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Prospective study of nocebo effects related to symptoms of idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF)

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ABSTRACT

The exact causes of Idiopathic Environmental Intolerance Attributed to Electromagnetic Fields (IEI-EMF, i.e., experience of somatic symptoms attributed to low-level electromagnetic fields) are still unknown. Psychological causation such as nocebo effects seem plausible. This study aimed to experimentally induce a nocebo effect for somatic symptom perception and examined whether it was reproducible after one week. We also examined whether these effects were associated with increased sympathetic activity and whether interoceptive accuracy (IAcc) moderated these relationships. Participants were recruited from the general population and instructed that electromagnetic exposure can enhance somatosensory perception. They participated twice in a cued exposure experiment with tactile stimulation and sham WiFi exposure in 50% of trials. The two sessions were scheduled one week apart (session 1: $N = 65$, session 2: $N = 63$). Before session 1, participants watched either a 6-min film on adverse health effects of EMF or a neutral film on trade of mobile phones. IAcc was assessed with the heartbeat detection paradigm. Electrodermal activity served as a measure of sympathetic activation. Evidence for a nocebo effect (i.e., increased self-reported intensity and aversiveness and electrodermal activity) during sham WiFi exposure was observed in both sessions. IAcc moderated the nocebo effect, depending on stimulus intensity. Contrary to previous findings, no difference emerged between the health-related EMF and the neutral films. Based on negative instructions, somatic perception and physiological responding can be altered. This is consistent with the assumption that IEI-EMF could be due to nocebo effects, suggesting an important role for psychological interventions.

1. Introduction

Individuals with idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) experience various medically unexplained symptoms (e.g., paresthesia, headache, dizziness), which they attribute to exposure to weak electromagnetic fields emitted by electrical devices like mobile phones, WiFi routers, and similar devices (Baliatsas et al., 2012). Although the prevalence of IEI-EMF is considerable (on average 6% across nine countries; Huang et al., 2018) and the strain on affected individuals is severe (Baliatsas et al., 2014; Kjellqvist et al., 2016), treatment options remain limited, since the underlying cause of the condition has not been conclusively determined.

Accumulating evidence suggests that psychological mechanisms, like misattribution of bodily symptoms (Dieudonne, 2016; Dieudonné, 2019) and nocebo effects based on negative expectations as well as learning experiences (Webster et al., 2016) rather than bio-electromagnetic processes might contribute to the development of IEI-EMF (Roosli, 2008; Roosli et al., 2010; Rubin et al., 2010). Recently, an integrative model for the aetiopathogenesis of IEI, including IEI-EMF has been proposed (Van den Bergh et al., 2017a). This model relies on predictive processing to understand how perception can diverge from actual sensory input. The brain constructs perceptual experiences out of generated prior beliefs on the one hand and actual sensory input on the other hand across multiple hierarchical levels. Depending on the relative reliability (precision) of the prior beliefs and the actual sensory input, the eventual percept can be closer to the prior beliefs than to actual input. Because interoception (perception of sensory signals from inside the body) has been shown to highly depend on prior expectations (Barrett and Simmons, 2015), it follows that the experience of symptoms can emerge as a result of imprecise bodily sensations interacting with

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highly precise prior beliefs about symptoms. In extreme cases, sensory input may not be present at all. According to this model, symptoms may emerge in response to specific environmental stimuli (e.g., WiFi router, mobile phones) as a result of strong (highly precise) prior beliefs that particular sources of EMF are dangerous and health damaging. These latter beliefs may in turn develop from the experience of actual or perceived contingencies (associative conditioning) between symptom episodes from whatever cause (see Van den Bergh et al., 2017a) and EMF-sources, and/or vicarious, informational experiences linking health complaints to EMF, qualifying the latter as health damaging. Several personality characteristics have been proposed as potential moderators of symptom generation, including interoceptive accuracy, trait negative affectivity, and gender (Van den Bergh et al., 2017a; Van den Bergh et al., 2017b).

In a previous study, we showed that watching a short film on adverse health effects of EMF can enhance the perception of tactile stimuli during sham WiFi exposure and increase worries concerning EMF in healthy participants (Bräscher et al., 2017). The results of this and other studies (Eltiti et al., 2018; Schweiger and Parducci, 1981; Szemerszky et al., 2010; Verrender et al., 2018; Witthöft and Rubin, 2013) suggest that nocebo effects might play a role in the development of IEI-EMF. To truly describe a potential aetiological pathway for the development of IEI-EMF, the induced nocebo effects should generalize beyond and outside the lab situation, but so far, no study has provided evidence supporting this hypothesis. In addition, physiological correlates of the nocebo effect in the context of IEI-EMF have rarely been investigated. One such study focused on neurobiological correlates using functional magnetic resonance imaging (Landgrebe et al., 2008) and showed increased activation in the anterior cingulate and insular cortex in electrosensitive compared to healthy participants during sham mobile phone radiation. Further, a study on healthy participants found no changes in electrodermal activity, heart rate, and heart rate variability during sham exposure to a magnetic field that led to perceived deficits in cognitive performance (Szemerszky et al., 2016). Yet, more studies are needed involving the physiological response level to obtain an integrated understanding of the phenomenon of IEI-EMF and to assess the potential role of response biases, demand effects and/or social desirability that may explain effects on the self-report level only.

Therefore, the current study aimed to model the development of IEI-EMF in healthy participants by giving negative information on health-related effects of EMF (film presentation, instructions, experimental set-up) and test the reproducibility of induced changes in the perception of tactile stimuli after one week on both self-report and physiological variables. We hypothesized that a nocebo effect would be induced, i.e., participants would experience increased intensity and aversiveness of tactile stimuli when sham-exposed to WiFi radiation and that watching a short film about adverse health effects of electromagnetic exposure would further increase this effect. We assumed that this nocebo effect would be reflected in increased skin conductance responses (SCR) and that increases in both the self-reports and physiological measures persist until the follow-up assessment after seven days. Finally, we expected that interoceptive accuracy (Schandry, 1981) contributes to the vulnerability for nocebo effects in the context of IEI-EMF, as suggested by predictive processing accounts (Van den Bergh et al., 2017a). In particular, we expected that lower interoceptive accuracy increases the relative influence of the experimentally induced prior and hence the nocebo effect.

2. Methods

2.1. Participants

Participants from the general public were recruited via e-mail and social media channels. Exclusion criteria were checked with a questionnaire and included chronic or acute pain, regular intake of analgesic drugs or psychopharmacological medication, use of illegal drugs, chronic diseases (e.g., diabetes, high blood pressure, liver dysfunction), neurological and psychiatric disorders, and allergy to plasters. All participants signed a first informed consent before starting the experiment and a second informed consent after completion and a full explanation of the purpose of the experiment. Participants received 25 € for compensation. Ethical approval for the study was granted by the local Ethics Committee (2017-JGU-psychEK-010).

