Respiratory Variability during Different Auditory Stimulation Periods in Schizophrenia Patients

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Keywords
Schizophrenia; respiration depth, respiration rate, classical Turkish music, white noise

Summary
Background: Schizophrenic patients are known to have difficulty processing emotions and to exhibit impairment in stimuli discrimination. However, there is limited knowledge regarding their physiological responsivity to auditory stimuli.

Objectives: The purpose of this study was to compare the respiratory effects of two types of auditory stimuli with emotional content, classical Turkish music (CTM) and white noise (WN), on schizophrenia patients and healthy control subjects.

Methods: Forty-six individuals participated in the experiment, and respiratory signals derived from a strain-gauge were recorded. Two important respiratory patterns, respiration rate and depth, were analyzed.

Results: The results indicated that patients presented a significantly higher respiration rate than control subjects during the initial baseline and WN exposure periods.

Conclusions: Further studies are needed to correlate respiratory differences with emotionally evocative stimuli and to refine our understanding of the dynamics of these types of stimuli in relation to clinical state and medication effects.

1. Introduction
Schizophrenia is a serious mental disorder characterized by psychosis, apathy and social withdrawal, motor abnormalities and cognitive impairment, which results in impaired functioning in school, work, interpersonal relationships and leisure time.

These abnormalities are generally classified into three categories: 1) positive symptoms, which include delusions, hallucinations, and other reality distortions; 2) negative symptoms, which are expressed as abulia (loss of motivation), alogia (poverty of speech), anhedonia (inability to experience pleasure), avolition (lack of initiative), apathy (lack of interest), and reduced social drive; and 3) cognitive impairment [1]. These symptoms are evaluated using the Positive and Negative Syndrome Scale (PANSS), which measures symptom severity in schizophrenia [2].

Although there are some models and theories for analyzing the causes and outcomes of schizophrenia, the cause of schizophrenia is unclear; evidence suggests that genetic factors, early environmental influences and social factors are key contributors [3]. Theories about symptom development in schizophrenia have long been related to autonomic dysfunction as being central to the manifestation of psychosis. Pupillary, vasomotor, perspiration, heart rate, salivation and temperature changes are some of the autonomic alterations observed in schizophrenic patients; these changes were first identified by Kraepelin [4] and confirmed in later studies [5, 6]. In addition to these alterations, respiration patterns, which are influenced not only by cortical and limbic factors but also by behavioral, mental and emotional factors, have been investigated in several studies [7, 8]. Studies also show that stressful or effortful mental tasks can increase respiration rates and that respiratory dysregulation is associated with several diagnostic groups, including panic disorder, depression and anxiety [9–11].

A previously reported meta-analysis and literature review emphasized the inconsistent nature of the results found in studies investigating distinct emotion-specific patterns of physiological activity and reported that respiration and cardiovascular patterns are two psycho-physiological measures that have been identified for indexing emotional states [12]. Emotional responses can be induced by stimuli in different sensory modalities. A number of
studies have suggested that the experience of emotional states, which can be induced by auditory and visual stimulation, is accompanied by respiratory changes [13, 14]. In a study that included anxious and fearful imagery, respiration was measured, and several breathing parameters were explored in healthy control subjects. In this study reported by Van Diest et al., inter-individual differences in anxiety were found that could be associated with respiratory variability. However, in a study on cardiovascular and respiratory reactions of normal subjects and schizophrenic patients, exposure to pictures with differing emotional content triggered higher respiration rate levels in schizophrenic patients compared to the control subjects [16]. Similarly, in another study investigating the cardio-respiratory parameters of schizophrenics, an increase in respiration rates was found in schizophrenia patients [17].

