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Short communication

Deeper than skin deep – The effect of botulinum toxin-A on emotion processing

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ABSTRACT

The effect of facial botulinum Toxin-A (BTX) injections on the processing of emotional stimuli was investigated. The hypothesis, that BTX would interfere with processing of slightly emotional stimuli and less with very emotional or neutral stimuli, was largely confirmed. BTX-users rated slightly emotional sentences and facial expressions, but not very emotional or neutral ones, as less emotional after the treatment. Furthermore, they became slower at categorizing slightly emotional facial expressions under time pressure.

It is difficult to imagine today's aesthetics medicine industry without the use of BTX as a treatment of facial wrinkles. But recent indications suggest that the effects BTX injections into facial mimetic muscles may go well beyond that of a cosmetic one and also have the potential to affect our emotional state (e.g. Kruger and Wollmer, 2015) and perception of emotional stimuli (e.g. Davis et al., 2011; Havas et al., 2010). Within the concept of embodied emotions, proprioceptive facial feedback supports the experience and comprehension of emotions (e.g., Niedenthal, 2007). The interruption of this feedback in healthy populations has been associated with impaired processing of emotional sentences, words, or facial expressions (Baumeister et al., 2015; Foroni and Semin, 2009; Havas et al., 2010; Korb et al., 2014; Niedenthal et al., 2009; Oberman et al., 2007).

The paralyzing effect of BTX could lead to similar effects interrupting the feedback loop from the face. Even though this may be beneficial in treating depression (see Kruger and Wollmer, 2015 for a review), the possible downside effects in healthy populations maybe detrimental in our daily lives where recognizing emotional states and understanding emotional content is a fundamental competence. Yet, so far evidence is vague, as studies showed that modulations in facial feedback do not necessarily affect the interpretation of emotional stimuli (Blairy et al., 1999; Fischer et al., 2012; Kim et al., 2014). One possible factor never systematically investigated, that could modulate the disruptive effect of BTX-injection in emotion perception, is the emotional intensity of the stimulus material. In line with this idea, it was found that BTX-blocked mimetic muscles did not alter participants' perception of very emotional video clips but instead weakened the perception of slightly emotion ones (Davis et al., 2011), originally introduced as control stimuli. This finding overlaps with other coincidental finding that stimuli low in emotional intensity or difficult to encode were particularly affected by any interruptions of the facial-feedback loop (Maringer et al., 2011; Oberman et al., 2007). It is therefore crucial to fully understand the significances of facial BTX treatments on emotion processing of different intensity and, thus, also reconciling previous conflicting results.

The present study aimed at bridging this gap by assessing the speed and quality with which BTX-users judge slightly emotional (SE) and very emotional (VE) stimuli before and two weeks after treatment. The SE stimuli consisted of slightly sad (S-SAD) and slightly happy (S-HAP) stimuli. Likewise the VE stimuli consisted of very sad (V-SAD), and very happy (V-HAP). Neutral (N) stimuli were added for control purposes. Participants were eleven healthy native Italian-speaking females (mean age 52.3, range 35–66), who received for the first time cosmetic BTX-injections into the glabellar

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region, including the corrugator and procerus muscles (involved in frowning, pulling eyebrows together or downwards, respectively) and into the orbicularis oculi muscles (lateral to the eyes and involved in producing laugh lines). Two participants received only injections into the corrugator/procerus muscles but not in the orbicularis oculi muscle. The obtained paralysis was intentionally not complete in order to obtain a more natural appearance in facial expressions. One BTX participant was excluded from all analyses because she had been unintentionally informed about the study hypothesis by the hospital staff prior to session two. Further 11 age-matched (mean = 50.3, range = 34–60) female participants, who had never received any BTX-injections served as the control (CTR) group. All participants gave written informed consent for the participation. Participants were tested 2 times: before their BTX-treatment and two weeks later when the BTX had unfold its full effect. Each time, participants conducted three tasks: 1) Rating the emotional intensity of emotional sentences ("sentences rating task"); 2) rating emotional intensity of facial expressions ("faces rating task"); 3) Categorization of facial expression into "sad" and "happy" under time pressure ("Reaction time task (RT-task)"). For two BTX participants, no data for the RT-task were available. The tasks and stimuli are described in Fig. 1. The procedure was the same for the CTR group, except that they did not receive any BTX injections.

We expected that if facial feedback specifically supports the processing of SE stimuli, then after a BTX-treatment there should be a decrease in emotionality for SE stimuli but not (or less so) for VE stimuli. No effect was expected for N stimuli. Similarly, when categorizing facial expressions, RTs should increase after BTX-treatment for SE but less so for VE stimuli.

1. Data preparation for the ratings tasks

For the analyses of the two rating tasks all data were cleaned by removing extremes (i.e., values more than 2.5 SD) from the average rating for each stimulus, within group and session. The original scale from 0 (very sad) – 100 (very happy) was transformed to reflect emotional intensity ratings regardless of emotion type by subtracting 50 from the original rating score and calculating its absolute value. The new scaling from 0 to 50 (neutral-slightly-very emotional) allowed better comparability of the hypothesized general effect across emotions. Separately for each time point (T1 & T2), the averaged ratings were calculated for both S-HAP and S-SAD stimuli and for V-HAP and V-SAD and then averaged to obtain respectively SE and VE scores. Averaged scores were used for the analyses. Control analyses for mood and affect ensured that the results were not influenced by these factors (see the Supplementary Material for the full analysis).

