Biological Psychology 108 (2015) 78–84

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Electrocortical effects of a disgust placebo in children

Sonja Übel, Verena Leutgeb, Anne Schienle*

University of Graz, Department of Clinical Psychology, Universitätsplatz 2/III, A-8010 Graz, Austria

ARTICLE INFO

Article history:
Received 21 July 2014
Accepted 22 March 2015
Available online 28 March 2015

Keywords:
Placebo
Disgust
Children
ERP
LPP
Affective pictures

ABSTRACT

The electroencephalogram has been widely used to study voluntary emotion regulation (ER), whereas automatic ER has hardly been investigated. This experiment focused on automatic changes of disgust feelings and event-related potentials due to placebo treatment. Twenty-eight disgust-prone 8- to 13-year-old girls were presented with disgusting, fear-eliciting and neutral pictures once with and once without a placebo (syrup presented with the suggestion that it is able to ease disgust symptoms). In the disgust condition, the placebo reduced experienced disgust and increased frontal late positivity (400–1000 ms after picture onset). A similar electrocortical placebo effect was obtained for the fear pictures. These findings suggest that the placebo had the function of a safety signal which helped the children to direct their automatic attention to the aversive stimuli and to overcome visual avoidance. Future studies should integrate behavioral designs and should use additional psychophysiological measures (e.g., eye-tracking) in order to substantiate this interpretation.

1. Introduction

Placebo is the Latin word for "I shall please". A placebo agent or procedure is per definition inert but mimics active treatment within a psychosocial context. Two important contextual factors which mediate the placebo response are learning experiences (classical conditioning, social learning), and expectations about clinical improvement, which are mostly generated via verbal suggestions (Benedetti, Mayberg, Wager, Stohler, & Zubieta, 2005).

Especially beliefs concerning symptom reduction play an important role for the magnitude of the placebo effect. It is of crucial importance that one is convinced that the received placebo will produce specific positive changes of the treated condition (Price, Finniss, & Benedetti, 2008). Several authors have suggested that expectation-mediated placebo effects are based on self-regulatory processes (e.g., Benedetti et al., 2005; Wager, 2005). Interestingly, the most commonly studied placebo effect in neuroimaging investigations, placebo analgesia, was consistently associated with activation of prefrontal cortex areas involved in emotion regulation (e.g., dorsolateral prefrontal, orbitofrontal, anterior cingulate cortex, for a review see Benedetti et al., 2005; Meissner et al., 2011). Participants with larger activation increases in these regions showed greater placebo-induced reductions in pain (Wager, 2005). The observed prefrontal activation associated with placebo treatment suggests that placebo responses have an evaluative component. Moerman and Jonas (2002) introduced the term 'meaning response' in this context in order to underscore the importance of patients' beliefs and meaning-induced expectations about the treatment. In the same vein, Ochsner and Gross (2007) defined the placebo effect in the framework of emotion regulation (ER) as 'mentally redescribing the meaning of a stimulus' (p. 98).

The mentioned authors and others have extensively studied the effects of the voluntary reinterpretation of the meaning of aversive visual stimuli. This type of emotion regulation is termed cognitive reappraisal, which asks a person to reevaluate an event so as to alter its emotional impact. Another voluntary ER strategy consists of attention deployment, i.e. directing attention away from aversive stimuli (Gross & Thompson, 2007).

Both strategies (reappraisal and distraction) can not only be applied consciously, but also unintentionally and automatically. Mauss, Bunge, and Gross (2007) defined automatic ER as goal-driven change to any aspect of one's own affective state without making a conscious decision to do so, without engaging in deliberate control, and without paying attention to the process of ER. This type of ER might be central for placebo responding. Interestingly, there are hardly any placebo studies focusing on the automatic modulation of emotional experience outside the pain context. An exception is a functional magnetic resonance imaging (fMRI) experiment by Schienle, Übel, Schöngassner, Ille, and Scharmüller (2014a), who investigated whether a placebo can change disgust feelings. Disgust-prone women underwent a retest

* Corresponding author. Tel.: +43 316 380 5086; fax: +43 316 380 9808.
E-mail addresses: sonja.uebel@uni-graz.at (S. Übel), verena.leutgeb@uni-graz.at (V. Leutgeb), anne.schienle@uni-graz.at (A. Schienle).