It is known that respiratory variability is related to dynamic behaviors of the autonomic nervous system [18] and that respiration is influenced by factors other than physiological requirements, including factors that induce emotions. Nylicek et al. [19] investigated a large number of measures of respiratory and cardiovascular activity to characterize the specific emotional states (e.g., happiness, sadness, serenity, and agitation) induced while subjects listened to music or neutral stimuli, i.e. white noise (WN). The results showed that respiratory measures were the parameters that were best able to distinguish between emotional states (i.e., an increase in happiness/agitation relative to sadness/serenity). Similar results were reported in a study by Krumhansl [20], where an increased respiration rate was observed during exposure to clips chosen to induce happiness and fear in comparison to baseline measurements. Other studies in which the physiological effects of WN were investigated include those of Nylicek et al. [19] and Bishop et al. [20], which considered healthy subjects, and Chait et al., Pishkin and Hershiser, and Todd et al. [22–24], which considered schizophrenics. In an earlier study conducted by Pishkin and Hershiser, WN was used as an auditory stimulus to soothe or calm the body and senses of schizophrenia patients. These researchers found that schizophrenic patients showed a stronger response than healthy subjects who possess a WN stress reduction ability [23].

It has been noted that patients with schizophrenia have mental difficulties processing emotions [24–26], and they are thought to experience emotion in a slightly different way than normal subjects during specific situations or conditions. Additionally, it has been reported that schizophrenic patients exhibit stronger emotions when exposed to unmeasured emotional conditions, as opposed to pleasurable conditions [25]. In a preliminary study [26] based on investigating the autonomic reactions and recognition of schizophrenic patients according to basic emotional conditions (e.g., fear, joy, and sadness), it was found that schizophrenic individuals may exhibit differences in physiological activity compared to healthy people. Although most of the research reported in the literature on healthy control subjects or schizophrenic patients consists of simple comparisons of positive emotion and negative emotion, the data indicate that parameters related to respiratory patterns, which can be used to measure an individual’s emotional responses objectively and express them numerically, may be correlated with emotional experiences induced in a variety of ways, such as by music or video.

The present study expands the literature on psycho-physiological measurements of auditory-induced emotions by examining both schizophrenia patients and healthy control subjects during exposure to stimuli. The main purpose of the present study was to determine whether consistent respiratory changes occur during exposure to auditory stimuli and to compare the respiratory effects of stimuli between the two groups. To this end, the auditory stimuli chosen were acoustic WN and a makam (form) of classical Turkish music (CTM) that was shown to induce serenity [27]. Respiration signals were recorded for a total of eight minutes for each participant during four periods of exposure to different stimuli: silence, WN, CTM and silence. To our knowledge, no study has previously explored respiratory patterns in response to CTM between schizophrenia patients and healthy control subjects to understand their autonomic differences. Thus, this investigation can be evaluated as the first study that investigates the relationship between the coordination of respiration with preferred stimuli and the emotional induction during these periods.

It was expected that respiratory changes in response to different stimuli would be consistent with the results of previous studies: increased respiration rates would be observed during happiness inductions [8]. Thus, we expected that respiration rates would increase more during CTM exposure due to its positive emotional content. Based on the results of a previous study by our group [28], we hypothesized that the induction of emotion would be associated with changes in respiration, that there would be some differences in respiration characteristics between the two groups during exposure to stimuli, and that there would be respiratory differences between schizophrenia patients depending on their symptom severity. Considering the high levels associated with respiratory patterns found in schizophrenic patients compared to control subjects [17], we expected that the respiratory differences between schizophrenia patients and control subjects would be diminished after CTM exposure because of its serenity effect. By combining respiratory responses with clinical symptoms, we aimed to extend the knowledge about the physiology and disturbances related to auditory-induced emotions in schizophrenia patients.

