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1 **An assessment of the autonomic nervous system in the electrohypersensitive**
2 **population: a heart rate variability and skin conductance study**

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11 *Running title: Evaluation of autonomic nervous system in electrosensitive*

12 **ABSTRACT**

13 The aim of the study was twofold: first, to compare the activity of the autonomic nervous
14 system (ANS) between the population self-declared as electrohypersensitive (EHS) and their
15 matched control individuals without intended exposure to electromagnetic fields (EMF). The
16 second objective was to determine whether acute exposure to different radiofrequency
17 signals modifies ANS activity in EHS. For that purpose, two different experiments were
18 undertaken, in which ANS activity was assessed through heart rate variability (HRV) and skin
19 conductance (SC). In the first experiment, a comparison between the EHS group (n=30) and
20 the control group (n=25) showed that the EHS has an increased number of responses to
21 auditory stimuli as measured by skin conductance activity, and that none of the short-term
22 heart rate variability parameters differ between the two matched study groups.

23 The second experiment, performed in a shielded chamber, involved 10 EHS from the first
24 experiment. The volunteers participated in two different sessions (sham and exposure). The
25 participants were consecutively exposed to four EMF signals (GSM 900, 1800, DECT and
26 Wi-Fi) at environmental level (1 V/m). The experiment was double blinded and
27 counterbalanced. The HRV variables studied did not differ between the two sessions.
28 Concerning electrodermal activity, the data issued from skin conductance and tonic activity
29 did not differ between the sessions, but showed a time variability.

30 In conclusion, the HRV and SC profiles did not significantly differ between the EHS and
31 control populations under no exposure. Exposure did not have an effect on the ANS
32 parameters we have explored.

33 **New & Noteworthy:** This study provided analysis on the skin conductance
34 parameters using a newly developed method (peak/min, extraction of skin
35 conductance responses) which had not been performed previously. Additionally, the
36 skin conductance signal was decomposed, considering tonic and phasic activities to
37 be a distinct compound. Moreover, this is the first time a study has been designed
38 into two steps to understand whether the autonomic nervous system is disturbed in
39 the EHS population.

40 **Keywords:** *electrohypersensitivity, symptoms, autonomic balance, idiopathic environmental*
41 *intolerance, electromagnetic fields, galvanic skin response, electrodermal activity,*
42 *environmental intolerance.*

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45

46 **INTRODUCTION**

47 Electrohypersensitivity, also known as idiopathic environmental intolerance attributed
48 to electromagnetic fields (IEI-EMF) (18), is a controversial condition whose
49 pathogenesis and clear etiology is so far unknown. Characterized by a wide range of
50 symptoms (23) and multiple incriminated sources of electromagnetic fields (12),
51 electrohypersensitive (EHS) patients reported that they mainly suffered from
52 symptoms such as tiredness, vertigo, tachycardia, headaches, etc. Some studies
53 have attempted to suggest different mechanisms of triggering symptoms or that
54 individuals are predisposed to become EHS, but nowadays no consensual
55 physiopathological mechanism has been accepted. One of the suspected causes of
56 the appearance of symptoms could be the disturbed activity (or imbalance) of the
57 autonomic nervous system (ANS).

58

59 The very few studies that have been conducted on EHS did not find there to be any
60 effect of acute exposure to electromagnetic fields (EMF) on cardiac autonomic
61 control (6, 20, 21, 26, 15, 8). An imbalance of the ANS has been suggested by
62 studies on the neurophysiological characteristics of EHS subjects (16). In terms of
63 visual testing, a significantly higher critical flicker frequency (CFF) and visual evoked
64 potential (VEP) has been found in patients suffering from symptoms related to visual
65 display terminal- and from EHS. Furthermore, an imbalance of the autonomic
66 nervous system and deviation of the circadian rhythm (as assessed by Heart Rate
67 Variability) (16) and the hyper-reactivity of the CNS (25) were reported.

68 A non-invasive and simple method to analyze sympathovagal balance (at the
69 sinoatrial level) is measuring heart rate variability (HRV). HRV is widely believed to
70 reflect changes in cardiac autonomic regulation. Skin conductance (SC), mostly
71 known as electrodermal activity or sympathetic skin response, results from the
72 activation of the reflex arch to different stimuli; the electrical activity of the eccrine
73 glands is simultaneously analyzed. The latter is thought to reflect sympathetic
74 arousal.

