnieszka

5   Nowak[3]

7   [1]Faculty of Medicine and Health Science, Andrzej Frycz Modrzewski Krakow University,

8   Kraków, Poland

9   [2]Department of Basic Biomedical Science, Faculty of Pharmaceutical Sciences in Sosnowiec,

10   Medical University of Silesia, Katowice, Poland,

11   [3]Józef Babiński Clinical Hospital in Krakow, Psychiatric Ward, Kraków, Poland

13   Corresponding Author:
14   Joanna Witkoś
15   G Herlinga-Grudzinskiego Street 1, Andrzej Frycz Modrzewski Krakow University, 30-705
16   Kraków, Poland
17   Email address: joannawitkos@yahoo.com
18

20 Abstract

21   **Background** Perception is the process or result of the process arising from the mental

22   interpretation of the phenomena occurring, therefore it depends not only on physiology, but is

23   also psychologically and socially conditioned**.** The aim of this study was to assess if there is a

24   difference in the sensory sensitivity to an electrical stimulus in women suffering from depression

25   and what the hedonic rating is of the lived experience of TENS.

26   **Methods**. Depression group - 44 women, who were inpatients treated for depression at the

27   Psychiatric Ward in the Clinical Hospital and control group - 41 women, matched by the age,

28   height and weight, with no mental illness. Measures: threshold for sensing current, type of

29   sensation evoked, hedonic rating.

30   **Results**. Median sensing threshold of electric current (depression vs. control: 7.75mA vs.

31 8.35mA; no significant), type of sensation evoked (depression vs. control: tingling 90.9% vs.

32 92.7%, no significant), hedonic rating (depression vs. control: unpleasant 11.4% vs. 2.4%;

33 p=0.003), hedonic rating (mildly ill vs. moderately ill vs. markedly ill: unpleasant 5.3% vs. 6.3%

34 vs. 33.3%; p=0.066).

35 **Conclusions**. Women suffer from depression exhibit a similar threshold of sensitivity to an

36 electrical stimulus as mentally healthy women, however the hedonic rating of the stimulus acting

37 on the skin in the group of clinically depressed women was more negative than in the mentally

38 healthy subjects. The stimulus was described as 'unpleasant' for many of the mentally unhealthy

39 women. The most negative sensations related to the electrical stimulus were experienced by

40 women with the highest severity of mental illness according to The Clinical Global Impression -

41 Severity Scale.

42

43 ## Introduction

44   The sensory perception process involves subjective evaluation of a stimulus acting on the

45 human body, therefore, it is considered as an individual variable. The sensations experienced

46 during a person's life, including, in particular, cutaneous perception, are associated with various

47 factors (e.g., sex, hormonal differences, genetic, social and cultural conditions) that can influence

48 their interpretation, modification, and degree of perception (Racine et al., 2012a, 2015b).

49 However, stimulus perception depends not only on physiology, but is also psychologically and

50 socially conditioned (Landa et al., 2020). Perception is the process or result of the process arising

51   from the mental interpretation of the phenomena occurring. These can be modified e.g., by

52 previous experiences and individual psychosomatic conditions, including cognitive factors which

53 receive information from the environment, store and transform it and introduce it back into the

54 environment in the form of reactions and behaviours (Racine et al., 2012a, 2015b). Therefore,

55 differences in tactile or pain sensitivity assessed only in terms of physiology are insufficient and

56 should be combined with an assessment of the overall quality of life of the person examined.

57 Stress, mood, and psychosocial factors contribute significantly to differences in pain perception

58 in people (Landa et al., 2020). The available literature indicates that people "satisfied" with their

59 lives and who have a family and social support react to external stimuli differently from those

60 who experience so-called "interpersonal pain" and cope with a sense of rejection at different

61 levels of functioning (Landa et al., 2020).

62 Physical medicine is an important component of a comprehensive physiotherapy

63 treatment. The vast majority of physical medicine procedures are electrotherapy treatments,

64 including transcutaneous electrical nerve stimulation (TENS) that change the sensitivity to

65 sensory stimuli, especially pain stimuli, with the use of an electric current. The main goal of

66 therapeutic management is pain relief, and an essential role in the process of physiotherapeutic

67 treatment is played by neuromuscular excitability (Jauregui et al., 2016; Gladwell et al., 2016).

68 Electrical stimuli applied during treatments may be perceived by patients as pleasant or

69 unpleasant, even if they refer to the same type of current, e.g., TENS (Martimbianco et al., 2019,

70 Gibson et al., 2017; Johnson et al., 2019). Therefore, it is necessary to consider what makes one

71 person perceive a certain electrical stimulus as pleasant, while another perceives a stimulus with

72 identical parameters using the same type of electrical current as unpleasant. In this situation,

73 there must be additional factors that modify the perception of the stimulus by a particular person,

74 and depression could be one of those factors.

75 Depression is one of the most common psychiatric disorders, associated with the highest

76 global burden of disease (Ferrari et al., 2010), and a leading cause of disease-related disability

77 throughout the world (GBD 2019 Diseases and Injuries Collaborators, 2020).

78 More than 300 million people are living with depression, with an 18% increase from

79 2005 to 2015 (World Health Organization 2017). Epidemiological studies have shown that the

80 lifetime prevalence of a major depressive disorder in women (21.3%) is almost twice that of men

81 (12.7%). This ratio has been documented in different countries and ethnic groups (Noble 2005).

82 Depression is associated with a variety of symptoms, high rates of relapse, and many

83 physical and psychological disorders. Symptoms of depression can be psychological, physical

84 and/or social (Sassarini 2016; de Girolamo et al., 2020; Brockbank et al., 2021). It is

85 characterised by a low mood, anhedonia, feelings of worthlessness and hopelessness, sadness,

86 loss of interest or pleasure, feelings of guilt or low self-worth, feelings of tiredness, poor

87 concentration and disturbances of sleep, appetite, and libido. Moreover, symptoms may include

88 lack of motivation or interest, difficulty in making decisions and thoughts of self-harm or

89 suicide, avoidance of social activities and friends and difficulty with home and family life (De

90 Giorgi et al., 2021; Pinheiro Campos et al., 2020).

91 This study aimed to assess if there is a difference in the sensory sensitivity to an electrical

92 stimulus in women suffering from depression and what the hedonic rating is of the lived

93   experience of TENS. Therefore, the research question was: do women who suffer from

94   depression experience an electrical stimulus applied during electrotherapy treatments in the same

95   way as women who are mentally healthy?

96   Detailed research hypotheses were as follows:

97   Women with depression have a different sensory threshold to TENS electrical stimuli than

98   mentally healthy women.

99   Women with depression differ in terms of sensations they experienced when the TENS electrical

100   stimulus was applied, when compared to mentally healthy women.

101   Women with depression differ in their hedonic rating of TENS when compared to mentally

102   healthy women.