2. Methods

2.1 Participants

Twenty-three adults with a DSM-IV (Diagnostic and Statistical Manual, Fourth Edition, 2000) [29] diagnosis of schizophrenia spectrum disorders from Bakirköy Mental and Nervous Diseases Training and Research Hospital, which specializes in the diagnosis and treatment of psychiatric disorders, and twenty-three age- and gender-matched healthy control participants (aged from 18 to 60 years old) participated in this study (Table 1). An experienced psychiatrist diagnosed these schizophrenic patients, and the severity of their schizophrenia symptoms was measured by PANSS [30] administered on the day of the respiration recordings. PANSS is a 30-item...
rating scale for evaluating the absence/presence and the severity of positive, negative and general psychopathology of schizophrenia. The total PANSS score is obtained using the scores of positive (7-item scale), negative (7-item scale) and general psychopathology (remaining 16-item scale) scales [30]. The exclusion criteria for patients included respiratory diseases, cardiovascular diseases, and exhibiting comorbidity. Respiration recordings were collected from all normal hearing subjects (confirmed using audiometry).

This study was approved by both the university and hospital ethics committee, and written informed consent was obtained from all subjects. Participants volunteering as the control group were excluded if they showed a history of cardiovascular or respiratory diseases or psychotic disorders, or if any of their first-degree relatives had been diagnosed with schizophrenia, schizophrenia spectrum or bipolar affective disorders.

2.2 Affective Stimuli

The auditory stimuli selected in this study were acoustic WN and CTM. The WN used was comprised of the sound of rain on a river and was selected based on results from previous experiments [31, 32] due to its evaluation from participants of being uncomfortable and annoying. Following the WN, a wordless clip in the Hüseyi makam called "Çeçen Kızı" was used as a second stimulus. The scientific principles concerning treatment using this traditional music were first established by Turkish scientists and doctors [33]. According to the Turkish philosopher Farabi (870–950 AD), the effects of the makams of Turkish music on the soul are as follows [27, 33]: the Rast makam brings happiness and comfort; the Behavi makam evokes the idea of eternity; additionally the Hüseyi makam induces serenity and ease. After a period of silence, a 2-minute period of acoustic WN was used as the first stimulus, followed by two minutes of CTM. All participants listened to these stimuli binaurally through headphones with an intensity of 75 dB. To compare the frequency range of these two stimuli, graphs of the power spectrum (Fast Fourier Transform, FFT) are presented in Figure 1. It can be observed that the Hüseyi (CTM) had a relatively narrow

| Table 1: Clinical and demographic data of participants |
|---------------------------------|----------|----------|
| Patients                        | Controls | Patients |
| Participants                    | 23       | 23       |
| Male/Female                     | 11 / 12  | 11 / 12  |
| Age (years ± std. deviation)    | 33.95 ± 8.33 | 33.39 ± 6.86 |
| Age of onset in male/female     | 20.82 ± 5.21 / 20.08 ± 6.37 |
| Smoker / non-smoker             | 8 / 15   | 16 / 7   |
| Positive symptoms score         | 16.13 ± 5.22 |
| Negative symptoms score         | 14.70 ± 6.15 |
| PANSS (total) score             | 62.13 ± 13.29 |

PANSS: Positive and Negative Syndrome Scale

Fig. 1
Spectral analysis of both stimuli used in the procedure. Top: FFT of white noise stimulus. Bottom: FFT of Classical Turkish Music stimulus
bandwidth of approximately 11 kHz, which is typical for this makam.

2.3 Procedure

The study was conducted in a quiet, illuminated, temperature-controlled room at Ba-kirköy Hospital. Recordings were collected for approximately eight minutes for each participant. Figure 2 shows a block diagram for the periods comprising the procedure. Respiration rate data were collected for a 2-minute baseline period prior to auditory stimuli exposure (resting1, R1); followed by a 2-minute period of acoustic WN exposure, a 2-minute period of wordless CTM exposure, and a 2-minute post-exposure period (resting2, R2) without any stimulation. The subjects were seated on a chair and asked to participate through the entire procedure with their eyes closed to avoid distractions.