75 According to the last proceeding of the World Health Organization (WHO) on EHS
76 (18), more studies focusing on the sympathetic nervous system are required to define
77 the role it has to play in the occurrence of EHS or EHS symptoms. Firstly, we aimed

78 to analyze the characteristics of the ANS in EHS volunteers under baseline
79 conditions (without exposure to EMF), before comparing them to a non EHS (control)
80 group. The HRV and skin conductance (SC) parameters were then analyzed. A
81 second study was performed to identify the possible effects of acute exposure to
82 EMF signals on the HRV and SC of EHS volunteers. To our knowledge, this is the
83 first time a study has been designed into two steps to understand whether the
84 autonomic nervous system is disturbed in the EHS population when compared to the
85 control one, and to characterize the effects of EMF exposure, if there are any, on the
86 autonomic nervous system of EHS individuals.

87

88 **PATIENTS AND METHODS**

89 **Approval**

90 For the whole study, ethical approval was obtained from the appropriate local
91 committee (Comité de Protection des Personnes CPP Nord-Ouest N°: CPP/2014/8;
92 CPP/2015/38) and informed consent was obtained from all participants.

93 **Study Population**

94 In the first part of this study (Experiment 1), a total of 30 EHS (mean age: 47 ± 9) and
95 25 non EHS (mean age: 46 ± 10) individuals participated in the experimental
96 protocol. EHS patients (aged from 18 to 65), who declared that they suffered from
97 symptom(s) when exposed to various EMF sources such as mobile phones (54%)
98 and ELF-emitting sources (24%), were included in this study. Participants were
99 recruited through self-help groups or from the general population. None of the EHS
100 participants were on medication such as anti-depressants, analgesics or muscle
101 relaxants. They were recruited after they had stopped taking any medication that
102 could affect the autonomic nervous system. The control group of this first experiment
103 was recruited through an advertisement. The control and EHS groups were matched
104 in terms of age, body mass index and gender. The control group was on no
105 medication and presented no evidence of disease. All participants were instructed to
106 abstain from consuming alcohol and coffee for the 24 hours prior to and during the
107 study. The first study protocol, with the results of biological analysis, can be found in
108 (2).

109 In the second part of our study (Experiment 2), only 10 EHS individuals who had
110 participated in the previous study (Experiment 1) consented to exposure to EMF.
111 They reported being EHS and were aged between 35 and 63 years (mean age: $48 \pm$
112 10). The participants reported being sensitive, or attributed their symptoms to any
113 one of the following sources: GSM 900, GSM 1800, DECT and Wi-Fi 2.45 GHz. The
114 study group was composed of eight female and two male participants.

115 All of the participants gave informed consent and were informed of the purpose, aims
116 and procedure of the experiments.

117

118 **Experimental conditions**

119 In Experiment 1 (Figure 1), all of the volunteers participated in one experimental day
120 session. No intentional EMF exposure was performed and the experiment took place
121 in a shielded chamber. No EMF source was allowed, and both the EHS and control
122 individuals were advised to switch off all EMF sources and to stop using all possible
123 EMF sources at least two hours before being tested. The participants arrived in the
124 experimental room in the morning for a series of biological tests, the results of which
125 were published in part in (2). All the recordings were taken between 4 pm and 4.30
126 pm in a noise-free chamber, following a period of acclimatization. Blood pressure
127 (systolic and diastolic) was measured using a commercial device upon the
128 participants' arrival.

129 Experiment 2 consisted of two sessions (sham and real exposure) (Figures 2 and 3).
130 No external EMF sources were allowed, and the exposure consisted of a series of
131 EMF signals emitted from a generator (Rhode & Schwarz) and a horn antenna
132 (Schwarzbeck BBHA9120b). Consecutive RF signals were applied: GSM 900, GSM
133 1800, DECT and Wi-Fi signals for five minutes per signal. Each exposure period was
134 followed by 10 minutes' rest. A dosimeter was placed near the participant to record
135 the level of exposure. The participants arrived in the experiment room at 9 am and all
136 recordings began at 10 am. Two blood pressure measurements were taken: the first
137 upon arrival and the second at the end of the experiment. The two sessions (sham
138 and real) were separated by an interval of at least one week.