103   In women with depression, the sensory threshold, the type of sensation and the hedonic rating of

104   TENS depend on the disease severity.

105

106   **Materials & Methods**

107

108   **1.1. Participants.** The study involved 85 women aged 18 to 49 years, of which 44 women were

109   inpatients treated for depression at the Psychiatric Ward in the Clinical Hospital and formed the

110   depression group (D), and 41 women were recruited from the city of Krakow and formed the

111   control group (C). The control group consisted of the authors' acquaintances together with

112   members of their families who were matched by age, height and weight to the group of women

113   suffering from depression. None of the women in the control group had any diagnosed mental

114   illness. Detailed information on the subjects is presented in Table 1. The number of examined

115   women was limited by Coronavirus pandemic.

116   The criteria for inclusion in the study was depression confirmed by medical diagnosis.

117   The women were qualified for the research by the Head of the Psychiatric Ward in consultation

118   with the attending psychologist. The exclusion criteria were the patient's lack of consent to

119   perform the sensory threshold test, the presence of psychotic symptoms, organic mental

120   disorders, incapacitation (partial or complete), neurological diseases, including neuropathies and

121   diabetes. Contraindication to the examination was also any skin diseases or damage in the place

122   where the sensory threshold was tested.

123   **1.2. Examination of the sensory threshold**. As a sensory stimulus, an electrical impulse of

124   increasing amplitude (intensity) was used, until the sensory threshold (minimally perceptible

125   tingling) was reached. The current was increased slowly and gradually at 0.1 mA intervals, until

126   the studied person informed the physiotherapist that she felt the minimum current under

127   electrodes, then the current was not increased anymore and its value was read. The point at

128   which this superficial sensation was felt, i.e., the sensory threshold (stimulation of thick Aβ

129   sensory fibres), was defined as the minimally perceptible level of electrical stimulation that the

130   subject was able to consciously feel. For this purpose, an electrotherapy device (BTL5818SLM)

131   was used, as it allows the current intensity to be read with an accuracy of 0.1mA. TENS with

132   100Hz and 100μs parameters and biphasic current waveform was used. The room in which the

133   tests were performed had a constant ambient temperature of 22ºC, The subject sat on a chair,

134   with the upper limb bent at the elbow joint and placed on a table with the forearm in supination.

135   Surface electrodes with 12 cm^2 pads, which had been dipped in warm water, were used. The

136   electrodes were placed on the interior of the subject's forearm on the group of flexor muscles of

137   the wrist of the dominant hand and fastened with straps. One of the electrodes was 1 cm from the

138   elbow and the other was in a straight line 2 cm from the first one. An important element of the

139   examination of the sensory threshold in which the electric stimulus was used, was the fact that

140   the same portable electrotherapy device was used to test all the women i.e., depression group and

141   control group.

142   **1.3. Examination of the description of the sensations**. The women were additionally asked to

143   indicate what type of sensation they felt when the current was applied. The following responses

144   were suggested: tingling, 'pins and needles', scratchy, burning, stinging, numbness, and tickling.

145   **1.4. Examination of the hedonic rating.** In addition, the women were asked to give a hedonic

146   rating to the electrical stimulus acting on the skin by indicating whether the sensation induced by

147   the current was pleasant, neutral, or unpleasant for them. The hedonic rating of the current felt by

148   studied people was performed for the current level that was recorded as the sensory threshold.

149   **1.5. Procedure**. The electric current parameters selected for the study resulted from their

150   specific impact on the human nervous system. The 100 Hz frequency is a prerequisite for

151   effective stimulation of Aβ sensory fibres. Whereas, with regard to the effect of the pulse

152   duration on skin sensation, especially in the case of high-frequency (100Hz) TENS stimulation,

153   the pulse width range should generally be from about 100 μs to about 200 μs (Geng et al., 2011;

154   Cheing et al., 2009). The duration of an impulse within these limits causes a delicate and

155   pleasant tingling sensation on the skin, and at the same time allows the effective stimulation of

156 the nerve fibres as planned in this research. Due to the use of biphasic current waveform, it did

157 not matter exactly where the anode (positive current pole) and where the cathode (negative

158 current pole) were located on the above-mentioned group of muscles. The biphasic waveform of

159 the current prevented both possible errors in the arrangement of the electrodes and a distortion of

160 the results which can differ when stimulating the nerve fibres with the opposite poles of the

161 current.

162   The research protocol has been reviewed and approved by the Bioethical Committee:

163 permission number KBKA/65/O/2019. In accordance with the Declaration of Helsinki, before

164 starting the study, the participants obtained information about the purpose of the study and the

165 principles of conducting the research. They also gave their written consent to participate in the

166 study, and were informed and made aware that they could refuse to participate in the study at any

167 time.

168 **1.6.   Statistical analysis.** The statistical analysis was performed in the Statistica 13 program.

169 The Shapiro-Wilk test was used to statistically assess the normality of the data distribution. U

170 Mann-Whitney and χ^2 tests were used to compare the groups. The results were considered

171 statistically significant at p <0.05.

172

Results

174   On the basis of The Clinical Global Impression - Severity Scale (CGI-S) (Busner et al.,

175 2007), the condition of 19 women suffer from depression (43.18%) was mildly ill, 16 women

176 (36.36%) were moderately ill and 9 women (20.45%) were markedly ill. The women had been

177 treated for depression for between 1 month and 24 years, mean 6.7 years ±6.6 years. The women

178 were being treated with selective serotonin reuptake inhibitors (SSRIs), benzodiazepines, and

179 lamotrigine/pregabalin.

180   The median value (Me) and the first and third quartiles (Q1 and Q3) of the threshold of

181 current sensation in the group of people with depression were: Me: 7.75 mA, Q1: 6.15 mA and

182 Q3: 9.95 mA respectively and in the control group: Me: 8.35 mA, Q1: 7.00 mA and Q3: 10.65

183 mA respectively (Figure.1). The differences in the threshold of current sensation between the

184 groups did not reach statistical significance (The Mann-Whitney U test, U=808.5, p=0.413).

185   In both the Group D and the Group C, the most frequently reported sensation caused by

186 TENS stimulation was "tingling" (Figure 2). The percentage of women experiencing tingling

187   after reaching the sensory threshold in the Group D was 90.91%, and in the Group C it was

188   92.68%. The second most frequent feeling after the activation of the electrical current was

189   "heat/burning", in Group D this was the response of 25.00% of the women, and in Group C

190   17.07% of the women. "Pinching " was reported by around a dozen percent of women from both

191   groups, and "numbness" was reported by only a few percent. The differences in the description

192   of the perceived stimulus caused by the current did not differ significantly in terms of which

193   group the woman belonged to.

194   The hedonic rating of the current-induced stimulus differed significantly between the

195   groups ($\chi^2 = 11.26496$, df=1, p = 0.003) (Figure 3). For 11.36% of clinically depressed women,

196   the perceived electrical stimulus was unpleasant, while in the Group C it was unpleasant for only

197   2.44%. Additionally, 19.51% of the mentally healthy women stated that the feeling caused by the

198   current was pleasant for them.

199   It was also observed that in the group of clinically depressed women, depending on the

200   degree of depression as per the CGI-S scale, there was a tendency towards a more negative

201   hedonic rating caused by the current ($\chi^2 = 5.43$, df=2, p = 0.066) (Figure 4). As many as 33.33%

202   of markedly ill women perceived the applied stimulus negatively, while in the group of mildly ill

203   women the electric stimulus was assessed negatively by 5.26% of the women. The study also

204   noted that the duration of the depression did not significantly affect the hedonic rating of the

205   current-induced stimulus.

