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The Influence of Olanzapine on Facial Expression of Emotions in Schizophrenia – An Improved Facial EMG Study

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Abstract

Background: The purpose of the study was to investigate the facial expression of emotions (FEE) and its correlation to psychopathology in schizophrenic, olanzapine-treated patients, using an improved facial-EMG method.
Method: We compared fifteen olanzapine-treated, schizophrenic patients with nineteen healthy subjects over a period of two weeks. Emotions were induced by showing pictures from the International Affective Picture System. The activity of five facial muscles was measured with a new, highly sensitive and discriminative facial EMG, recording pre-visible facial muscle activity. The Positive and Negative Syndrome Scale (PANSS) and the Simpson-Angus rating scale for extrapyramidal side effects (EPS) were administered.
Results and Conclusion: Unmedicated schizophrenic patients showed fewer joy/smile reactions than the control group. Compared to healthy controls, the relative smile frequency was not significantly changed by olanzapine. The smile frequency and its changes over time are not significantly correlated with the PANSS depressive syndrome. The changes of facial muscle activity do not correlate with EPS (German J Psychiatry 2004; 7: 14-19).

Keywords: Olanzapine, facial expression of emotions; mimic disturbance; psychopathology

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Introduction

Ever since the development of atypical neuroleptics (NL), intense research has been conducted to investigate effects and side effects of these compounds. So far, the most intensely investigated topics have been: clinical efficacy, side effects, effects on cognitive functions, impact on quality of life and subjective well-being.

However, still largely unknown is the influence of atypical NL on emotions and on the most important medium of emotional communication, i.e. the facial expression of emotions (FEE). FEE and especially the 'smile' as an expression of joy, is one of the main components of psychosocial interaction. Moreover, the ability to conduct psycho-social interactions is crucial for the course of illness and prognosis. This fact is now well established (Baenninger-Huber, 1996; Colby et a., 1977; Scherer, 1984, 1986, 1990).

Several studies have examined the disturbances of FEE in schizophrenic patients. They were all based on the hypothesis of Ekman (1967, 1982, 1992) which postulates six basic expression emotions. These are supposed to be culturally independent and universal in humans regarding their pattern of facial expression. Joy, expressed via different kinds of smile, is said to be the most important of the six basic expression emotions with regard to psychosocial action. Ekman postulates that at least two types of smile can be distinguished: The so-called "felt smile", expressed by M. zygomaticus plus M. orbicularis oculi and the so-called "phony smile", expressed by M. zygomaticus alone.

Ekman developed an objective method for analyzing visible facial activity, the video based Facial Acting Coding System (FACS), which allows the reconstruction of expressed emotions, e.g. the two kinds of smile. One shortcoming is that Ekman's method only measures the visible movements and that he uses them to draw conclusions about the emotions initiating the movements.

Therefore, some studies are currently being conducted to differentiate these movements with a microcomputer-based method (Katsikitis, 1990; Pilowsky et al., 1994; Thornton et al., 1982). The most important but not surprising finding is that visible movements of the face are only a small part of the complete facial muscle activity.

Measuring the complete muscle activity can only be achieved by using a sensitive EMG-method (Ekman et al., 1978; Smith, 1973; Tomkins, 1962, 1963). Dimberg's (1982, 1990, 1998) studies were the first to prove the validity of this attempt and to relate EMG-data to emotions in intensity and quality. In addition, Dimberg showed the existence of so-called "rapid facial reactions" (1998). However, the methods employed so far entail considerable disadvantages regarding sensitivity and cross talks between muscle activities.

Therefore, in order to examine disturbances of FEE in schizophrenic patients mostly visible FEE were applied. Only Kring (1996) used a facial EMG, measuring three muscles, but was confronted with uncontrollable interference, the so called "cross talks". In general, her unmedicated schizophrenic patients showed an overall reduction of FEE and less smile responses than the controls. Other researchers found - more than anything else - a reduced frequency of joy (Schneider et al., 1992; Walker et al., 1993), a preponderance of negative emotions (Martin et al., 1990) and an increased activation of the "disgust muscle" M. levator labii sup. (Steimer-Krause 1990). One important study (Schneider et al., 1992) investigated the influence of typical NL on FEE in schizophrenic patients and showed that typical NL reduces FEE and the smiling frequency.

While the clinical importance of atypical NL is growing rapidly, no studies have been conducted which measure the influence on FEE and especially on the smiling frequency. Hence, the aim of our project was to investigate the influence of the atypical NL olanzapine on FEE and its effect on the frequency of smiling. We used a new, highly sensitive EMG. This EMG method allows an improved analysis and discrimination of minimal pre-visible emotion-related facial muscle activity, which consecutively allows the use of standardized induction methods like the IAPS. This set-up has not been applied successfully in conjunction with the IAPS up to now.