In previous studies [34, 35], it was found that approximately 2 to 4 minutes are sufficient for measuring physiological parameters in relation to excitation, such as fear, stress, and anxiety. Thus, in this study, the duration of each period was selected as two minutes. In conclusion, the respiration signals were recorded for a total of eight minutes. In the procedure, including another resting period between auditory stimuli was not selected because of the long duration of the recordings. Both healthy and schizophrenic subjects are usually exposed to continuous auditory stimuli without any pause in their daily lives. Therefore, the ability to discriminate sequential stimuli and to respond to them differentially was investigated in this study.

2.4 Measurement System

Respiration patterns were recorded using a Model MP150WSW data acquisition system (BIOPAC Systems Inc., Santa Barbara, CA). The system’s respiratory effort transducer (TSD201) and amplifier (RSP100C) were utilized to measure the changes in thoracic or abdominal circumference that occur during breaths.

Changes in respiration were measured with a strain gauge type transducer (belt) that wrapped around the subject at the approximate height of the sternum and was fastened to fit snugly, but not uncomfortably tight. The respiration signals were low-
pass filtered at 1 Hz, high-pass filtered at 0.05 Hz and sampled at 250 Hz.

2.5 Data Analysis

The respiration recordings were analyzed using the MATLAB 7.0® software package (The Mathworks, Natick, MA, USA). Respiration rate and depth are two important parameters that should be observed and counted together to identify any respiratory changes. While the normal respiration rate is known to rest between 6 and 20 breaths per minute, the respiratory amplitude is defined as the depth of inspiration.

A min-max detection was implemented in MATLAB to compute the time stamp for each peak and valley in the waveform, thereby indicating the timing of each respiration pattern. This information was visually double-checked to ensure that all breaths in the waveform were identified and that they corresponded to actual breaths taken by all subjects. The respiration rate was calculated in terms of breaths per period, where each period had a duration of 120 seconds. The peak of each individual breath detected in the respiratory waveform of a schizophrenia patient is indicated with circles in Figure 3. An example of representative R1, WN, CTM and R2 periods of respiration data for a subject with a respiration rate of 0.24 Hz (29 breaths in 2-minute), 0.26 Hz (31 breaths in 2-minute), 0.26 Hz (31 breaths in 2-minute) and 0.23 Hz (27 breaths in 2-minute), respectively, is shown in the same figure. The respiration amplitude or depth during a stimulus period was calculated as the mean of the difference between the maximum and minimum values of each breath.

Data were analyzed using the SPSS (v.13.0) statistical package (SPSS Inc., Chicago, IL). To detect differences in respiration between patients and controls, the mean values of the respiration rate and depth during each period were compared between groups using an independent sample Student’s t-tests. Each sequential recording period was paired. Student’s t-test was chosen due to the result of Levene’s test, which was used to test whether variances among the groups were homogeneous. In the statistical analysis, a confidence level of 95% was used and differences between groups of p < 0.05 were considered statistically significant.

3. Results

In this study, respiration signals were recorded and analyzed for both schizophrenia patients and healthy control subjects.

<table>
<thead>
<tr>
<th>Periods</th>
<th>Controls (n = 23)</th>
<th>Patients (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1*</td>
<td>35.74 (6.56)</td>
<td>39.83 (9.62)</td>
</tr>
<tr>
<td>WN*</td>
<td>37.87 (8.09)</td>
<td>41.26 (9.98)</td>
</tr>
<tr>
<td>CTM</td>
<td>40.52 (9.40)</td>
<td>41.22 (7.34)</td>
</tr>
<tr>
<td>R2</td>
<td>37.61 (8.87)</td>
<td>37.74 (6.36)</td>
</tr>
</tbody>
</table>