206

Discussion

207

208   This study has shown that for women suffering from depression, this condition does not

209   affect either the threshold for sensing the electrical stimulus, or the way the stimulus acting on

210   the skin is described (tingling, burning, stinging). However, the interpretation of the perceived

211   stimulus in the form of a hedonic rating is what distinguishes mentally healthy women from

212   women suffering with depression. For women with clinical depression, the electrical stimulus

213   applied, using TENS stimulation, was never pleasant, and the percentage of women who said the

214   stimulus was unpleasant was higher in these women than in the mentally healthy women. It can

215   also be observed that the percentage of women negatively perceiving electrical stimulation

216   increased with the severity of their condition expressed in the CGI scale.

217   Anhedonia is one of the key features of major depressive disorder. It is mostly being
218   considered as a decreased ability to experience pleasant feelings and influences many processes
219   like, for example, motivation and cognition. Apart from an overall reduction in emotional
220   response to pleasant activities and a loss of interest, it was found that anhedonia may lead to
221   changes in perception of sensory stimuli, e.g. touch or taste (Lambert et al., 2018). When
222   anhedonia is considered as an multifaceted construct referring to all major emotional,
223   motivational, cognitive, sensory and social processes, it may actually explain negative
224   assessment of the stimulus in depressive women observed in our study. As there is little research
225   evidence for sensory impairment being one of anhedonia symptoms, further studies in the field
226   are required (Rømer Thomsen, et al., 2015).
227   The results of our research presented above are related to a so far unexplored, yet
228   important and worthwhile scientific issue, which cannot be overlooked when discussing this
229   research, and which may have significant impact on the course of all physical treatment in health
230   centres. Namely, if physical treatments are unpleasant for the patient, does the person still
231   perceive them as therapeutic? Is physical medicine treatment effective to the same degree when
232   the stimuli applied are unpleasant to the patient? All electrotherapy is based on ascending and
233   descending analgesic mechanisms, but are these mechanisms activated when the procedure
234   brings discomfort to the patient? It is known that painful stimulation of tissues and repeated pain
235   induces hyperalgesia (Schug et al., 2011), i.e., excessive sensitivity to the stimuli used. However,
236   it is not known whether this also applies to stimuli described by patients as 'unpleasant'. In
237   addition, procedures in the field of physical medicine and electrotherapy are characterised by
238   repeatability in a treatment series. Therefore, the question arises of whether the daily repetition
239   of stimulation, that is unpleasant for a given patient, will continue to result in the analgesic effect
240   of the electric current used during the procedures? The mechanism that leads to the perception of
241   a stimulus by the brain is complex and is not yet fully understood. The complexity of this process
242   results from the fact that the nervous system is not a 'ductile' system, but shows plasticity, which
243   enables it to change its function under various conditions (Schug et al., 2011). No answers to the
244   questions posed above have been found yet, but it is known that in some patients physical
245   procedures do not result in the expected analgesic effect.
246   Depression can be characterised by psychological and physical symptoms, is considered a
247   public health problem and is also one of the major contributors to global disease burden

248   (Whiteford et al., 2013). In many people, depression may accompany various painful conditions

249   treated in primary care but go undiagnosed by a psychiatrist, because the patient does not seek

250   this type of help. Research (Bair et al., 2003) has shown that at least 75% of primary care

251   patients with depression present with physical complaints exclusively and seldom attribute their

252   pain symptoms to depression or other psychiatric illness.

253   Depression and pain can trigger and perpetuate each other due to overlapping neuronal

254   and emotional changes (Bair et al., 2003; Williams et al., 2003). Scientific studies show that, on

255   average, 65% of depressed patients experience one or more painful conditions. It has also been

256   estimated that 85% of people affected by chronic pain suffer from severe depression (Bair et al.,

257   2003; Williams et al., 2003). The above shows that depression and pain are often co-morbid and

258   decrease the quality of life of many individuals worldwide. An exact understanding of the

259   pathophysiology of chronic pain and depression and of why comorbidity of these two disorders

260   is so common is still a matter for research (Thompson et al, 2016; Nitzan et al., 2019; Malejko et

261   al., 2021). However, although the biological mechanisms are still to be explained, it has been

262   hypothesised that depression and pain may share the same descending tracts of the central

263   nervous system, possibly involving serotonin, noradrenaline, and dopamine (Pinheiro Campos et

264   al., 2020; Thompson et al., 2016). This association, called depression-pain syndrome (Cox et al.,

265   2020), supports the concept that both conditions co-exist and exacerbate one another (Currie et

266   al., 2005; Cox et al., 2020).

267   Depression and pain share biological pathways and neurotransmitters, so there are

268   implications for treating both simultaneously. Depression has been found to be less effectively

269   treated if patients experience co-morbid pain, and patients with pain are less responsive to

270   treatment if they are suffering from depression at the same time (Pinheiro Campos et al., 2020).

271   The presence of pain negatively affects the diagnosis and treatment of depression (Currie et al.,

272   2005; Cox et al., 2020). In addition, as pain worsens, depression worsens and because pain may

273   limit the person's capacity to function, i.e., their ability to do their job as well as limiting any

274   social contact, this leads to a drastic reduction in the quality of life of a person already affected

275   by illness (Currie et al., 2005; Cox et al., 2020). Based on this information, it can be assumed

276   that a significant proportion of patients who come to health centres for pain relief and to benefit

277   from physical treatments, including electrotherapy, suffer from depression.

278   Moreover, it can also be assumed that in some of these people the pain is a consequence
279   of a depressive state, and not of any actual musculoskeletal disorder.
280   Sensory processing refers to the organism's ability to register and modulate sensory
281   information (Serafini et al., 2017; Abraira et al., 2013; Ulashchik 2017), such as visual, auditory,
282   motor, or tactile information, and to process it in order to recognise a specific stimulus (Serafini
283   et al., 2017; Abraira et al., 2013; Ulashchik 2017). Research (Serafini et al., 2017), has found that
284   sensory processing disorders, in particular sensory intolerance, combined with mood disorders
285   and difficulties in adapting to specific situations, leads to maladjusted behaviour and impaired
286   functioning in everyday life. It has been shown that sensory disorders occur in patients with
287   affective and anxiety disorders and these are mainly expressed in the form of increased
288   sensitivity to external stimuli, this, in turn, leads to these people avoiding any sensory
289   impressions. In this study, it was not shown that people with depression were more sensitive to
290   electrical stimuli compared to the group of mentally healthy women, but, what was shown, was
291   that TENS stimulation was unpleasant for a certain percentage of women with depression.
292   There is little research available in scientific reports on the perception of electrical stimuli
293   in people with depression. Most of the published studies focus on how pain is experienced by
294   these patients. In this research, the pain threshold was not examined as it was considered
295   unethical. The sensory threshold test showed no difference. Examination of the hedonic rating,
296   however, showed a tendency to a more frequent unpleasant perception of TENS stimulation in
297   the group of women suffering from depression, especially in those with a higher degree of
298   severity according to the CGI-S scale. This appears to be in line with other research (Serafini et
299   al., 2017) in which it has been shown that the relationship between mood disorders and sensory
300   processing problems is related to the severity of symptoms and the duration of the episode.
301   The results of existing studies on pain sensitivity in patients with depression are
302   inconclusive. Some studies show a lower pain threshold compared to mentally healthy subjects
303   (Lautenbacher et al., 1994; Marazziti et al., 1998), others show the opposite results (Adler et al.,
304   1993). In research (Parker et al., 2017) it was also interesting to note that in patients with bipolar
305   disorder, which is known to consist of depressive and manic phases, patients in the depressive
306   phase reported reduced sensory sensitivity. This fact was not confirmed by this research, as the
307   sensory sensitivity of mentally healthy and mentally ill women did not differ significantly. There
308   is no doubt that the relationship between mood disorders and sensory sensitivity requires further

309   investigation (Engel-Yeger et al., 2016).