Our study aims to investigate whether atypical NL induce an improvement of FEE in schizophrenic inpatients and how FEE is related to psychopathology.

Method

Subjects

The sample group consisted of fifteen inpatients with schizophrenia (DSM-IV 295) and nineteen healthy subjects. Patients had to meet the DSM-IV (APA, 1994) criteria for schizophrenia, with no other current diagnosis. All of them were inpatients, tested on their first day after admission (T0). Patients had to be without any antipsychotic medication for at least one month, without any benzodiazepines for at least three half-life periods of the respective compound and without any other medication for at least three months. The patients were medicated with olanzapine. The follow-up measurements were done one week (T1) and again two weeks (T2) after starting the medication. Only Caucasian subjects were chosen to participate due to the somewhat culture-specific content of the presented pictures from the International Affective Picture System (IAPS, Lang, 1993). The normal controls had never suffered from any psychiatric illness, had no family history of psychiatric disturbances and had not received any medications for at least three months (for sample characteristics see Table 1).

The medication with olanzapine was dosed according to clinical needs and ranged from 7.5–20 mg. The mean dosage at T1 was 11.5 mg (SD 3.85), and 12.6 mg (SD 4.03) at T2. The study was approved by the local ethics committee of Hamburg and written informed consent was obtained from all participants prior to the study.

Induction of Emotions

All subjects were tested under video observation in an electrically shielded, soundproof chamber with reduced light, sitting in a comfortable chair. All tests were scheduled between 1 p.m. and 3 p.m. Subjects were allowed to adapt to the surroundings in the room for 30 minutes prior to testing,

Table 1. Sample Characteristics

	OLA Schizophrenic Patients (N = 15)	**CON Healthy Controls (N = 19)**
Age in years, mean (SD)	28.44 (5.3)	25.23 (3.19)
Males, N (%)	9 (60.0%)	12 (63.1%)
Females, N (%)	6 (40.0%)	7 (36.9%)
Educational level	No school degree, N = 1 (6.6%) elementary school, N = 5 (33.3%) middle school, N = 3 (20.0%) high school[1], N = 6 (40.0%)	high school[1], N = 19 (100%)
Diagnosis DSM-IV	295	-
Number of psychiatric admissions, mean (SD)	1.5 (1.6)	-
Duration of illness[2] (years), mean (SD)	3.4 (4.1)	-

[1]qualifying for entrance to university
[2]age at time of investigation minus age at first prodromal sign

while they were asked about their present psychosocial situation. Afterwards the patients and the healthy subjects were exposed to slides with neutral, joyful, and sad stimuli. The exposure time (10 sec per picture) was controlled electronically. The first picture before showing the stimulating slides was a gray-colored baseline-picture, presented for 2 minutes, inducing a relaxed psychophysiological state.
For testing, eleven pictures were chosen from the IAPS, with different series for women and men in order to acknowledge sexual preferences. Each picture was preceded by a gray-colored baseline-picture (presentation time 15 sec.). Two neutral pictures were followed by a picture of flowers and a picture of a landscape, expecting the emotion of relaxed joy. Then an erotic picture of a single person was presented, followed by an erotic picture of a couple, expecting the emotions of joy plus arousal, based on the results of the IAPS research by Lang. After showing two pictures - one depicting a family and the second one showing a child - one picture with sad content was presented as a control picture. Finally, the landscape picture and the erotic picture of a single person were presented again. The results are based on the analysis of the fifth of the eleven pictures. The fifth picture is the erotic picture of a single person, which was presented in different versions during the trial: IAPS No. 8041 (T0), No. 4510 (T1), No. 4533 (T2) for women and IAPS No. 4180 (T0), No. 4210 (T1), No. 4220 (T2) for men. We chose these pictures because – based on the studies of Lang (1993) – they are expected to trigger a higher emotional response and facial muscle activation than funny pictures or smiling faces. In choosing a small sample size we hoped to reach significant results sooner with this kind of picture than we would have been able to achieve with other pictures.