2. Results of the sentences rating task

A 2(*group*: BTX vs. CTR) X 2(*time*: T1 vs. T2) X 3 (*emotionality*: N vs. SE vs. VE) mixed-measures-ANOVA (first factor between-subjects and the others within-subjects), revealed, as the most important finding, an interaction between *emotionality*, *time*, and *group* ($F(2,38) = 4.62$, $p = 0.02$, $\eta^2_p = 0.20$), see Fig. 2. Two repeated measures-ANOVAs 2 (*time*: T1 vs. T2) X 3 (*emotionality*: N vs. SE vs. VE) for each group separately resulted in a significant interaction within the BTX group ($F(2,18) = 7.04$, $p < 0.01$; $\eta^2_p = 0.44$), confirming a differential change in emotionality ratings across time, while the CTR-group showed no change ($F = 1.4$, $p = 0.26$). Follow-up paired-samples *t*-tests, indicated that the BTX-group showed a significant drop in emotionality only for SE sentences ($t(9) = 3.97$, $p < 0.01$, *Cohen's d* = 1.14) and not for VE ($t(9) = 1.98$, $p = 0.08$, *Cohen's* d = 0.72) and N ($t(9) = 1.33$, $p = 0.21$) sentences. A paired-sample *t*-test comparing the proportional difference scores (calculated with the formula: [(T2-Rating − T1-Rating)]/[((T1-Rating + T2-Rating)/2)]) for SE ($M = 0.50$, $SD = 0.27$) and VE sentences ($M = 0.18$, $SD = 0.16$) confirmed that the SE drop was significantly larger than the one of VE ($t(9) = 3.51$, $p < 0.01$, *Cohen's d* = 1.44). Additional pairwise comparisons confirmed that the effect was present for both S-HAP and S-SAD stimuli ($ts(9) > 2.00$, $ps < 0.05$); see Supplementary Material for full details on the analyses on the effect of BTX on specific emotions.

3. Results of the faces rating task

The same analysis routine described for sentences was applied here. This time the interaction between *time*, *emotionality*, and *group* did not reach significance ($F(2,38) = 16.91$, $p = 0.13$, $\eta^2_p = 0.10$). That this effect was weaker than the effect observed for the sentences, may be due to the larger differences in emotionality ratings between the SE and VE sentences in comparison with the less extreme ratings for SE and VE facial stimuli (see Fig. 1). Due to the a priori interest, the faces rating analysis was continued with 2 separate ANOVAs for BTX and CTR group, which resulted in a marginally significant interaction within BTX-group ($F(2,18) = 3.00$, $p = 0.08$, $\eta^2_p = 0.25$) and no interaction within CTR ($Fs > 0.40$, $p = 0.53$; see Fig. 2). Follow-up paired-sample *t*-test within BTX-group showed a significant drop in emotionality ratings of SE faces after BTX-treatment ($t(9) = 3.27$, $p = 0.01$, *Cohen's d* = 1.22), while ratings of the N stimuli ($t(9) = 1.39$, $p = 0.20$) did not change and those of VE changed only marginally ($t(9) = 2.1$, $p = 0.06$, *Cohen's d* = 0.40). A paired-samples *t*-test using the proportional difference scores confirmed that the drop in perceived emotionality of SE expressions ($M = 0.53$, $SD = 0.34$) was significantly stronger ($t(9) = 3.2$, $p = 0.01$, *Cohen's d* = 1.19) than the decrease observed for VE ($M = 0.22$, $SD = 0.14$). Two pairwise comparisons confirmed that the effect was present for both S-Hap and S-Sad stimuli ($ts(9) > 2.55$, $ps < 0.05$, see Supplementary Material for full description).

4. Results of the RT task

Only correct trials were considered (leaving 90% of data for BTX-group and 92% for CTR-group). Trials with a RT more than 2.5 SD away from the mean for each participant within each emotion condition and a given time point (T1, T2) were excluded (affecting 5.6% of data from BTX-group and 4.5% from CTR-group). Log-transformed RTs were analysed with a 2 (*group*: BTX vs. CTR) X 2 (*time*: T1 vs. T2) X 2 (*emotionality*: SE vs. VE) ANOVA (first factor between-subjects and the others within-subjects). The 3-way interaction showed a slight trend ($F(1,17) = 2.00$, $p = 0.14$, $\eta^2_p = 0.10$). Due to the a priori interest in the effect of time on emotionality within each group, two separate 2 (*time*: T1 vs. T2) X 2 (*emotionality*: SE vs. VE) ANOVAs were conducted. The two-way interaction was significant for the BTX-group ($F(1,7) = 13.90$, $p < 0.01$, $\eta^2_p = 0.67$) but not for the CTR-group ($F = 2.00$, $p = 0.18$), suggesting that only the BTX-group showed a differential rating pattern across times (see Fig. 2). Follow-up paired-sample *t*-tests within the BTX-group, revealed a significant slowing in RTs from T1 to T2 for both SE ($t(7) = 4.66$, $p < 0.01$, *Cohen's d* = 1.63) and VE stimuli ($t(7) = 3.46$, $p = 0.011$, *Cohen's d* = 1.20). Yet, pairwise-comparisons of the proportional differences (calculated with the formula [(T2-RTs − T1-RTs)]/[((T1-RTs + T2-RTs)/2)]) confirmed that the slowing from T1 to T2 was significantly larger for the SE stimuli than for the VE stimuli ($t(7) = 3.76$, $p < 0.01$, *Cohen's d* = 1.26). Two pairwise comparisons indicated a strong slowing in response to S-SAD facial expressions ($t(7) = 4.25$, $p < 0.01$) and only a marginal one for S-HAP facial expressions ($t(7) = 2.04$, $p = 0.08$;