310   With regard to the drugs used by the women suffering from depression in this research, it
311   is worth noting that literature on the subject states that psychotropic drugs may affect the
312   response to pain, i.e., antinociceptive effects (Klauenberg et al., 2008; Blier et al., 2008;
313   Bouwense et al., 2012). It is important to also take into account that the obtained study results
314   may, to some extent, reflect the effect of medications taken by mentally ill women. Since mood
315   stabilisers have analgesic properties, an effect on the response to sensory stimuli can also be
316   expected. The antidepressant effect of psychotropic drugs leads to an increase in the transmission
317   of neurotransmitters (norepinephrine, serotonin and dopamine) in cortical and subcortical
318   structures responsible for mood regulation through, among others, a mechanism blocking the
319   reuptake pumps of these neurotransmitters (Andrade et al., 2010). Among the drugs used by the
320   women suffering from depression was, for example, pregabalin, which like some SSRIs, is
321   sometimes used to relieve pain of central and peripheral origin. It is not clear if it has an effect on
322   sensory sensitivity, but in research (Engel-Yeger et al., 2016) there were no differences in pain
323   responsiveness between those patients taking and not taking SSRIs. Benzodiazepines do not
324   change pain sensitivity, which may give a possible picture of their effect on sensory sensitivity
325   (Klauenberg et al., 2008; Blier et al., 2008; Bouwense et al., 2012).

326   As is known, however, pain-reactivity is not the same phenomenon as sensory-reactivity,
327   as they are related to the stimulation of different nerve fibres. In order to be sure which drugs had
328   or had no effect on the changes in sensory sensitivity in the women with depression in this study,
329   an additional control group of women with depression who were not taking any drugs would
330   have been required. This approach is impossible in a psychiatric hospital, however such study
331   could be conducted in a sample of patients receiving various forms of psychological support in
332   outpatient settings.

333   It is worth to mention here that a diagnosis of major depression in patients with pain-
334   related symptoms is difficult, although those two conditions often co-occur (Choi et al., 2014). A
335   patient with a mental illness is often treated in primary care only for the pain that he/she has
336   reported to their general practitioner. In primary care facilities, the medical team, by design,
337   focuses more on the physical ailments than on the patient's depressed mood and mental
338   despondency, and this is clearly the role of these specialists. However, since the results of studies
339   by other authors (Holmes et al., 2013; Bair et al., 2003; Williams et al., 2003) show such a strong

340 relationship between pain and depression, is it not worth paying attention to the patient more
341 holistically? If the patient's somatic pain is the result of psychological issues, physical treatments
342 could be less effective. Moreover, recognizing and addressing depressive symptoms by applying
343 a complex and interdisciplinary approach would lead to a better treatment response.
344 Physiotherapists can offer a holistic, biopsychosocial assessment which includes an enquiry
345 about the presence of any mental health issues, and the impact of pain on mood and morale.

346 The main implications of this paper, based on the Author's findings, indicate that that
347 TENS procedures applied in patients with depression may possibly have only a limited analgesic
348 effect. The results of this research show a different hedonic rating in the perception of electrical
349 stimuli in women with depression, when compared to mentally healthy women. Therefore, the
350 fundamental question which arises is: should electrotherapeutic procedures be performed in
351 people suffering from depression, since procedures using TENS, one of the mildest existing
352 electrical currents used in treatment, are known to be unpleasant? As people suffering from
353 depression informed that the stimulus was unpleasant to them at the lowest current doses that
354 represented only the sensory threshold, it is likely that with the increase in the current to the dose
355 representing a therapeutic stimulus it would become increasingly unpleasant or even impossible
356 to tolerate, and result in the need to stop the procedure.

357 In the physical medicine, too weak stimuli acting on tissues do not have the required therapeutic
358 effect like, for example, pain relief (Geng et al., 2011; Cheing et al., 2009). The TENS
359 stimulation intensity must be high enough to stimulate sensory fibers at a level resulting in
360 presynaptic inhibition of pain conducted through pain fibers, i.e., closing of the control gate
361 (Moayedi et al., 2013) . Thus the authors are of the opinion that TENS treatments applied at
362 healthcare centers in people with depression may not result in the expected analgesic effect due
363 to a limited possibility to increase the current in those patients. Therefore, it seems justified to
364 expand the research to include those assumptions and verify whether physiotherapy procedures
365 using TENS performed at healthcare centers in people with depression have the expected
366 analgesic effect.

367 The main limitation of this study emerge from the characteristics of the group of people
368 suffering with depression who participated in this study. Due to these limitations, the presented
369 conclusions cannot be applied to other groups of patients suffering from depression, e.g., men
370 and women with stage VI and VII depression on the CGI-S scale. When planning successive

371 studies, it would be worthwhile to introduce a detailed evaluation of the ahedonia degree in
372 studied people with depression, to determine whether it is this phenomenon that is responsible
373 for the negative perception of the TENS stimulus in the women with depression, described in this
374 study. It would be interesting to include typical sensory aspects of ahedonia in that evaluation.
375 An attempt should be made to divide the study subjects into groups with primary depression and
376 with secondary depression caused, for example, by chronic physical pain.
377   Moreover, it would be beneficial to conduct studies involving people who are suffering
378 from depression of varying degrees and experiencing pain. It would be worth, for these people,
379 assessing the sensations that emerged in a complete series of TENS treatment, observing the
380 course of the full therapy, e.g., the level of intensity achieved on individual treatment days,
381 asking patients for a hedonic rating, and finally assessing whether the therapy had brought a
382 satisfactory final result for the patient, as in the elimination of pain.
383   Additionally, in our study all women were during treatment. It would be advantageous to
384 conduct studies in subjects with depression in whom no pharmacotherapy was initiated, and
385 compare sensations caused by the current in those two groups of patients. It would be interesting
386 to evaluate occurrence of possible psychosomatic symptoms in the study group and their
387 influence on reception of the sensory stimuli and treatment effectiveness. Extending research in
388 this area is justified.
389
390 ## Conclusions
391   In conclusion, it should be stated that women suffering from depression present a similar
392 threshold of sensitivity as mentally healthy women to an electrical stimulus. Moreover, the
393 sensations caused by the electric current were described by depressed women in a similar way to
394 those given by the mentally healthy women - most often it was tingling. However, the hedonic
395 rating of the electrical stimulus acting on the skin in the group of women suffering depression
396 was more negative than in the mentally healthy group. The electrical stimulus was described by
397 many of the mentally ill women as 'unpleasant'. The electric stimulus was most negatively
398 perceived by women with the most severe depression, i.e., those with the highest severity of
399 illness on the CGI scale.
400
401
402