EMG Measures

We used a modified EMG device, based on the Varioport™ system (Becker MEDITEC™, Karlsruhe, Germany), without interference between muscles, which allows a sufficient discrimination even between facial muscles close to one another. Bipolar EMG recordings were taken from the left M. frontalis medialis, M. corrugator supercilii, M. orbicularis oculi, M. levator labii and M. zygomaticus region on the face, using Hellige miniature surface Ag/AgCl electrodes (internal diameter 0.6 cm) filled with Med-Tek/Synapse conductive electrode cream. Electrodes were placed according to the recommendations of Fridlund and Cacioppo (1986) (Pic.1).The inter-electrode distances were 12 mm. Skin was prepared by abrasion with 70% clinical alcohol first, followed by Hellige Epicont abrasive skin preparation cream. The electrodes were connected to Becker MEDITEC™ amplifiers, the raw EMG signal was analyzed automatically by a two channel contour-following integrator (Becker MEDITEC™, Karlsruhe, Germany). The frequency range (-3dB) was 90-500 Hz with a time constant of 0.0018s. The amplification factor was 5000 (+/-2%), CMRR (Common Mode Rejection Ratio) 77dB at 50 Hz, time constant of integrator 0.1s, range +/- 250μV, resolution of AD-Converter 12 Bit (= 4096 steps), resolution of signal 0.122μV per step. The input impedance is theoretically 1Gohm, but due to our cable capacities it is about 500Mohm at 50Hz. The sampling rate was 32 Hz. The output signals were recorded and stored in computer files (Variograph™ software on a Macintosh Power book, Becker MEDITEC™, Karlsruhe, Germany) for off-line analysis. With the help of video recordings, the complete EMG data were screened for artifacts like eye blinking. Artifacts were interpolated with the Variograph™ software.

Psychopathologic symptoms

The patient's psychopathological status was determined with the Positive and Negative Syndrome Scale (Kay et al., 1987). The extrapyramidal side effects were calculated with the Simpson-Angus rating scale (Simpson et al., 1970). Factor analysis (Mass et al., 2000) yielded five PANSS syndromes: positive syndrome (POS; PANSS items P1, P3, G9), negative syndrome (NEG; N4, N2, N1, N3, G16, N6), cognitive syndrome (COG; N5, G11, P2), depression (DEP; G6, G2, G3), and hostile excitement (EXC;P7, P4, G14, G4, G8, P5, G5). For the present analyses, we considered the depression syndrome only.

Statistical Analyses

As our EMG baseline value we established the average of the measures obtained during the last 3 sec of the 15 sec presentation of the gray-colored picture, which was shown before each IAPS stimulus. As a trial phase we used the 10-sec presentation of the IAPS stimulus.

A facial muscle reaction was defined as an increase in mean muscular voltage during the trial (i.e. picture exposure). The increase had to be greater than the mean value of the preceding baseline plus two baseline standard deviations. A smile response was defined as a reaction of the M. zygomaticus major alone or in combination with a reaction of M. levator labii and/or M. orbicularis oculi.

To calculate changes of facial muscle activity we determined the difference between mean voltage observed during the trial and mean voltage observed during baseline.

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), Version 10.08 for Macintosh. Baseline-to-trial changes of muscular activity (averaged mean) were tested with the Wilcoxon test for both groups and within the groups, separately for each muscle. Group differences of smile response frequencies were tested with Chi-Square tests. To examine the relationship between facial muscular reactions and psychopathologic symptoms, parametric correlation coefficients (r_{xy}) were calculated for the schizophrenic patients. A repeated measures ANOVA was conducted with the five PANSS syndrome scores of the schizophrenia group. Hypothesis testing was two-tailed.

Table 2. Muscle activities for each muscle over the schizophrenics (SCH) and the controls (CON) at T0, unmedicated (Wilcoxon tests). After Bonferroni correction, only the decrease of M. frontalis and the increase of M. orbicularis of the CON group would remain significant

	SCH (n=15)			CON (n=19)		
	Median of baseline means (mV)	Median of trial means (mV)	Z	Median of baseline means (mV)	Median of trial means (mV)	Z (p)
M. frontalis	4.41	3.85	-0.114	5.56	5.21	-2.777 * (.005)
M. corrugator	3.39	3.43	-0.966	2.64	2.56	-2.299 (ns)
M. orbicularis	-0.10	-0.07	-1.704	0.13	1.15	-2.696* (.007)
M. levator	4.33	3.70	-1.079	2.48	2.55	-1.938 (ns)
M. zygomaticus	0.53	0.31	-0.454	0.58	2.98	-2.045 * (.011)

*: p < .05 (asymp. significance, 2-tailed)