Sixty-five participants ($M = 27.3$ years, $SD = 7.38$; $n = 41$, 63% females) took part in the study. Two persons (one female, both in the experimental group) participated in the first session only. Members of the EMF-film ($n = 32$, 49%) and the Control-film group ($n = 33$, 51%) did not significantly differ on any of the reported items at baseline (T0; Table 2, Table 3).

2.2. Experimental design and procedure

After filling in questionnaires on personality traits and state variables, participants at first performed the heartbeat detection task (Schandry, 1981; cf. Table 1). In an experimental mixed (between- and within-groups) design, participants were then assigned to the experimental or control group by a computerized random allocation process. Participants in the experimental group watched a television report on the adverse health effects of electromagnetic radiation ('EMF-film group'). In this film, a health physicist tested and demonstrated the negative impact of electromagnetic radiation on a patient with Multiple Sclerosis in a pseudoscientific setting and the extent of electromagnetic radiation in an ordinary family's home was measured by an environmental engineer. Participants in the control group watched a television report on the illegal trade of mobile phones ('Control group'). In this film, people's reactions were displayed when they were offered stolen mobile phones. Both reports lasted approximately 6 min, had previously

Table 1
Timeline of the study including the different assessments and experimental tasks.

	online survey	session 1	session 2
Sequence of events per appointment …	**T0 assessment:** SSA MHW-R STAI-T SSAS	heart beat detection task **T1 assessment:** STAI-6 television report (EMF-film or Control-film) **T2 assessment:** film rating STAI-6 MHW-R cued sham exposure experiment **T3 assessment:** SSAS MHW-R CSD STAI-6 first funnel debriefing	**T4 assessment:** SSAS MHW-R CSD STAI-6 cued sham exposure experiment **T5 assessment:** SSAS MHW-R CSD STAI-6 second funnel debriefing

SSA, Somatosensory Amplification Scale; MHW-R, radiation subscale of the Modern Health Worries Scale; STAI-T, State Trait Anxiety Inventory, trait version; SSAS, Sensitive Soma Assessment Scale; STAI-6, 6-item State Trait Anxiety Inventory, state version; CSD, Checklist for Symptoms in Daily Life.

Table 2
Demographics, detection threshold for the tactile stimuli, and statistical comparison of both experimental groups.

	Experimental film condition		Test statistic for differences between groups (*p*-value)
	EMF-film ($n = 32$)	Control-film ($n = 33$)	
Number of female participants (%)	19 (59.4)	22 (66.7)	0.371 (.543)[a]
Mean age (standard deviation)	26.8 (7.74)	27.7 (7.10)	476.0 (.424) [b]
Detection threshold for tactile stimuli (in milliampere) session 1	0.57 (0.17)	0.55 (0.17)	528.5 (.995) [b]
Detection threshold for tactile stimuli (in milliampere) session 2	0.57 (0.14)[c]	0.55 (0.11)	−0.822 (.415)[d]

[a] X^2-test.
[b] Mann-Whitney-U-test due to non-normally distributed data.
[c] $n = 30$.
[d] Independent samples *t*-test.

been broadcasted on public German TV and successfully applied in a previous study (Bräscher et al., 2017). After watching the respective film, participants took part in a cued sham exposure experiment with two different kinds of trials: sham WiFi ON and sham WiFi OFF (Fig. 1). During the trials, tactile stimuli of a low, medium, and strong intensity (in the non-painful range) were presented to the participants' index fingers. The cued sham exposure experiment was repeated about one week later (+/− one day, $M = 7.03$, $SD = 0.47$) in a follow-up appointment to test for longer-lasting nocebo effects (without prior film presentation or reminder of the instructions). At the end of the second session, participants answered a series of questions in a funnel debriefing manner (i.e., asking increasingly specific questions (Chartrand et al., 2006)) to assess whether they believed the cover story. Finally, they were fully debriefed.

Experimental testing took place between November 2017 and May 2018 at the University of Mainz, Germany. The first session took about 80 min, the second session took about 50 min. Throughout both cued sham exposure experiments, participants' electrodermal activity was assessed.

Cover story. The cover story was similar to the one used in a previous study (Bräscher et al., 2017). Before entering the testing room, participants were asked to shut down their mobile phone "due to interference with electromagnetic radiation" and were told that the purpose of the experiment was to test body and symptom perception during electromagnetic radiation as well as memory effects. In the testing room, a "signal-increased" router was placed on the left-hand side of the participant's seat, and a big antenna was attached on the right side "to achieve a homogeneous EMF" around the participant. The experimenter took place behind a movable wall, covered with aluminum foil. This set-up was intended to make the participants believe that "an electromagnetic WiFi field will be created in the room, twice as strong as a regular one". Once seated, the participants read the (first) study information and signed the first informed consent. We instructed the participants that some people experience transient symptoms (like dizziness, headache, etc.) under exposure with EMF and that some evidence exists showing enhancement of somatosensory perception by EMF. To give a rationale for the second session and to seemingly check for the memory effects of the electromagnetic radiation, participants had to answer three questions concerning the film at the end of the first session.

Questionnaires. To assess trait and state anxiety, we used the trait (Cronbach's α at T0: α = 0.91) and 6-item state version (Marteau and Bekker, 1992); Cronbach's α between α = 0.48 and α = 0.77) of the State Trait Anxiety Inventory (Spielberger et al., 1970). Worries about adverse health effects of electromagnetic radiation were assessed with a modified version of the radiation subscale of the Modern Health Worries Scale (MHW-R; Petrie et al., 2001); Cronbach's α between α = 0.84 and α = 0.89) comprising six items. The EMF version of the Sensitive Soma Assessment Scale (SSAS; Nieto-Hernandez et al., 2008); Cronbach's α at T0: α = 0.98), including five items, was used to assess sensitivity to EMF. Perceived bodily symptoms were assessed using a modified version of the Checklist for Symptoms in Daily Life (CSD; Wientjes and Grossman, 1994). The CSD (Cronbach's α between α = 0.72 and α = 0.81) comprised 25 items with a 5-point Likert scale ranging from "not at all" to "extremely". The perception of the films was assessed with a self-generated questionnaire (Bräscher et al., 2017; Cronbach's α: α = 0.75) with the subscales absorption (3 items), interest (1 item), novelty (3 items), perception of danger (2 items), personal relevance (3 items), concreteness (3 items), and reliability (3 items), rated on 5-point scales from "not at all" to "very much".