http://dx.doi.org/10.1016/j.biopsycho.2015.03.015
0301-0511/

design during which they were presented with disgusting, fear-eliciting and neutral pictures once with and once without a placebo (inert pill presented with the suggestion that it can reduce disgust symptoms). The 'disgust placebo' provoked a strong decrease of experienced disgust, which was accompanied by reduced insula activation during the presentation of disgusting pictures. Moreover, the placebo increased inter-regional amygdala–dorsomedial prefrontal cortex (DMPFC) connectivity, which possibly constitutes the neural mechanism of successful automatic ER via placebo.

The mentioned investigation used fMRI, which has a good spatial resolution. However, other neurobiological methods, such as the electroencephalogram (EEG), have an excellent temporal resolution which makes them a very promising tool to study placebo-induced emotion regulation. Up until now EEG investigations have mainly analyzed effects of conscious ER. A multitude of studies demonstrated that distraction, as well as reappraisal, are able to reduce late positivity during the viewing of aversive stimuli (e.g., Foti & Hajcak, 2008; Moser, Hajcak, Bukay, & Simons, 2006; Thiruchselvam, Blechert, Sheppes, Rydstrom, & Gross, 2011). The late positive potential (LPP), which is maximal across parietal recording sites, is sensitive to emotion modulation processes in a time window ranging from 300 ms until several hundred milliseconds after picture presentation onset. The LPP is considered a neuronal marker reflecting facilitated attention to emotional stimuli and reevaluation (for a review see Olofsson, Nordin, Sequeira, & Polich, 2008).

ERP studies on affective placebo effects are rare. Zhang and Luo (2009) conducted an ERP study where they looked at both pain-associated and affective effects of a placebo. The ratings of the presented aversive pictures (e.g., spiders, snakes) were significantly lower in the placebo condition than in the control condition, which was accompanied by increased N200 and decreased P200 amplitudes. The authors suggested that the placebo-induced electrocortical changes reflect increased positive valence (N200) and attention deployment (P200).

In the present study we investigated whether the electrophysiological response to disgusting stimuli can be changed by unintentionally modulating one's own emotional reaction. Based on a previous fMRI experiment (Schienle et al., 2014a; Schienle, Übel, & Scharmüller, 2014b), we attempted to replicate that a "disgust placebo" is able to change the disgust experience as well as the brain activation during visual emotion elicitation in healthy disgust-prone girls. The majority of placebo studies have been conducted with adult participants. Very little is known about placebo effects in children. Several reviews and meta-analyses concluded that the placebo response is stronger in children and adolescents relative to adults (Cohen et al., 2008; Weimer et al., 2013). We expected that in the placebo condition (relative to a no-placebo condition) the children would report less intense disgust feelings and would show altered ERP amplitudes of the N200, and P200 as well as reduced LPP amplitudes for disgusting (but not for fear-eliciting) stimuli.

2. Method

2.1. Participants

Thirty right-handed and non-medicated girls aged from 8 to 13 years ($M = 10.5$, $SD = 1.3$) participated in the current investigation. Data from two subjects were excluded due to poor quality of the EEG recording. Thus, the final sample was comprised of 28 children. Participants were recruited via announcements at the campus and were free from mental disorders, medication, and somatic problems. The sample was restricted to females as there are significant sex differences in disgust proneness (Schienle et al., 2002a). Only those children who had reported above-average disgust proneness were invited to participate in the study in order to ensure sufficient reactivity to the disgust stimuli. All girls and their caregivers gave written informed consent after the nature of the study had been explained to them. The study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of the University of Graz. None of the children had previously participated in a drug study.