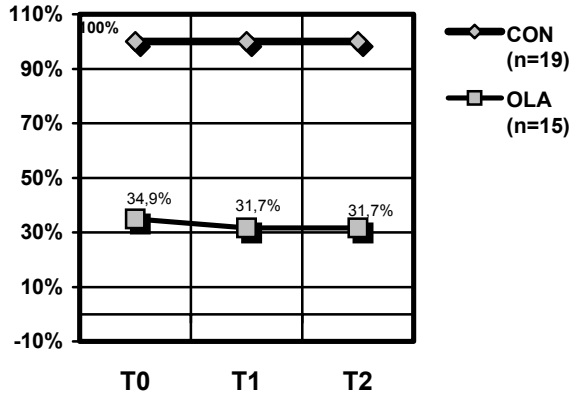
Results

Unmedicated schizophrenic patients show a less pronounced smile response in comparison to healthy subjects. Table 2 shows the muscle reactions after presentation of erotic stimuli. While control subjects showed a significant decrease in the activity of the "fear muscle" M. frontalis, there was no significant change in unmedicated schizophrenics. Control subjects show a significant increase in activity of the two "smile muscles" M.orbicularis and M.zygomaticus. In comparison, schizophrenics only show a significant increase in activity of the M.orbicularis. Control subjects and unmedicated schizophrenics showed no activation of the "disgust muscle" M. levator labii sup. or the M. corrugator, representing negative emotions in general and used as a control picture.

Figure 1 shows the smile frequency of the healthy controls group vs. olanzapine group at T0, at T1 (after one week of medication with olanzapine) and at T2 (after two weeks of medication with olanzapine). Setting the healthy groups smile frequency as 100 %, only 34.9 % of the unmedicated olanzapine patients show a relative smile response at T0. Compared to the healthy controls group, olanzapine shows a parallel course of smile frequency (34.9% at T0 and each 31.7% at T1 and T2).

The analysis of variance for the PANSS depression syndrome showed no significant correlations to the changes of FEE.

Figure 1. Smile frequency of controls (CON) set as 100% vs. relative smile frequency of olanzapine (OLA) at T0 (unmedicated), T1 (1 week of medication), T2 (2 weeks of medication). (Fisher's exact test, 2-tailed of CON vs. OLA at T0: p=0.029, T1: p=0.128, T3: p=0.128; X^2 tests of CON vs. OLA at T0 4.97, df=1, p=.026; at T1 and T2 3.342, df=1, p=0.068)



Discussion

This is the first study simultaneously measuring pre-visible activities of five muscles (M. frontalis, M. corrugator supercilii, M. orbicularis oculi, M. levator labii, M. zygomaticus).

Two of these five muscles, M. orbicularis and M. zygomaticus, are important role-players in schizophrenic mimic disturbances. M. frontalis is known as a "fear muscle", M. corrugator is used as a control muscle - representing negative emotions - which should not become active when erotic pictures are presented. M. levator is a "disgust muscle", shown to be activated in unmedicated schizophrenic patients (Steimer-Krause 1990). In contrast to the measurement of visible muscle activity with the video-based FACS (Ekman & Friesen 1978) or microcomputer-based methods (Katsikitis 1990, Pilowsky & Katsikitis 1994, Thornton et al. 1982) our method allows a significantly better differentiating analysis using a standardized induction method like the IAPS.

Our EMG device shows a compatible sensitivity, while not allowing interference from facial muscles activated nearby.

The major results are: Unmedicated patients show a lower activation of the two 'felt smile' muscles M.orbicularis and M.zygomaticus and an overall lower smile frequency than healthy subjects. At T0 healthy subjects show a decrease of activity in the M.frontalis, which is known as a main fear muscle. This decrease can be seen as a sign of relaxation. Unmedicated schizophrenics do not show this particular muscle relaxation. In contrast to the results of Steimer-Krause (1990), unmedicated schizophrenic patients do not show an activation of the "disgust muscle" M. levator labii. Neither subject controls nor schizophrenic patients show an activation of the M. corrugator. This is concurrent with our expectation.

The atypical NL olanzapine does not change the relative FEE in schizophrenic patients over two weeks of treatment (Fig.1). This is an important finding, since we know from a study by Schneider (1992) that typical NL reduce FEE and smile frequency.

The changes in smile frequency during olanzapine are neither significantly correlated with changes in the PANSS depression syndrome, nor with the EPS.

To understand these results in depth, it will be necessary to collect larger samples and to include groups with typical and with other atypical NL. Our present results demonstrate the necessity for further studies in schizophrenic patients. These should include the analysis of nine or more muscles in order to be able to distinguish between different basic emotions. We suggest the use of a highly sensitive EMG method and standardized emotion induction methods like the IAPS. This will help us to find out more about the influence of different atypical NL on FEE and to establish the beneficial effects of NL on FEE as a new criteria of quality.

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