Table 2: Mean values of respiration rate for the control group and patient group

*, Significant difference between groups, p < 0.05

Fig. 4 Changes in respiration rates (mean and standard deviation) with the 95% Confidence Interval (CI) during the periods of the procedure in the control and the schizophrenic group. The respiration rate increased in both the control group (p = 0.01) and patient group (p = 0.05) under auditory stimuli exposure. (Abbreviations: R1 – resting 1, WN – white noise, CTM – Classical Turkish Music, R2 – resting 2).
3.1 Respiration Rate

In Table 2, the results are shown for the respiration rate values in each measurement period. The respiration rate was calculated using the number of breaths per period (120 seconds). It is possible that the respiration rate has an inaccuracy of a maximum of 1 breath in each period due to the calculation of the algorithm. The patients showed a higher mean respiration rate than the control subjects during all periods of the procedure; however, a significant difference between two groups was obtained for the R1 period and WN exposure period (p < 0.05). Our results showed that there was an increase in the mean of respiration rate in both the control subjects (p = 0.01) and schizophrenic patients (p < 0.05) when stimulated with auditory exposure (Fig. 4). The greatest increase in the respiration rate of schizophrenia patients was observed during both auditory stimulus periods when compared to the resting baseline periods. In the control group, the highest mean value of the respiration rate was obtained during the CTM period. Stimulus with WN after a period of rest caused an increase in the mean respiration rate in both groups. This increase continued in the CTM period (p = 0.02) for the control group. However, for the schizophrenic patients, no significant change was reported over these two periods of respiration (i.e., the WN period and the CTM period). There was a decrease from the CTM to R2 period in the control group (p < 0.01) and the patient group (p = 0.007). In the control group, the results indicated that there as an insignificant increase in the number of breaths per period between periods R1 and R2 (p > 0.05), but the rate of respiration in schizophrenia patients decreased between periods R1 and R2 (p < 0.05).

3.2 Respiration Depth

The respiration amplitude or depth in a period was calculated by averaging the value of the peak minus the minimum for each breath in that period. The mean values of respiration depth for the patient and control groups in each measurement period are listed in Table 3. Figure 5 presents the mean respiration depth of each period for both the control subjects and schizophrenia patients. The patients exhibited a greater respiratory depth than the control subjects over all periods; however, a significant difference between the patient and control groups was obtained in the R2 period and CTM exposure period (p < 0.05). For the control group, the highest mean value of respiration depth was obtained during the R1 period, with a non-significant decreasing pattern towards the end of the procedure. Only CTM exposure caused a significant decrease (p = 0.05) in terms of respiration depth. For schizophrenic patients, no significant differences in respiration depth patterns were found between periods.

The respiration rate and depth values were correlated with each of the two subscales of the PANSS (positive and negative symptoms score) and with the total PANSS score to explore the relationships between the severity of clinical symptoms and respiration rate. Table 3 Mean values of respiration depth for the control group and patient group.

<table>
<thead>
<tr>
<th>Periods</th>
<th>Controls (n = 23)</th>
<th>Patients (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1</td>
<td>1.13 (0.17)</td>
<td>1.70 (0.68)</td>
</tr>
<tr>
<td>WN</td>
<td>1.07 (0.47)</td>
<td>1.69 (0.48)</td>
</tr>
<tr>
<td>CTM*</td>
<td>0.86 (0.02)</td>
<td>1.61 (0.35)</td>
</tr>
<tr>
<td>R2*</td>
<td>0.88 (0.09)</td>
<td>1.86 (0.82)</td>
</tr>
</tbody>
</table>

R1: Resting 1, WN: White noise
CTM: Classical Turkish Music, R2: Resting 2
*Significant difference between groups, p < 0.05