Participants at first completed the SSA, MHW-R, STAI-T, and SSAS at home via Sosci Survey (Leiner, 2014; T0; cf. Table 1 for a timeline). In the first session, before watching the film, participants filled in the STAI-6 (T1). Directly after watching the film, participants completed the film rating, the MHW-R and again the STAI-6 (T2). After the cued sham exposure experiment in the first session (T3), before the experiment in the second session (T4), and after the experiment in the second session (T5) participants filled in the SSAS, MHW-R, CSD, and STAI-6. At T3 and

Table 3
Questionnaire data for both experimental groups at baseline (T0), before watching the film (T1) after watching the film (T2), and after completing the experiment (T3) at session 1 and before (T4) and after completing the experiment at session 2 (T5; means and standard deviations) and statistical comparisons of the two experimental groups at baseline.

questionnaire	Experimental film condition												Group difference at T0 (*p*)
	EMF-film						Control-film						
	T0	T1	T2	T3	T4	T5	T0	T1	T2	T3	T4	T5	
STAI-T	36.97 (8.40)	–	–	–	–	–	38.52 (9.65)	–	–	–	–	–	0.69 (.494)[1]
STAI-6	–	10.03 (1.20)	9.44 (1.29)	9.09 (1.61)	8.33 (1.97)	7.97 (1.65)	–	10.64 (2.01)	10.45 (2.40)	9.18 (1.83)	9.36 (2.54)	8.94 (2.26)	–
SSAS	20.53 (6.25)	–	–	20.38 (3.48)	20.67 (4.05)	20.77 (4.22)	21.24 (5.47)	–	–	20.27 (3.87)	20.45 (5.09)	20.58 (5.20)	553.0 (.730)[2]
MHW-R	1.41 (0.43)		1.76 (0.57)	1.71 (0.51)	1.61 (0.52)	1.62 (0.52)	1.56 (0.63)	–	2.04 (0.89)	1.80 (0.73)	1.76 (0.70)	1.73 (0.79)	499.50 .713)[2]
CSD	–	–	28.72 (4.05)	29.53 (4.29)	27.73 (3.17)	28.63 (4.64)	–	–	39.39 (3.48)	30.48 (4.21)	28.36 (3.20)	29.30 (3.80)	–

STAI-T, State Trait Anxiety Inventory, trait version; SSA, Somatosensory Amplification Scale; STAI-6, 6-item State Trait Anxiety Inventory, state version; SSAS, Sensitive Soma Assessment Scale; MHW-R, radiation subscale of the Modern Health Worries Scale; CSD, Checklist for Symptoms in Daily Life; [1] Independent samples-t-test; [2] Mann-Whitney-U-test due to non-normally distributed data.

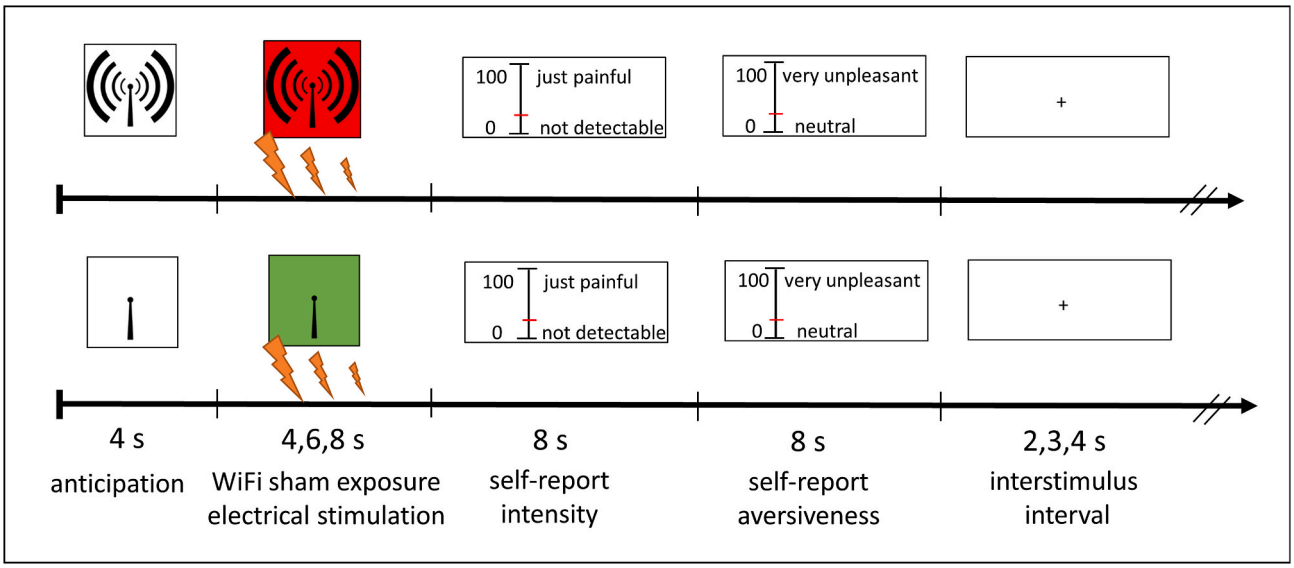

Fig. 1. Trial procedure of the cued sham exposure experiment. Trials were randomized and in the anticipation interval either announced sham WiFi exposure (WiFi ON trial, upper half of the figure) or no WiFi exposure (WiFi OFF trial, lower half of the figure), which supposedly was effective during the presentation of an electric stimulus (of high, medium or low intensity, cf. flash in the figure). The time interval of the sham WiFi exposure/no exposure was indicated with a colored symbol and varied between 4, 6, and 8 s. After self-reported intensity and aversiveness of the electric stimulus, a fixation cross was displayed for 2, 3 or 4 s before the next trial started.

T5, they also answered a funnel debriefing procedure (Chartrand et al., 2006) to assess whether they believed the cover story. Answers to open questions from funnel debriefing were coded into non-overlapping categories summarizing equivalent contents. In this context, participants also rated their anxiety concerning the tactile stimuli and the WiFi radiation and their belief in WiFi exposure during the experiment on scales ranging from 0 (none) to 100 (maximum anxiety/belief).

Heartbeat detection task. The procedure was identical to a previous study (Schaefer et al., 2012). An ECG was obtained by attaching Ag–AgCl electrodes (35 mm) to the lower left rib cage, the right mid-clavicle, and the left mid-clavicle (serving as a ground electrode). Signals were recorded (sampled at 512 Hz) and analyzed by a Varioport system (Becker Meditec, Germany). Custom-built software (programmed by Gerhard Mutz) detected R-waves, computed the mean heart rate, and presented the task. Participants were instructed to silently count their heartbeats by concentrating on bodily sensations that might be associated with heart activity. They were not allowed to take their pulse or attempt any other manipulations to facilitate the discrimination of their heartbeats (Schandry, 1981). The task was performed three times (for 25 s, 35 s, and 45 s), while the duration of these intervals was unknown to the participants. The beginning and the end of each interval was signaled by a tone. In the current sample, Cronbach's α (based on the perception scores of the three intervals) was 0.90. Accuracy of heartbeat detection task was quantified by a perception score calculated from the relative difference between the actual and the counted number of heartbeats: perception score = 1 - 1/3 ∑(|recorded heartbeats – counted heartbeats|/recorded heartbeats).