403 **References**

404

405   Abraira VE, Ginty DD. 2013. The Sensory Neurons of Touch Neuron 21:618-639

406   Adler D, Gattaz WF. 1993. Pain perception threshold in major depression. Biol Psychiatry

407   34:687-689

408   Andrade C, Rao NS. 2010. How antidepressant drugs act: A primer on neuroplasticity as the

409   eventual mediator of antidepressant efficacy. Indian J Psychiatry 52:378-386

410   Bair MJ, Robinson RL, Katon W, Kroenke K. 2003. Depression and pain comorbidity: a

411   literature review. Arch Intern Med 163:2433–2445

412   Blier P, Abbott FV. 2001. Putative mechanisms of action of antidepressant drugs in affective

413   and anxiety disorders and pain. J Psychiatry Neurosci 26:37–43

414   Bouwense SAW, Olesen SS, Drewes AM, Poley JW, van Goor H, Wilder-Smith OHG. 2012.

415   Effects of pregabalin on central sensitization in patients with chronic pancreatitis in a

416   randomized, controlled trial. Plos One 7:e42096

417   Brockbank J, Krause T, Moss E, Milthers Pedersen A, Morup MF, Ahdesmaki O, Vaughan J,

418   Brodtkorb T-H. 2021. Health state utility values in major depressive disorder treated

419   with pharmacological interventions: a systematic literature review. Health Qual Life

420   Outcomes 19:94

421   Buster J, Targum SD. 2007. The clinical global impressions scale: applying a research tool in

422   clinical practice. Psychiatry 4:28-37.

423   Cheing GL, Chan WW. 2009. Influence of choice of electrical stimulation site on peripheral

424   neurophysiological and hypoalgesic effects. J Rehabil Med 41:412–417

425   Choi Y, Mayer TG, Williams MJ, Gatchel RJ. 2014. What is the best screening test for

426   depression in chronic spinal pain patients? Spine J 14:1175-1182

427   Cox DR, Ashby S, Mace JC, DelGaudio JM, Smith TL, Orlandi RR, Alt JA. 2017. The pain-

428   depression dyad and the association with sleep dysfunction in chronic rhinosinusitis. Int Forum

429   Allergy Rhinol 7:56–63

430   Currie SR, Wang J. 2005. More data on major depression as an antecedent risk factor for first

431   onset of chronic back pain. Psychol Med 35:1275–1282

432   De Giorgi R, De Crescenzo F, Cowen PJ, Harmer CJ. 2021. Statins for major depressive
433   disorder: A systematic review and meta-analysis of randomized controlled trials. PLOS One
434   16:e0249409

435   de Girolamo G, Barattieri di San Pietro Ch, Bulgari V, Dagani J, Ferreri C, Hotopf M, Iannone
436   G, Macis A, Matcham F, Myin-Germeys I, Rintala A, Simblett S, Wykres T, Zarbo C. 2020.
437   The acceptability of real-time health monitoring among community participants with
438   depression: A systematic review and meta-analysis of the literature. Depress Anxiety 37:885–
439   897

440   Engel-Yeger B, Gonda X, Muzio C, Rinosi G, Pompili M, Amore M, Serafini G. 2016. Sensory
441   processing patterns, coping strategies, and quality of life among patients with unipolar and
442   bipolar disorders. Rev Bras Psiquiatr 38:207–215

443   Ferrari AJ, Norman RE, Freedman G, Baxter AJ, Pirkis JE, Harris MG, Page A, Carnahan E,
444   Degenhardt L, Vos T, Whiteford HA. 2014. The burden attributable to mental and substance
445   use disorders as risk factors for suicide: findings from the Global Burden of Disease Study
446   2010. Plos One 9:e91936

447   Geng B, Yoshida K, Jensen W. 2011. Impacts of selected stimulation patterns on the perception
448   threshold in electrocutaneous stimulation. J Neuroeng Rehabil 8:9

449   Gibson W, Wand BM, O'Conell NE. 2017. Transcutaneous electrical nerve stimulation
450   (TENS) for neuropathic pain in adults. Cochrane Database Syst Rev 9:D011976

451   Gladwell PW, Badlan K, Cramp F, Palmer S. 2016. Problems, solutions, and strategies
452   reported by users of transcutaneous electrical nerve stimulation for chronic musculoskeletal
453   pain: qualitative exploration using patient interviews. Phys Ther 96:1039–1048

454   GDB 2019 Diseases and Injuries Collaborators. 2020. Global burden of 369 diseases and
455   injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global
456   Burden of Disease Study 2019. Lancet 396:1204-1222

457   Holmes A, Christelis N, Arnold C. 2013. Depression and chronic pain. Med J Aust 199:17-20

458   Jauregui JJ, Cherian JJ, Gwam CU. 2016. A meta-analysis of transcutaneous electrical nerve
459   stimulation for chronic low back pain. Surg Technol Int 28:296–302

460   Johnson MI, Jones G, Paley CA, Wittkopf PG. 2019. The clinical efficacy of transcutaneous
461   electrical nerve stimulation (TENS) for acute and chronic pain: a protocol for a meta-analysis
462   of randomised controlled trials (RCTs). BMJ Open 9:e029999

463   Klauenberg S, Maier Ch, Assion HA, Hoffmann A, Krumova EK, Magerl W, Scherens A,
464   Treede R-D, Juckel G. 2008. Depression and changed pain perception: hints for a central
465   disinhibition mechanism. Pain 140:332-343

466   Lambert C, Da Silva S, Ceniti AK, Rizvi SJ, Foussias G, Kennedy SH. 2018. Anhedonia in
467   depression and schizophrenia: A transdiagnostic challenge. CNS Neurosci Ther 24:615-623

468   Landa A, Fallon BA, Wang Z, Duan Y, Liu F, Wagner TD, Ochsner K, Peterson BS. 2020.
469   When it hurts even more: The neural dynamics of pain and interpersonal emotions. J
470   Psychosom Res. 128:109881

471   Lautenbacher S, Roscher S, Strian D, Fassbender K, Krumrey K, Krieg JC. 1994. Pain
472   perception in depression: relationships to symptomatology and naloxone-sensitive
473   mechanisms. Psychosom Med 56:345-352

474   ~~Leo RJ. 2005. Chronic pain and comorbid depression. Current Treatment Options in~~
475   ~~Neurology 7:403-412~~

476   Malejko K, Brown RC, Plener PL, Bonenberger M, Graf H, Abler B. 2021. Differential neural
477   processing of unpleasant sensory stimulation in patients with major depression. Eur Arch
478   Psychiatry Clin Neurosci 271:557-565