Fig. 5 Respiration depth changes in the baseline (R1), auditory stimulation (WN-CTM), and post-stimulation rest (R2) periods for both the schizophrenic and control groups (Abbreviations: R1 – resting 1, WNm – white noise, CTM – Classical Turkish Music, R2 – resting 2). There was no significant change between two stimulation periods in the schizophrenia group.
piratory responsiveness. According to Pearson’s Correlation test, only the respiration depth response to CTM with emotional content showed a significant negative correlation with the PANSS subscales negative (R = –0.46, p < 0.05) score, as shown in Figure 6. The line appears in the graph with R² values (R Sq Linear = 0.216) resulting from the linear correlation analysis. This squared correlation coefficient, which is also known as the determination coefficient for evaluating the strength of a relationship, determines how much of the respiration depth response to CTM is related to the PANSS negative score. Therefore, (R Sq Linear = 0.216) 21.6% of the respiration depth during CTM exposure was determined by the PANSS negative score. Here, it is shown that the respiration depth of some patients is characteristic of very shallow respiration (nearly 0.2 liters) due to the rapid respiration rate during this period.

3.3 Symptom Severity and Respiratory Features

In this study, patients were divided into two classes according to their total PANSS score: a moderately ill group of 12 patients with scores of 44–61 and a severely ill group of 11 patients with scores of 68–87. Respiration rates were evaluated in each group (Fig. 7). Moderately ill patients showed slight respiration rate variation for all periods of the procedure, except the R2 period, in which they exhibited a decrease in the mean respiration rate (p = 0.03). As the severity of symptoms increased, such as in the severely ill patients group, a small change in the respiration rate was observed, but this was not evaluated to represent a significant difference. The moderately ill patients and severely ill patients did not differ in their respiration rate responses over sequential periods of the procedure.

The respiration depth results for the patient sub-groups are shown in Figure 8. In both the moderately ill and severely ill patient groups, different exposure periods resulted in different response curves. Furthermore, the severely ill patients showed a more elevated response during all periods of the procedure in comparison with the control subjects and moderately ill patients. While listening to WN, the moderately ill patients showed a small increase in respiration depth, followed by a decrease during the CTM period, whereas the severely ill patients showed an initial decrease during WN exposure, followed by a slight decrease during the CTM period. No significant differences were found for respiration depth in the response patterns within sub-patient groups.

4. Discussion and Conclusion

Studies reported in the literature have suggested that both auditory and visual stimulation have the property of evoking emotions that are detectable through central and autonomic nervous system measures and that the experience of emotional states is accompanied by respiratory changes [8, 19, 36–38]. However, these studies have been limited to investigations in healthy people. Only a few authors have reported results related to the physiological response of schizophrenics to stimuli with emotional content [16, 39].

The purpose of the present study was to investigate respiratory variability in response to two different auditory stimuli with emotional content for schizophrenic patients and healthy control subjects. Motivated by the influence of CTM on psychiatric patients, which although it has not been scientifically proven, was described by Kalender [27] and Somakci [33], we aimed to examine the autonomic responses of schizophrenics to CTM. To this end, the Hüseyni makam was used as a stimulus that induces positive emotions. To clarify and improve the interpretability of the respiratory responses of schizophrenics to CTM, a second auditory stimulus, acoustic WN, was employed as an alerting control condition based on the results of previous studies [31, 32].

Auditory stimuli were presented in a fixed order: WN exposure and followed by a CTM period. In the literature, the order of stimuli differs according to the study and their expected effects. In some studies on healthy subjects, WN has been used as a neutral stimulus to distinguish the effects of music fragments on cardiovascular differences associated with auditory-induced
emotions [19]. In other studies, WN is selected because of its annoying, uncomfortable and alerting effects [31, 32], but in our study, WN was used before CTM exposure because of its alerting effect. Therefore, to investigate the serenity effect of CTM on respiratory patterns, we preferred to use the stimuli in this fashion.

In the present study, two auditory stimuli were used to evoke an emotional situation, and the differences in the respiratory response between two groups associated with schizophrenia were investigated. Many factors, both physiological and emotional, are involved in the regulation of ventilation and the rate and depth of breathing. Therefore, respiration rate and depth were analyzed, similarly to studies that investigate physiological responses to mental workload [40]. Considering the total eight-minute recording time, we chose respiration signals instead of cardiovascular patterns due to their ability to objectively measure emotional responses and quantitatively distinguish between emotional states [19] and their correlation with the PANSS scores of schizophrenic patients, as reported by Hempel et al. [16].