Cued sham exposure experiment. Before the experiment, participants were familiarized with two visual analog scales (VAS). The intensity VAS was labeled with 0 *'not noticeable'* and 100 *'just painful'*. The aversiveness VAS was labeled with 0 *'neutral'* and 100 *'very unpleasant'*. During the cued sham exposure experiment, participants repeatedly had to rate the intensity and aversiveness of tactile stimuli in six different kinds of trials. In half of the trials participants, were told that the WiFi router was switched on, indicated by a picture with an antenna surrounded by radiation waves shown on the computer screen and in the other half of the trials the router was supposedly switched off, indicated by a picture of the antenna without radiation waves (Fig. 1). In each case, one of three different stimulus intensities of the tactile stimuli were applied to the index finger of the participants' dominant hand: low tactile, medium tactile, and high tactile stimulation with 12 trials each. This resulted in a total of 72 trials presented in random order. Trials lasted 29 s on average and started with 4 s of anticipation time, during which the picture was shown indicating a WiFi ON or OFF trial. Then an interval of four, six or 8 s of sham WiFi exposure or no WiFi exposure followed, during which the background of the picture turned green or red. In half of the participants green indicated 'WiFi ON', in the other half of the participants green indicated 'WiFi OFF' to control for possible effects induced by the colors. Subsequently, the participants had 8 s to rate the perceived intensity on the intensity VAS and 8 s to rate the perceived aversiveness on the aversiveness VAS. Finally, for four, six or 8 s (depending on the length of the sham WiFi exposure/no exposure interval), a fixation cross was displayed until the next trial started (Fig. 1).

2.3. Electrodermal activity

EDA was continuously recorded as skin conductance on the palm of the non-dominant hand with two Ag/AgCl electrodes (24 mm) and a sampling rate of 32 Hz (Varioport System, Becker Meditec, Karlsruhe, Germany). The data was baseline and range-corrected and further analyzed using the Matlab-based software Ledalab 3.4.9 (Benedek and Kaernbach, 2010); www.Ledalab.de). Preprocessing involved downsampling to 16 Hz and visual checking for artifacts. EDA was analyzed utilizing continuous decomposition analysis (CDA) with a response window of 1–4 s after the onset of the tactile stimulus and an amplitude threshold of 0.01 μS. The phasic activity within the response window (skin conductance response; CDA. SCR) returned by Ledalab was further analyzed.

2.4. Tactile stimuli

Tactile stimuli were applied by a bipolar constant-current stimulator (DS5; Digitimer, Welwyn Garden City, Hertfordshire, United Kingdom) and delivered to the index finger of the dominant hand, through a pair of Ag/AgCl electrodes (24 mm). The stimulator was coupled to a data acquisition system (DT9812-10V; Data Translation, Inc., Marlborough, Massachusetts, United States), which was controlled by a laptop

computer. Each stimulus consisted of a sinus wave with a duration of 100 ms (1000 Hz), defined in MATLAB (MATLAB and Data Acquisition Toolbox Release, 2015b, The MathWorks, Inc., Natick, Massachusetts, United States). The individual intensities of the stimuli applied were determined with the following calibration procedure. Each participants' detection threshold for the tactile stimuli was computed three times according to the method of limits (Levitt, 1971). Then the mean of these three thresholds was used as the final detection threshold. During the remainder of the experiment, three intensities were used. The intensity level of the participants' detection threshold was multiplied with 1.2 for the low tactile stimuli, with 1.8 for the medium tactile stimuli, and with 2.4 for the strong tactile stimuli. No stimulus was rated as painful (equals 100 on the intensity VAS) by any of the participants.

2.5. Statistical analysis

Independent samples *t*-test and Mann-Whitney-U-tests (for non-normally distributed data) were calculated to compare the WiFi and the Control group on baseline measures and some of the closed questions of the funnel debriefing procedure. Multiple choice questions of the funnel debriefing, as well as the comparison of the gender distribution of both groups, were tested with χ^2-tests. Mixed factorial ANOVAS with time (MHW-R: T0-T4; SSAS: T0, T2-T4; STAI-6: T1-T5; CSD: T2-T5) as repeated factor and group (WiFi vs. Control group) as between factor were calculated to assess changes in time and group differences in MHW-R, SSAS, CSD, and STAI-6, respectively. Mixed factorial ANOVAS with intensity (low, medium, high), time (session 1, session 2), and sham WiFi exposure (WiFi ON vs WiFi OFF) as repeated factors and group (EMF- vs. Control-film group) as between factor were calculated to test for nocebo effects in self-reported intensity and aversiveness and electrodermal activity, respectively. Adding gender (female vs. male) as an additional factor was waived in the presented analyses since it did not change the observed pattern of results. Greenhouse-Geisser correction and Bonferroni correction for post-hoc tests were applied where appropriate. Relations between questionnaire data, self-reported intensity and aversiveness, and electrodermal data were assessed with Pearson correlations or Spearman correlations in the case of non-normally distributed data. Analyses were performed with JASP 0.9.0.1 and SPSS V 23.

3. Results

3.1. Modern health worries related to radiation and self-perceived electrosensitivity

Compared to the baseline assessment (T0), worries related to radiation were increased constantly after entering the experimental setting (main effect of time: $F(2.60, 158.71) = 19.88$, $p < .001$, $\eta^2 = 0.241$; post hoc tests: T0 < T1-T4, T1 > T2-T4). Specifically, modern health worries related to radiation (MHW-R) increased from T0 after watching either one of the films in the first session, decreased after the experiment and again decreased in the second session, where they remained stable (Fig. 2). Increased worries relative to the baseline assessment correlated significantly, confirming the temporal stability of the induced effects (all $r_s > 0.63$, $p < .001$). No significant difference between the experimental groups emerged (WiFi vs. Control group; main effect of group: $F(1, 61) = 1.03$, $p = .314$, $\eta^2 = 0.017$).

With regards to self-perceived electrosensitivity (SSAS), no significant group difference and no change over time appeared, indicating that subjectively perceived sensitivity to EMF was not affected by the experimental manipulation (main effect of group: $F(1, 61) = 0.02$, $p = .879$, $\eta^2 < 0.001$); main effect of time: ($F(3, 183) = 0.19$, $p = .906$, $\eta^2 = 0.003$).

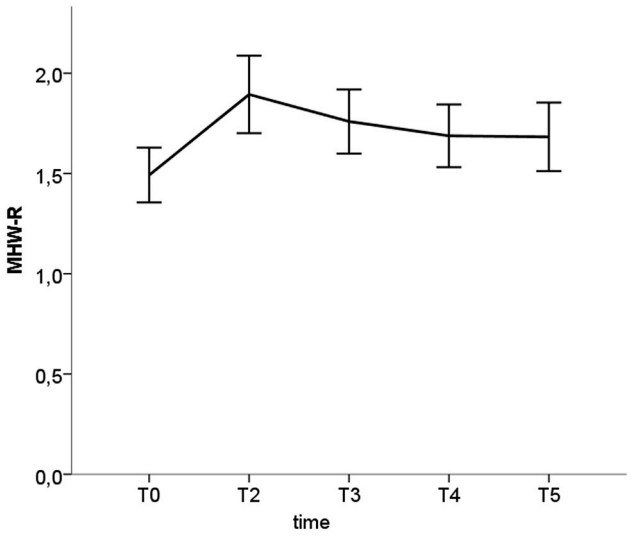

Fig. 2. Mean levels of worries regarding adverse health effects of electromagnetic fields (MHW-R mean scores) across the different assessments with standard errors.