479   Marazziti D, Castrogiovanni P, Rossi A. 1998. Pain threshold is reduced in depression. Int J
480   Neuropsychopharmacol 1:45-48

481   Martimbianco ALC, Porfirio GJM, Pacheco RL, Torloni MR, Riera R, Cochrane Back and
482   Neck Group. 2019. Transcutaneous electrical nerve stimulation (TENS) for chronic neck pain.
483   Cochrane Database Syst Rev 12:CD011927

484   Moayedi M, Davis DD. 2013. Theories of pain: from specificity to gate control. J Neurophysiol
485   109:5-12

486   Nitzan U, Hecht M, Brow Y, Maoz H, Levkovitz Y, Yarnitsky D, Granovsky Y, Bloch Y.
487   2019. Initial evaluation of pain intensity among depressed patients as a possible mediator
488   between depression and pain complaints. Front Psychiatry 10:48

489   Noble RE. 2005. Depression in women. Metab Clin Exp 54:49-52

490   Parker G, Paterson A, Romano M, Graham R. 2017. Altered Sensory Phenomena Experienced
491   in Bipolar Disorder. Am J Psychiatry 174:1146-1150

492   Pinheiro Campos AC, Antunes GF, Matsumoto M, Pagano RL, Ruiz Martinez RCh. 2020.

493   Neuroinflammation, Pain and Depression: An Overview of the Main Findings. Front Psychol

494   11:1825

495   Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choiniere M. 2012. A

496   systematic literature review of 10 years of research on sex/gender and pain perception – part

497   1: are there really differences between women and men? Pain 153:602-618

498   Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choiniere M. 2012. A

499   systematic literature review of 10 years of research on sex/gender and pain perception - part 2:

500   do biopsychosocial factors alter pain sensitivity differently in women and men? Pain 153:619-

501   635

502   Rømer Thomsen K, Whybrow PC and Kringelbach ML. 2015. Reconceptualizing anhedonia:

503   novel perspectives on balancing the pleasure networks in the human brain. Front Behav

504   Neurosci 9:49

505   Sassarini J. 2016. Depression in midlife women. Maturitas 94:149-154

506   Schug SA, Daly HCS, Stannard KJD. 2011. Pathophysiology of Pain. Mechanisms of Vascular

507   Disease. Barr Smith Press.

508   Serafini G, Engel-Yeger B, Vazquez GH, Pompili M, Amore M. 2017. Sensory Processing

509   Disorders are Associated with Duration of Current Episode and Severity of Side Effects.

510   Psychiatry Investig 14:51-57

511   Thompson T, Correll ChU, Gallop K, Vancampfort D, Stubbs B. 2016. Is pain perception

512   altered in people with depression? A systematic review and meta-analysis of experimental pain

513   research. J Pain 17:1257-1272.

514   Ulashchik VS. 2017. Skin receptors and therapeutic physical factors. Vopr Kurortol Fizioter

515   Lech Fiz Kult 94:48-57

516   Whiteford HA, Degenhardt L, Rehm J, Baxter AJ, Ferrari AJ, Erskine HE, Charlson FJ,

517   Norman RE, Flaxman AD, Johns N, Burstein R, Murray ChJL, Vos T. 2013. Global burden of

518   disease attributable to mental and substance use disorders: findings from the Global Burden of

519   Disease Study 2010. Lancet 382:575–1586

520   Williams LS, Jones WJ, Shen J, Robinson RL, Weinberger M, Kroenke K. 2003. Prevalence

521   and impact of depression and pain in neurology outpatients. J Neurol Neurosurg Psychiatry

522   74:1587–1589

523   World Health Organization. World Health Day. Retrieved from the WHO website 2017.

524   http://www.who.int/campaigns/world-health-day/2017/en/

525   Zeveke AV. 2013. An integrative framework of the skin receptors activation:

526   mechanoreceptors activity patterns versus "labeled lines". J Integr Neurosci 12:47-56

527

Figure 1

Figure 1: The threshold of current sensation in the group of women with depression
(N=44), and the Control group (N=41)

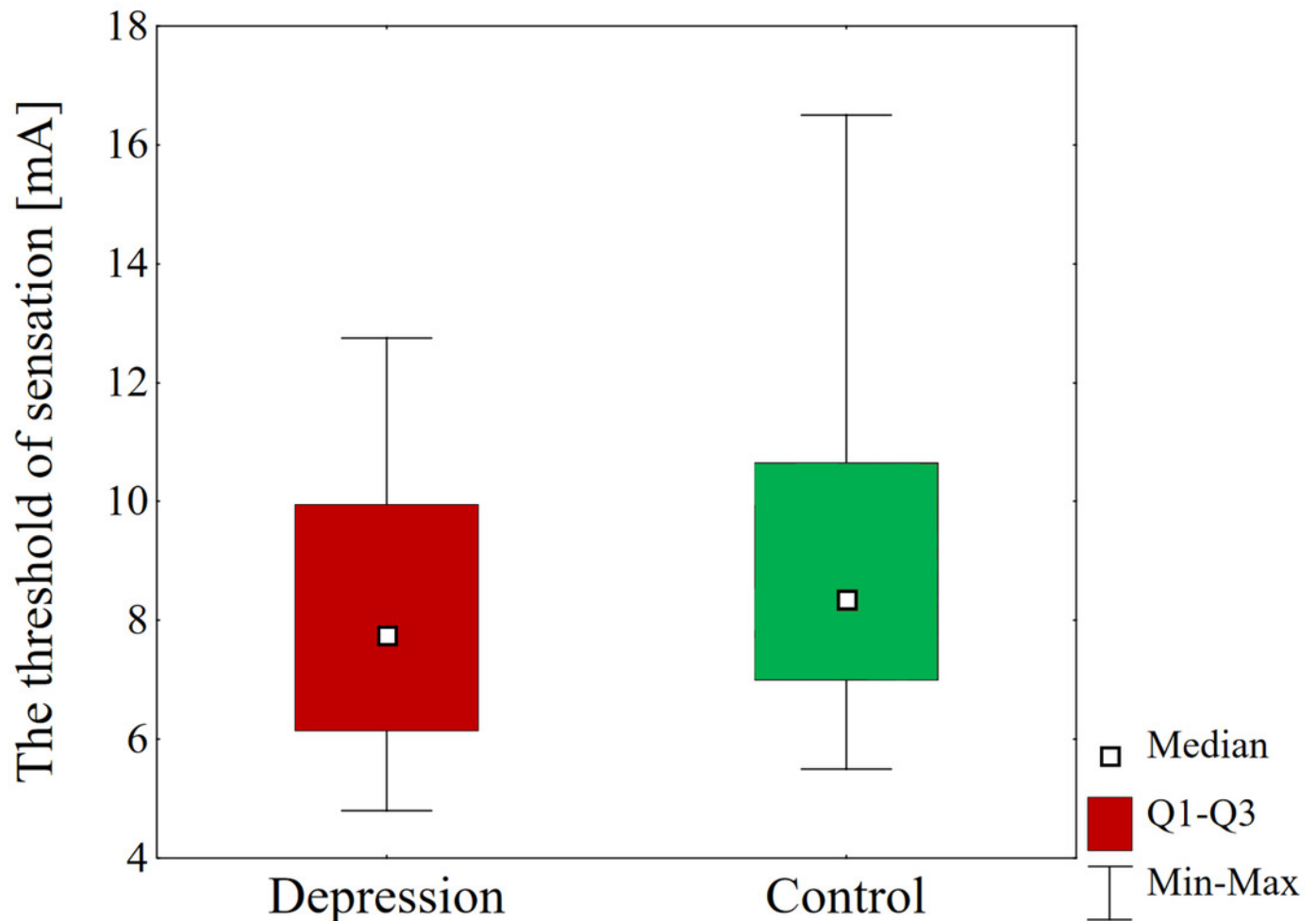



Figure 2

Figure 2: Subjective description of the sensations caused by the electrical current in the group of women with depression (N=44), and in the Control group (N=41)