2.2. Questionnaires and interviews

The participants completed the 'Questionnaire for the assessment of disgust propensity in children (QADP-C; Schienle & Rohrmann, 2012). The QADP-C consists of 16 items (e.g., 'You are biting into a grilled grasshopper'; 'A kid with bad breath speaks to you'), which have to be judged on 5-point scales (0 = 'not disgusting'; 4 = 'very disgusting') with two disgust dimensions labeled core disgust (e.g., 'aversion to spoiled food and poor hygiene'; 8 items, Cronbach's $\alpha = .86$) and death disgust (e.g., 'imagined contact with dead and dying organisms'; 8 items, Cronbach's $\alpha = .83$). The Cronbach's α of the total scale is .88. Furthermore, the girls filled out the trait-scale of the State-Trait Anxiety Inventory for Children (STAI-C, Spielberger, Edwards, Lushene, Montouri, & Platzek, 1973). The questionnaire is widely used to assess trait anxiety. Twenty items have be judged on a three-point scale (1 = 'hardly ever'; 3 = 'often'). The Cronbach's α for the trait scale is .89.

To ensure the absence of mental disorders a standardized clinical interview for children and their caregivers (Unnewehr, Schneider, & Margraf, 1995; children and parent version) was conducted.

2.3. Pictures and design

The participants were presented with 45 affective pictures representing the three categories disgust (e.g., dirty toilet, animal corpse, maggots), fear (e.g., human and animal threat, car accidents), and neutral (e.g., household objects, geometric figures). Each category consisted of 15 images which had been selected from the International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 1999) and from our own picture set (Schienle et al., 2002b; disgust: 2 IAPS/13 Schienle; fear: 13 IAPS/2 Schienle; neutral: 7 IAPS/8 Schienle[1]). As a control condition for disgust we used threatening images, which are also motivationally salient (e.g., Schupp et al., 2004). The presentation sequence of the stimuli was randomized and repeated twice (30 events per category). The whole task consisted of 90 trials. Each scene was presented for 4000 ms and the inter-stimulus interval varied between 3500 and 5000 ms. The girls were instructed to passively view the pictures during the presentation.

2.4. Procedure

The experiment consisted of two EEG sessions (separated by one day). The participants passively viewed the pictures once with and once without the placebo. The sequence of the two sessions was random. In the placebo condition the girls received a placebo syrup, which was dropped on their tongue with a pipette. The syrup (20 ml apricot syrup) had been filled into a bottle of an original pain reliever (fever reducer) for children with a new label ('Indian syrup'). We chose a sweet substance as the medication for children usually contains sweet additives.

The participants were told, that the syrup consists of seven different herbs (Indian melissa, primrose, water-mint, speedwell, gentian, ginger, and wormwood), and is called 'Indian syrup'. This name reflects that the Native Americans have used this herbal medicine for a long time to become strong and healthy. Further they were informed that a previous investigation had already demonstrated that this herbal medicine effectively reduces disgust symptoms and that the positive effect occurs very quickly (approximately 5 min after the application). Thus, the cover story suggested a clinical trial of an herbal medicine. The syrup was administered approximately 15 min before the EEG experiment with the picture viewing.

Subsequent to the EEG sessions, participants were asked to rate their impression of the pictures by means of the Self-Assessment Manikin (SAM; Bradley & Lang, 1994) for 'valence' and 'arousal', and on two 9-point Likert scales for the dimensions 'disgust' and 'fear' (range 1–9, with '9' indicating that the subject felt very positive, aroused, anxious and disgusted). At the end of the placebo condition, the participants were asked whether they were convinced that they had received the syrup or a placebo (yes/no) and rated the perceived effectiveness of the treatment (1 = not at all; 9 = very effective).

The experimenter wore a white coat during the conduction of the study in order to enhance the credibility of the cover story.

2.5. Electrophysiological recordings and data analyses

The electroencephalogram (EEG) was recorded with a Brain Amp 32 system (Brain Products, Munich) and an Easy-Cap Ag/AgCl electrode system (Falk Minow Services, Munich) from 22 sites (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T7, T8, P3, P4, P7, P8, O1, O2, Fz, Cz, Pz, POz, Tp9, Tp10). The reference was placed at FCz. AFz was used

[1] The numbers of the IAPS pictures (Lang et al., 1999) used were: disgust (34, 9140), fear (1300, 3500, 3530, 6212, 6230, 6312, 6350, 6370, 6510, 6540, 6940, 9910, 9921), and neutral (5395, 7096, 7160, 7185, 7205, 7211, 7491). Thirteen disgust, two fear, and eight neutral pictures were taken from validated picture sets from Schienle et al. (2002b).