3.2. Self-reported intensity

Participants rated the intensity of the tactile stimuli differently in accordance with actual intensity differences (main effect of intensity: $F(1.57, 95.58) = 493.41$, $p < .001$, $\eta^2 = 0.596$); Bonferroni-corrected post hoc tests indicated that the low intensity ($M = 7.35$, $SD = 11.31$) was rated lower compared to the medium ($M = 29.17$, $SD = 16.47$; $t(64) = -13.91$, $p < .001$, $d = 1.75$) and high intensity ($M = 56.53$, $SD = 16.81$; $t(64) = -31.35$, $p < .001$, $d = 3.95$) and that the medium intensity was rated lower than the high intensity ($t(64) = -17.44$, $p < .001$, $d = 2.20$). The main effect of time was not significant ($F(1, 61) = 1.00$, $p = .321$, $\eta^2 < 0.001$), indicating that self-reported intensity remained stable across both sessions. Further, the subjectively perceived intensity of the tactile stimuli was increased in sham WiFi exposure compared to no WiFi exposure trials (Fig. 3; main effect of sham WiFi exposure: ($F(1, 61) = 37.29$, $p < .001$, $\eta^2 = 0.001$), while the interaction effect between exposure and time was not significant ($F(1, 61) = 2.51$, $p = .118$, $\eta^2 < 0.001$). This suggests the successful induction of a nocebo effect in both sessions. Since the interaction between intensity and WiFi exposure was not significant ($F(1.81, 110.44) = 2.59$, $p = .085$, $\eta^2 < 0.001$), a nocebo effect across all intensities can be assumed.

However, the health-related film did not significantly increase the nocebo effect for the EMF-film group, as indicated by the non-significant interaction between WiFi exposure and group ($F(1, 61) = 0.93$, $p = .338$, $\eta^2 < 0.001$) and a non-significant main effect of group ($F(1, 63) = 0.03$, $p = .858$, $\eta^2 < 0.001$).

Interestingly, modern health worries related to radiation (MHW-R) at session 1 predicted the difference in self-reported intensity in session 2, supporting the notion that elevated worries lead to larger nocebo effects (after the film, T2: $r = 0.30$, $p = .016$; after the experiment, T3: $r = 0.26$, $p = .041$).

3.3. Self-reported aversiveness

The results of self-reported aversiveness were similar to the results of self-reported intensity (Fig. 4). Participants differentiated between the three stimulus intensities (main effect of stimulus intensity: $F(1.47, 89.76) = 320.53$, $p < .001$, $\eta^2 = 0.493$) confirmed by post hoc tests, in which the low intensity ($M = 7.40$, $SD = 11.71$) was rated lower that the medium ($M = 26.44$, $SD = 17.79$; $t(64) = -10.94$, $p < .001$, $d = 1.38$) and high intensities ($M = 51.36$, $SD = 20.00$; $t(64) = -25.24$, $p < .001$, $d = 3.18$) and the medium lower than the high intensity ($t(64) =$

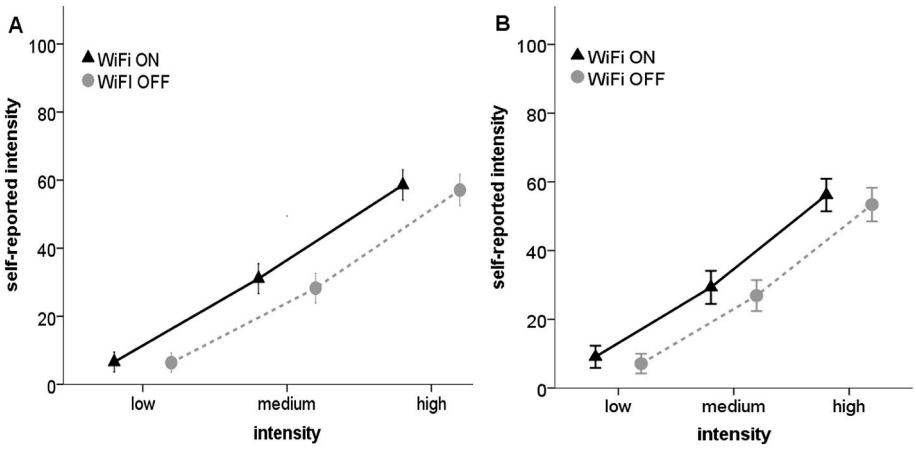

Fig. 3. Mean self-reported intensity regarding the tactile stimuli, session 1 (A) and session 2 (B) with 95% confidence interval.

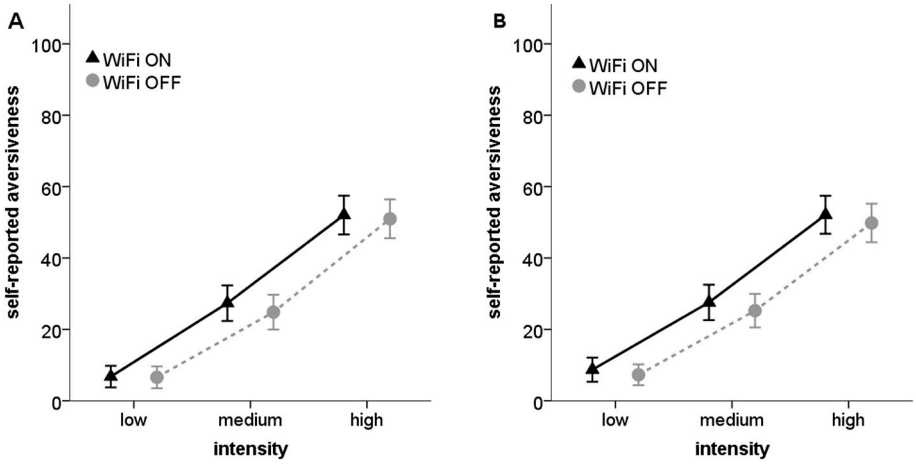

Fig. 4. Mean self-reported aversiveness, session 1 (A) and session 2 (B) with 95% confidence interval.