We observed that schizophrenic individuals may exhibit differences in respiratory responses to auditory stimuli in comparison to healthy people. The schizophrenic patients showed significantly higher respiration rates (p < 0.05) during the R1 period and WN exposure period and greater respiration depth levels during the R2 period and CTM exposure period compared to control subjects. This is consistent with the results of a previous study that compared the baseline respiratory patterns of schizophrenic patients and control subjects [17]. There are several possible explanations for this finding, one of which is that the patients chosen for this experiment presented respiration volume differences due to their high smoking percentage, as shown in Table 1. Another possible explanation is the effects of medication on schizophrenia patients [16, 17].

We found that respiration rates increased during auditory stimulation periods for both the control subjects and schizophrenia patients in comparison to the baseline rest period. Specifically, the increased respiration rate observed during the stimulation periods was associated with emotional

Fig. 7  Respiration rate changes during different periods (Abbreviations: R1 – resting 1, WN – white noise, CTM – Classical Turkish Music, R2 – resting 2) for two patient sub-groups classified by PANSS scores and the control group. To connect the mean values of respiration rate, straight lines were used. For moderately ill patients, a significant change was observed during the R2 period (p = 0.03). In the group of severely ill patients, a small but insignificant amount of change in respiration rate was observed.

Fig. 8  Changes in respiration depth during different periods for sub-patient and control groups. No significant differences were found in the response patterns within the sub-patient groups. (Abbreviations: R1 – resting 1, WN – white noise, CTM – Classical Turkish Music, R2 – resting 2)
arousal. This result confirms and extends previous reports on respiration rate changes during auditory stimulation [13, 19]. The control group showed a higher respiration rate during CTM exposure compared to the WN period. This result strongly supports the findings of a previous report [8] and our expectation that increased respiration rates would be associated with happiness induction during CTM exposure due to its positive emotional effect. Additionally, the rhythmic characteristics of music in contrast to the static nature of WN may partly explain this difference. Our observation of this response is largely in agreement with the results of previous studies about synchronization between rhythm and respiration [8]. However, it is not surprising that no respiration rate differences were found between stimulus periods for schizophrenia patients in the present study. Patients with schizophrenia have been noted to have deficiencies in emotional functioning [41] and are impaired in auditory stimuli discrimination [42]. Therefore, this result may be related to the inability of schizophrenia patients to discriminate between the rhythmic differences of auditory stimulation periods.

The schizophrenic group showed the highest respiration rate during both stimulation periods. During the first minute of WN exposure, the physiological response was typical of an orienting reflex accompanied with respiration rate acceleration, which is generally mediated by sympathetic activation because of the sudden initiation of a stimulus. During the second minute of WN exposure, an adaptation in the respiratory waveform was observed. Thus, the WN period can be evaluated as a transient period between silence and music exposure. The respiration rate differences observed in the control group and similarities between the WN and CTM periods observed in the patient group may be a result of the sequential exposure to these two stimuli. However, a decrease in respiration rates in both groups during the post-stimulation period was found, possibly as a result of increased parasympathetic activity.