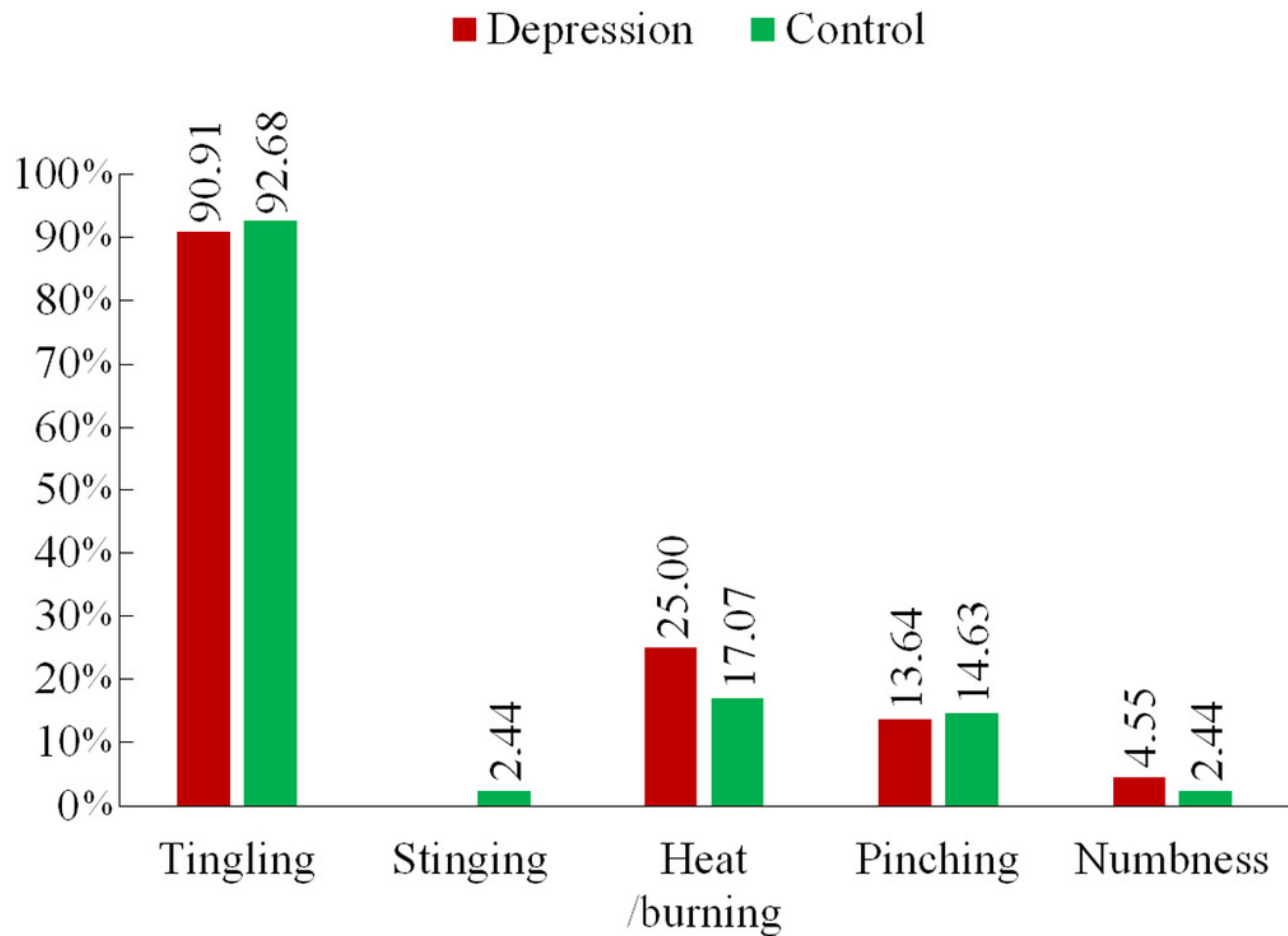



Figure 3

Figure 3: Hedonic rating of the current-induced stimulus in the group of women suffering from depression (N=44), and in the Control Group (N=41) ** p=0.003