-14.31, $p < .001$, $d = 1.80$). The main effect of time was not significant (F (1, 61) < 0.01, $p = .984$, $\eta^2 < 0.001$), indicating that self-reported aversiveness remained stable across both sessions. Participants showed nocebo effects (main effect of WiFi exposure, $F(1, 61) = 21.97$, $p < .001$, $\eta^2 < 0.001$) across both sessions (interaction effect between time and WiFi exposure: F (1, 61) $= 1.73$, $p = .193$, $\eta^2 < 0.001$). The interaction between intensity and WiFi exposure was not significant (F (1.93, 117.83) $= 2.91$, $p = .060$, $\eta^2 < 0.001$), confirming a nocebo effect across all intensities. Yet, again, the films had no additional effect (main effect of group: F (1, 61) $= 0.03$, $p = .876$, $\eta^2 < 0.001$; interaction between WiFi exposure and group: F (1, 61) $= 0.17$, $p = .679$, $\eta^2 < 0.001$).

3.4. Interoceptive accuracy

The mean perception score was 0.62 ($SD = 0.24$) in this sample. There were no significant correlations between the perception score (assessed at the first session) and self-reported intensity and aversiveness of the first session. Significant correlations between the perception score and self-reports of the second session emerged (Table 4). Correlations were negative for trials with low tactile stimuli and medium tactile stimuli, but positive for trials with high tactile stimuli. This means that higher interoceptive accuracy (IAcc) was related to smaller nocebo effects (i.e., the difference in the subjectively perceived intensity and aversiveness of WiFi ON and WiFi OFF trial) for weak and medium intense tactile stimuli. In the case of strong tactile stimuli, higher IAcc was positively associated with stronger nocebo effects in self-reported aversiveness and by trend self-reported intensity.

Table 4
Correlations (p-value) of interoceptive accuracy, assessed at session 1, with the nocebo effect reflected in self-reported intensity and aversiveness of low, medium and high intensities of the tactile stimuli.

	interoceptive accuracy r (p-value)
Session 1	
Self-reported intensity	
Low	.10 (.464)[a]
Medium	-.11 (.402)
High	-.12 (.356)
Self-reported aversiveness	
Low	.10 (.469)[a]
Medium	-.05 (703)[a]
High	-.04 (.758)
Session 2	
Self-reported intensity	
Low	-.27 (.043)[a]
Medium	-.31 (.017)[a]
High	.24 (.072)
Self-reported aversiveness	
Low	-.33 (.011)[a]
Medium	-.41 (.001[a]
High	.30 (.022)

[a] Spearman correlation due to non-normally distributed data.

3.5. Electrodermal activity

Skin conductance responses (SCR) 1–4 s after the tactile stimulus showed a pattern very similar to the self-reports (Fig. 5). SCR were graded according to the intensity of the tactile stimulus (main effect of intensity: F (1.12, 66.23) = 51.17, $p < .001$, $\eta^2 = 0.070$), indicated by post hoc tests that showed lower SCR for the low ($M = 6.21^{-4}$, $SD = 4.66^{-4}$) compared to the medium ($M = 8.96^{-4}$, $SD = 6.19^{-4}$; t (59) = −3.83, $p < .001$, $d = 0.49$) and high intensity ($M = 1.34^{-3}$, $SD = 9.31^{-4}$; t (59) = −10.02, $p < .001$, $d = 1.28$) and lower SCR for medium compared to high intensities (t (59) = −6.20, $p < .001$, $d = 0.79$). A significant effect of time (F (1, 59) = 9.05, $p = .004$, $\eta^2 = 0.012$) indicated that SCR were larger in the first ($M = 8.29^{-4}$, $SD = 6.35^{-4}$) compared to the second session ($M = 1.08^{-3}$, $SD = 6.35^{-4}$).

SCR was higher in trials with sham WiFi exposure compared to no WiFi exposure (main effect of WiFi exposure: F (1, 59) = 9.57, $p = .003$, $\eta^2 = 0.001$) in both sessions (interaction effect between WiFi exposure and time: F (1, 59) = 1.10, $p = .300$, $\eta^2 < 0.001$), confirming a stable nocebo effect. No difference between both experimental groups or interaction between group and WiFi exposure emerged, confirming that the films did not influence electrodermal responding (main effect of group: F (1, 59) = 0.01, $p = .932$, $\eta^2 < 0.001$; interaction effect between group and WiFi exposure: F (1, 59) = 0.07, $p = .786$, $\eta^2 < 001$).

3.6. Reported symptoms (CSD) and state anxiety (STAI-6)

Self-reported symptoms, assessed with the CSD before and after both experiments, showed an increase after the experiments compared to before and a decrease in symptoms in session 2 compared to session 1 (Supplementary Fig. 1; main effect of time: F (2.43, 148.45) = 8.53, $p < .001$, $\eta^2 = 0.122$, post hoc tests: T2 < T3, T3 > T4, T4 < T5). No difference between both film groups emerged (F (1, 61) = 0.69, $p = .410$, $\eta^2 = 0.011$).

Interestingly, the nocebo effect in session 1, as indicated by self-reported intensity and aversiveness, correlated with the increase in symptoms perceived (difference between T5 and T4) at session 2 (intensity: $r = 0.28$, $p = .026$; aversiveness: $r = 0.31$, $p = .014$). Further, the increase in symptoms perceived at session 2 correlated with reported anxiety concerning WiFi radiation at session 2 ($r = 0.36$, $p = .004$) as well as self-reported electrosensitivity at session 2 (SSAS T4: $r = −0.38$, $p = .002$, T5: $r = −0.40$, $p = .001$).

Concerning state anxiety (STAI-6), the groups differed by trend, with the control group presenting itself as more anxious compared to the experimental group (Supplementary Fig. 1; main effect of group: F (1, 61) = 3.59, $p = .063$, $\eta^2 = 0.056$). State anxiety decreased over the course of participation (main effect of time: F (2.71, 165.10) = 23.58, $p < .001$, $\eta^2 = 0.274$), confirmed by post-hoc tests (T1 > T3-T5, T2 > T3-T5). Trait anxiety did not significantly correlate with measures of the nocebo effect.

3.7. Film rating and funnel debriefing

The EMF-film was perceived as more novel, more interesting, and less concrete compared to the Control-film (novelty: EMF-film: $M = 3.57$, $SD = 0.64$, Control-film: $M = 2.92$, $SD = 0.92$; t (63) = 3.32, $p = .001$; interest: EMF-film: $M = 3.38$, $SD = 0.91$, Control-film: $M = 2.76$, $SD = 0.87$; $U = 715.00$, $p = .009$; concreteness: (EMF-film: $M = 3.57$, $SD = 0.64$, Control-film: $M = 2.92$, $SD = 0.92$; t (63) = 3.32, $p = .001$). No differences between both groups appeared for absorption (EMF-film: $M = 2.86$, $SD = 0.57$, Control-film: $M = 2.81$, $SD = 0.57$; $U = 553.00$, $p = .739$), perception of danger (EMF-film: $M = 2.55$, $SD = 0.83$, Control-film: $M = 2.20$, $SD = 0.79$; $U = 664.50$, $p = .068$), personal relevance (EMF-film: $M = 2.23$, $SD = 0.77$, Control-film: $M = 2.14$, $SD = 0.90$; $U = 577.00$, $p = .517$), and reliability (EMF-film: $M = 3.21$, $SD = 0.79$, Control-film: $M = 2.98$, $SD = 0.64$; $U = 608.50$, $p = .286$).