Moreover, while there was a significant respiration rate difference between the schizophrenic patients and the control subjects during the R1 period, no difference between two groups was observed during R2 period in the post-stimulation period. The significant difference between the groups in the R1 state may be related to the patients’ high smoking percentage or the effects of their medication usage which would be consistent with the results of previous studies [16, 17]. Although respiration rates increased during auditory stimulation periods, especially in the CTM period, for both the control subjects and schizophrenia patients in comparison to the R1 period, this increase was found to be higher in the control group. This significant difference confirms the results of a previous study conducted by Etzel et al. on respiration rate increases associated with an increasing tempo [8]. While control subjects synchronize their respiration with the tempo of auditory stimuli, the respiration rates of schizophrenia patients remain quite similar during exposure to stimuli because of their impairment related to auditory stimuli discrimination [42]. Additionally, respiration rates were found to be lower in the post-stimulation R2 period compared to the stimulation periods in both groups. Thus, in the R2 period, respiration rates recovered to the baseline value (R1). Post- vs. pre-stimulation respiration rate changes differentiate the effects of auditory stimuli in schizophrenia patients and healthy subjects. As a result of these effects and the expected response being observed in control subjects during CTM exposure, the respiration rates of patients and control subjects were not significantly different in the R2 period. Moreover, this supported our hypothesis that the respiratory differences between schizophrenia patients and control subjects will diminish after CTM exposure because of its serenity effect. We found that respiration rates of the control group showed higher values in the R2 period compared to the values in the R1 period most likely because of the increased sympathetic activity triggered by the sequential stimuli periods or the stressful situation of the procedure.

In the present study, no significant respiration depth differences were found between periods for the control and schizophrenia groups. Only the CTM stimulus compared to the R1 period was associated with a significant decrease (p = 0.05) in terms of respiration depth in the control group. This difference may be due to the acceleration of the respiration rate during the CTM period. Additionally, our results showed that the respiration depth in the control group during the R2 period did not recover to its higher value in the first resting state, which may be related to the persistence effects of the previous CTM period. Another possible explanation for this finding is the occurrence of an orienting response evoked by the different measurement periods. Sokhadze reported that this type of effect continues for nearly one minute [14] following a stimulus.

Furthermore, to assess the effect of the clinical severity of psychiatric symptoms on respiratory patterns, patients were divided into two classes according to their total PANSS score. As the severity of symptoms increased, a small amount of acceleration in respiration rates was observed. When we evaluated respiratory responsiveness to emotional stimuli in relation to clinical symptoms, none of the parameters, such as depth or rate, showed a significant correlation with the PANSS scores. In this study, we did not differentiate between different sub-groups of patients. For future research in this area, it may be useful to divide the schizophrenic group into different sub-groups according to their medication.

The novel aspects of this study include the examination of the respiration of schizophrenia patients during exposure to CTM and the evaluation of their auditory-induced emotions. In this study, stimuli were presented in a fixed order: a first WN exposure followed by a CTM period. To investigate the serenity effect of CTM on respiratory patterns, we chose to use the stimuli with this order. It will be interesting for future studies to examine the effects of the sequence of these periods. In this pilot study, the ability of schizophrenia patients to discriminate sequential stimuli was investigated. While during stimulation periods, the control subjects showed different respiration rate responses, the schizophrenic patients showed similar responses. This may be an indicator of problems corresponding to sequential stimuli in daily their lives. These findings shed new light on understanding the inability to discriminate stimuli and difficulties in emotional processing seen in schizophrenia patients.
In conclusion, our study has shown that respiration signals of schizophrenia patients in response to emotion-inducing music are different compared to healthy individuals. The obtained respiration rate results can be considered as strongly supporting our hypothesis that the induction of emotion is associated with changes in respiration and that there are differences in respiratory responses between the two investigated groups. In relation to the PANSS score, we found that patients with schizophrenia who exhibit high values for respiration rates and depths are more likely to suffer from a more severe illness. Although the some aspects of the respiratory differences observed between patients and controls in response to emotional stimuli are nuanced, these findings are likely to have broad implications for understanding emotional disturbances in schizophrenic patients. Our results show that to evaluate the dysregularities of the autonomic system and to clarify the effects of CTM, different physiological measurements should be taken into account. To understand emotional disturbances in schizophrenic patients and to obtain information about whether or not autonomic dysfunction is related to these disturbances, further investigations will be required.

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