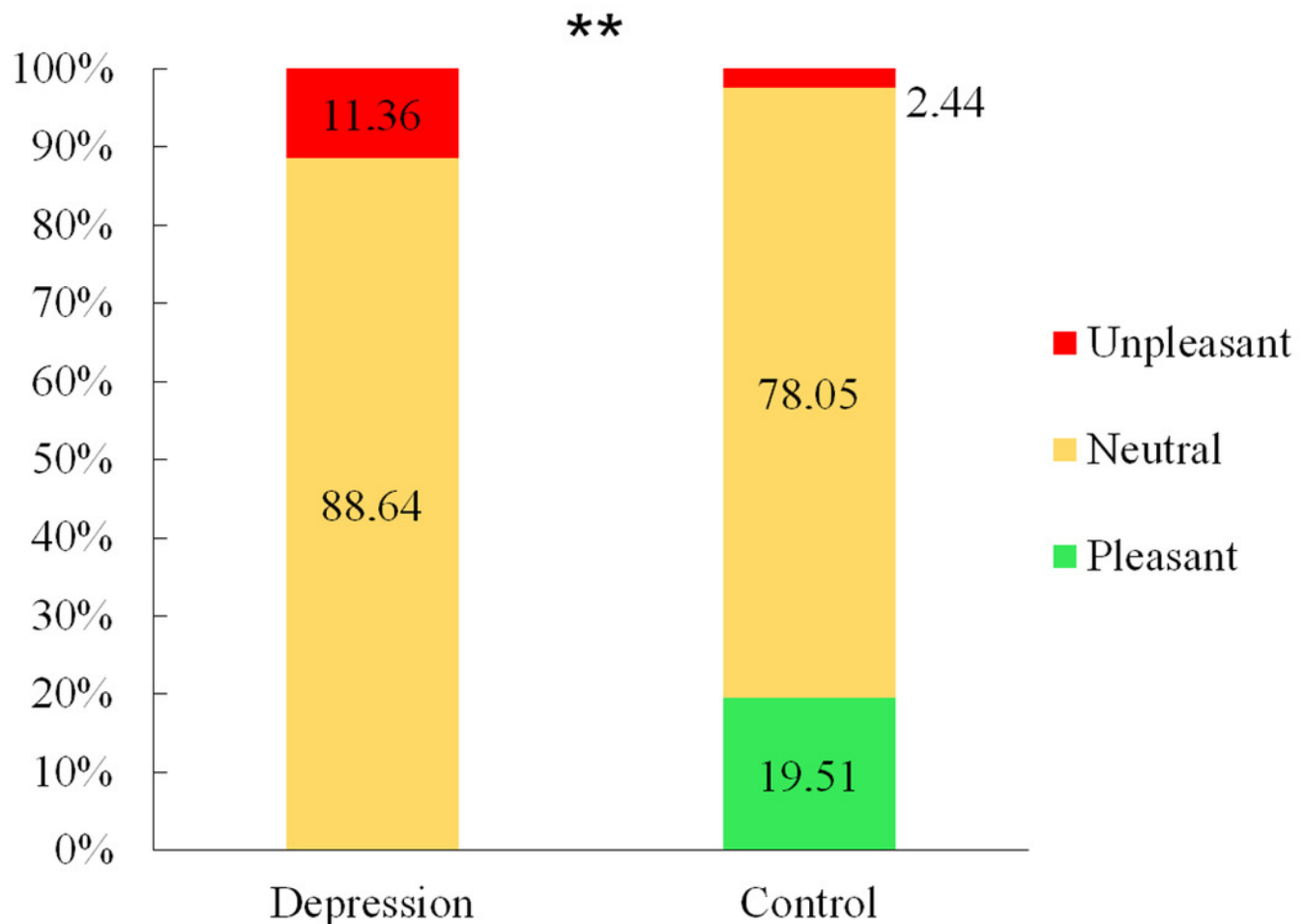
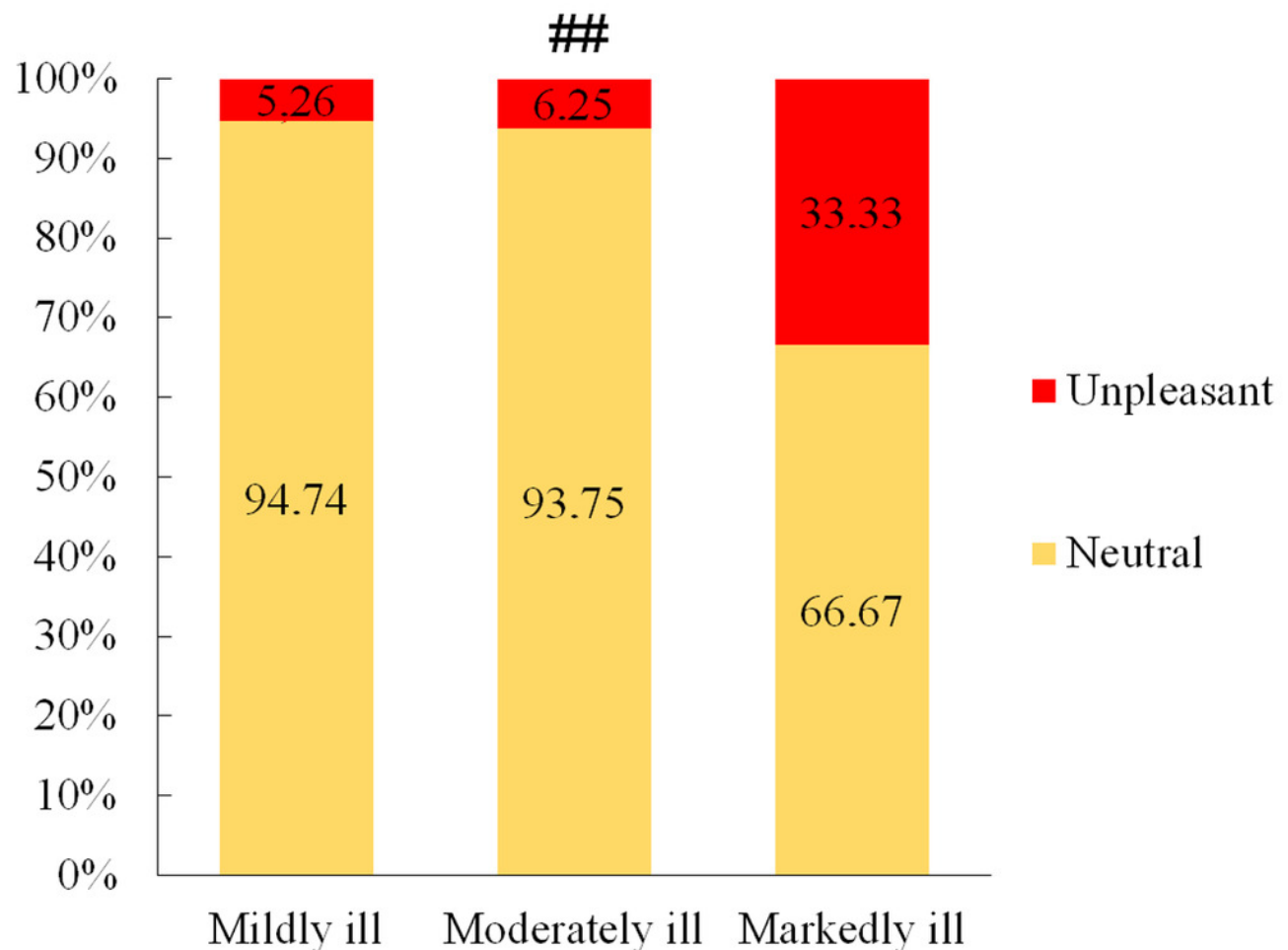



Figure 4

Figure 4: Hedonic rating of the current-induced sensation in mildly ill (N=19), moderately ill (N=16), and markedly ill (N=9) depressed women according to the CGI-S; ## p = 0.066

Characteristics of the women in the depression group (D) and control group (C)

1 **Table 1: Characteristics of the women in the depression group (D) (N=44) and control**

2 **group (C) (N=41); St. Dev - standard deviation, Me - median, Q1 and Q3 - first and third**

3 **quartile, Min -minimum, Max - maximum, p - level of statistical significance, the Mann-**

4 Whitney U test

	Group	Mean	St. Dev.	Me	Q1	Q2	Min	Max	U, p
Age [years]	C	34.44	9.09	36.00	24.00	41.00	21.00	49.00	785.5, 0.308
	D	32.36	9.93	33.50	22.00	41.50	18.00	49.00	
Height [cm]	C	166.59	6.93	167.00	160.00	172.00	152.00	179.00	894.5, 0.951
	D	166.50	6.23	166.50	163.00	171.00	154.00	179.00	
Weight [kg]	C	66.46	10.13	65.00	60.00	72.00	49.00	98.00	756.0, 0.200
	D	68.41	7.99	67.50	61.50	75.00	55.00	85.00	
BMI [kg/m^2]	C	24.03	3.90	24.22	21.14	25.95	18.59	34.31	766.0, 0.413
	D	24.72	3.01	24.45	22.09	27.25	18.93	32.05	