In the funnel debriefing, participants were asked some questions to test whether they believed the cover story (cf. Table 5 for closed questions). Concerning the open question of the first session, "Why, do you think, did you watch the movie in the beginning of the experiment?", participants assumed they saw the movie in order to test for memory effects or attention (EMF-film group: $n = 5$, 15%; Control group: $n = 19$, 58%), to induce anxiety (EMF-film group: $n = 6$, 19%; Control group: $n = 0$, 0%), as a manipulation (EMF-film group: $n = 7$, 22%; Control group: $n = 0$, 0%) or to inform about the topic (EMF-film group: $n = 14$, 44%; Control group: $n = 7$, 21%). Seven participants (all Control group, 21%) did not know or suggested another reason. In the second session, participants were openly asked: "What do you think was the purpose of this study?" They assumed that the effect of WiFi radiation on the perception (EMF-film group: $n = 19$, 63%; Control group: $n = 25$, 76%), the impact of color on the perception (EMF-film: $n = 0$, 0%; Control: $n = 3$, 9%) or the effect from anxiety/sham WiFi exposure (EMF-film group: $n = 8$, 27%; Control: $n = 3$, 9%) was tested. Three participants from the EMF-film group (10%) and two from the Control group (6%) assumed other purposes. At the end of the funnel debriefing, participants were asked in the second session: "Did you think that something was strange or suspicious concerning the experiment?" Fifteen participants of the EMF-film group (50%) and 21 of the Control group (64%) did not have any suspicion, whereas 15 participants of the EMF-film group (50%) and 12 of the Control group (36%) expressed some kind of suspicion due to various reasons (e.g., the movable wall, the ECG assessment, whether

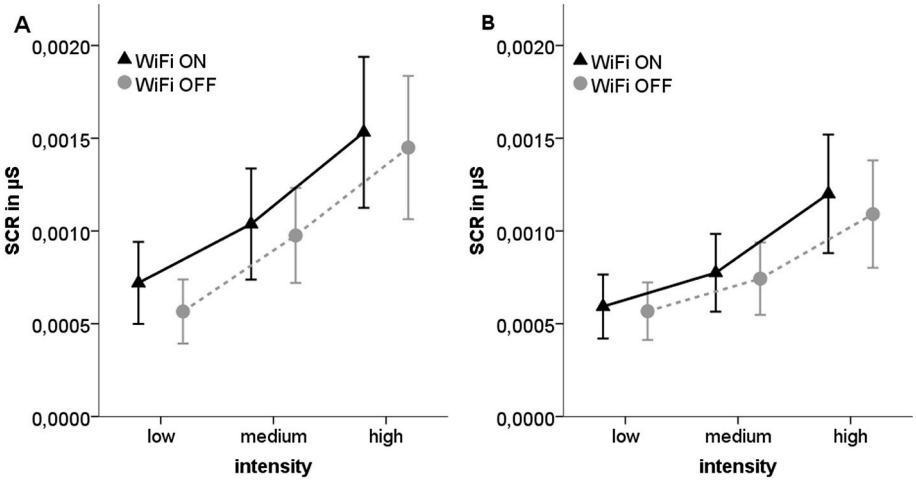

Fig. 5. Mean skin conductance response (SCR) in session 1 (A) and session 2 (B) with 95% confidence interval.

Table 5
Results of the funnel debriefing procedure for both experimental groups at the end of both sessions (see text for participants' responses to additional open questions) and statistical comparison of both groups.

	EMF-film group (*SD*)	Control-film group (*SD*)	U/χ^{b} (*p*-value)
How much did you fear the WiFi exposure during the experiment? [0; 100]			
Session 1	*M* = 10.84 (14.03)	*M* = 11.18 (19.87)	586.50 (.421)[a]
Session 2	*M* = 8.80 (14.27)	*M* = 10.00 (16.91)	510.00 (.826)[a]
How much did you fear the tactile stimulation? [0; 100]			
Session 1	*M* = 24.38 (24.03)	*M* = 26.30 (28.17)	531.00 (.968)[a]
Session 2	*M* = 21.87 (23.62)	*M* = 20.30 (23.72)	492.00 (.967)[a]
How did the WiFi radiation affect your perception of the tactile stimuli?			
Session 1			
stimuli felt stronger	*N* = 6	*N* = 8	1.46
stimuli felt weaker	*N* = 1	*N* = 3	(.481)[b]
no impact	*N* = 25	*N* = 22	
Session 2			
stimuli felt stronger	*N* = 5	*N* = 4	1.05
stimuli felt weaker	*N* = 1	*N* = 3	(.591)[b]
no impact	*N* = 24	*N* = 26	
During the experiment, did you believe that WiFi radiation was switched on or were you skeptical? (Session 2)			
WiFi was switched on all the time	*N* = 2	*N* = 7	3.38
WiFi was switched on sometimes (as indicated)	*N* = 10	*N* = 11	(.336)[b]
WiFi was switched on sometimes (different than indicated)	*N* = 10	*N* = 10	
WiFi was switched off all the time	*N* = 8	*N* = 5	
How confident have you been during the experiment, that WiFi radiation was switched on as indicated? [0; 100](Session 2)	*M* = 68.73 (28.56)	*M* = 48.33 (29.09)	700.00 (.005)[a]

[a] Mann-Whitney-U-test due to non-normally distributed data.
[b] X^{b}-test.

the WiFi router can be switched on and off as quickly, etc.).

4. Discussion

This study shows that negative expectations about harmful effects of electromagnetic fields can increase worries regarding electromagnetic radiation and increase both perceived intensity as well as aversiveness of somatosensory stimuli, suggesting the induction of a nocebo effect. Changes in self-reports concerning perceived intensity and aversiveness were accompanied by increases in physiological arousal (SCR) during sham WiFi exposure. Importantly, the induced changes were reproducible one week after their induction. Further, interoceptive accuracy, worries regarding electromagnetic radiation, and reported symptoms in daily life assessed at session 1 correlated with the nocebo effect in session 2. Other than expected, the presentation of a film on adverse health effects of electromagnetic fields compared to a neutral film on the trade of mobile phones did not enhance the induced nocebo effects.

Although the presentation of a film on adverse health effects of electromagnetic fields was not successful in the current study, a nocebo effect was observed. This nocebo effect possibly relied on information given by the instructions and the informed consent, as well as the experimental set-up (WiFi router, antenna, aluminum foil, etc.). In line with this interpretation, worries related to electromagnetic radiation increased after the participants entered the experimental context and received experimental instructions, despite an unchanged self-report of IEI-EMF. From a predictive processing perspective, this could be interpreted as the successful modulation of priors concerning symptom perception by giving written and verbal information.

IEI-EMF is a prevalent condition, but knowledge concerning its aetiopathology remains limited. The results of this study support the notion that nocebo effects play a role in the development and maintenance of IEI-EMF. Indeed, the induced effects were reproduced after one week without additional reinforcement (i.e., no repetition of negative instructions concerning WiFi radiation or film presentation), showing that a nocebo effect can lead to longer-lasting changes in interoceptive information processing. The temporally stable increases in worries regarding radiation and the significant prediction of the nocebo effect by worries support this notion. We are not aware of any other study investigating the longitudinal development of induced nocebo effects in the context of IEI-EMF in healthy participants. While few clinical studies (coronary heart disease, Rana et al., 2005; depression, Khan et al., 2008) and one experimental study (pain perception, Colloca and Benedetti, 2006) indicate that a *placebo* effect can be stable across several days or even longer time periods (Kaptchuk et al., 2008, for review), we are only aware of one clinical study investigating the longevity of the *nocebo* effect. That study demonstrated that patients taking finasteride due to benign prostatic hyperplasia reported significantly more sexual side effects up to twelve months when they previously received information that sexual side effects could occur compared to not receiving this information (Mondaini et al., 2007).

The fact that negative expectation effects were reflected in increased SCR suggest that nocebo effects also affect peripheral physiological markers of sympathetic nervous system activity. One previous study investigated skin conductance in experimentally induced nocebo effects in the context of IEI-EMF. In that study, skin conductance of healthy participants did not change during sham WiFi exposure with a magnetic field that led to perceived deficits in cognitive performance (Szemerszky et al., 2016). In contrast to this, the increased physiological reaction observed in the present study possibly mirrors increased arousal in the face of enhanced tactile perception by electromagnetic exposure. Since conscious efforts to manipulate SCR are highly unlikely in the current setting, it further confirms that the self-reported increases in intensity and aversiveness are not a product of response bias or socially desirable response style. Interestingly, a recent study investigating experimentally induced placebo and nocebo effects in pain perception showed that conditioned nocebo hyperalgesia but not placebo hypoalgesia seems to be resistant to extinction (Colagiuri and Quinn, 2018) and that anticipatory SCR mediated the resistance to extinction in nocebo hyperalgesia. In the present study, nocebo effects in SCR of the first session did not correlate with self-reports of the second session, yet the difference between WiFi ON and WiFi OFF trials in SCR was reduced, but still observable in the second session. The investigation of psychophysiological responses in the context of nocebo effects and IEI-EMF should be further pursued to gain a better understanding of the processes that take place during the acquisition and maintenance of IEI-EMF.

Consistent with predictive processing accounts, we hypothesized that higher interoceptive accuracy would lead to more reliable sensory input to the brain and thus reduce the impact of prior beliefs on the eventual conscious perception (Van den Bergh et al., 2017a; Van den Bergh et al., 2017b). Results show that interoceptive accuracy at session 1 predicted the nocebo effect in the second session. As expected, better interoceptive accuracy was related to a smaller nocebo effect with weak and medium stimuli. However, in strong tactile stimuli, higher interoceptive accuracy was related to a greater nocebo effect suggesting a larger influence of the prior in this context.

In line with previous studies that document the relevance of modern health worries in IEI-EMF (Bailer et al., 2008; Baliatsas et al., 2015; Witthöft and Rubin, 2013), we observed increased worries related to electromagnetic sham radiation after the participants first came to the lab. Interestingly, worries related to radiation in session 1 also predicted the nocebo effect in self-reported intensity at session 2, affirming the notion that worries related to radiation originally induced by experimental instructions and perceived somatosensory changes remain

elevated for at least one week and possibly contribute to increased perceptions in session 2 without additional reinforcement. Since state anxiety ratings were not affected, this seems to be a rather specific process.

Similar to a study by Witthöft and Rubin (2013), subjective symptom perception increased during the experiment in both sessions (although this might also just be an effect of time). The nocebo effect in the intensity and self-reported aversiveness of session 1 predicted the number of symptoms reported in session 2, which might reflect a self-reinforcing process. Further, the symptom increase in the second session correlated with increased self-reported anxiety concerning the WiFi exposure (funnel debriefing) and perceived electrosensitivity in session 2, rendering a mere effect of time unlikely.

Concerning the cover story, the funnel debriefing procedure indicated that most participants believed that there was some kind of WiFi exposure during the experiment and the EMF-film group, even more, believed that the WiFi signal was switched on as indicated. Although there was some extent of suspicion concerning the EMF-film and the whole experiment, only a few participants thought that the purpose of the experiment was to test the effect of sham exposure, anxiety, or similar. Interestingly, most participants did not think that the sham WiFi exposure influenced their perception of the tactile stimuli, although the results of the self-reports indicated the opposite.

4.1. Limitations

Other than in our previous (Bräscher et al., 2017) and another study (Verrender et al., 2018), no difference between participants watching the WiFi- or accordingly the Control-film emerged. The reasons for this remain unknown but could be related to the reception of the films. Using the same films, in the previous study the EMF-film was perceived as more worrisome and personally relevant than the Control-film, whereas in the present study, it was perceived as more novel and less concrete, but no differences in other subscales of the film rating emerged. Obviously, in this sample, the film did not increase the level of worries over and above the level of worries induced by the general instructions, which might be related to the aging of the film, which had been broadcasted in 2010. Further, the funnel debriefing indicated that the level of suspicion was increased in the EMF-film group, which might explain the absent film effect. The fact that self-reported sensitivity regarding electromagnetic exposure was not elevated by the experimental manipulation, other than in the previous study, might be a consequence of the absent effect of the film. Possibly, participants related less to the topic and the electrosensitive persons displayed. It could be speculated that this is a process relevant in the development of IEI-EMF.

This study gives first hints concerning the longevity of nocebo effects and suggests a possible route to the development of IEI-EMF. However, we cannot be sure whether the nocebo effect was stable across one week or whether it was re-elicited at session 2. Ambulatory assessment methodology could help to gain knowledge on the processes that take place in between sessions. To further investigate long-term effects, longer follow-up periods would be desirable, but should be carefully considered due to ethical restraints and to prevent participants from harm.

5. Conclusions

In sum, this study shows that a nocebo effect in tactile perception can be experimentally induced using verbal and written instructions and is detectable one week later without additional reinforcement. The results can be interpreted in the light of predictive processing and illustrate the impact of negative priors and interoceptive accuracy on tactile perception. Clinical implications concern the acquisition of IEI-EMF and confirm the possible role of the nocebo effect. Further, the results indicate the need to impinge on priors to treat persons concerned. The role of moderators like interoceptive accuracy should be further investigated but could be another target for treatment (e.g., training of interoceptive accuracy).

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2020.110019.

Credit author statement

Anne-Kathrin Bräscher: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization; Project administration; Stefan M. Schulz: Software, Formal analysis, Writing - review & editing; Omer van den Bergh: Conceptualization, Writing - review & editing, Supervision; Michael Witthöft: Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Funding acquisition.

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