139 During the second experiment, the tests were double-blind and the data analysis was
140 performed in blind, without any possible way of recognizing the real or sham
141 exposure.

142 For both experiments, the temperature and humidity were measured; the average
143 temperature in the laboratory was: 24 ± 1 °C in the morning and 25 ± 0.8 °C in the
144 afternoon. The mean humidity was: 44 ± 8 % during the experiments.

145 **Heart rate variability measurement**

146 The electrocardiogram (ECG) signal was recorded according to the instructions of the
147 European Society of Cardiology (14). Leads, attached to the left and right wrists and
148 ankles, were connected to a Biopac system and a laptop with a rate of 1000
149 samples/sec. Kubios HRV® signal analysis software (Biosignal Analysis and Medical
150 Imaging Group, Department of Physics, University of Kuopio, Kuopio, Finland) was
151 used to automatically detect QRS complexes in ECG signals. A visual inspection was
152 first performed to avoid any misdetection and to ensure that the records did not
153 contain any ectopic beats or artifacts.

154 Non-stationary trends were removed from the HRV signals by using a detrending
155 procedure based on smoothness prior to regularization. Next, time and frequency

156 domain parameters were extracted. The participants were seated in a comfortable
157 position in a normal, resting state. Due to the circadian rhythm of HRV, the
158 recordings were performed at the same time of day for each participant for
159 Experiment 1 and Experiment 2.

160 **Skin conductance and electrodermal responses measurement**

161 Two Ag/AgCl electrodes were attached to the phalanges of the non-dominant hand
162 and linked to a Biopac MP 36 system to record SC and the resulting skin
163 conductance responses (SCR). Auditory stimuli were generated to elicit specific
164 SCRs, which could then be analyzed and characterized. For Experiment 1, SC was
165 recorded without auditory stimulation for Run 1 and Run 7, and with stimulation from
166 Runs 2 to 6 (10 * auditory burst for each run) (Figure 1). For Experiment 2, SC was
167 continuously recorded before exposure, during all exposure runs (both real and sham
168 for GSM 900, GSM1800, Wi-Fi and DECT) and after exposure with repetitive auditory
169 stimuli (5 * auditory burst for each run) (Figure 2 and Figure 3). The software used
170 was Ledalab, which allowing continuous decomposition analysis (CDA), trough to
171 peak (TTP) or the general linear method. After visual inspection and artifact
172 correction, analysis was performed on the recordings. The software can separate SC
173 signals into phasic and tonic activities. The CDA method has been shown to be
174 beneficial for analyzing data with apparent superposition of SCR signals (3).

175 **Variables**

176 The RR intervals were acquired from the ECG recordings seven times and five times
177 respectively for Experiment 1 and Experiment 2 (Figure 1 and Figure 2). The time
178 domain parameters analyzed were: the average RR interval (RR), heart rate (HR),
179 the standard deviation of the instantaneous heart rate values (STD HR), the standard
180 deviation of the RR intervals (SDNN), the square root of the mean squared
181 differences between the successive RR intervals (RMSSD), the number of
182 successive RR interval pairs that differ by more than 50 ms (NN50) and NN50
183 divided by the total number of RR intervals (pNN50). Power spectral analysis was
184 then conducted using the non-parametric Fast Fourier Transform (FFT) method. The
185 frequency-domain metrics (ms^2) were: low frequency band (LF: 0.04 – 0.15 Hz), high
186 frequency band (HF: 0.15 - 0.4 Hz) powers. Furthermore, the LF in normalized units
187 (nu), the HF nu and the LF/HF ratio were extracted. The latter represents the
188 frequency at which the power spectral density is highest within the HF band.

189 Ledalab was used to extract SC, and hence tonic and phasic activities, after applying
190 the CDA method. The software was employed to extract the following parameters:
191 the total number of SCRs above the threshold, the response latency of the first
192 significant SCR within response window (wrw), the sum of amplitudes of significant
193 SCRs wrw, the average phasic driver wrw (SCR amplitude), area (i.e., time integral)
194 of the phasic driver wrw (ISCR) and mean tonic activity wrw (tonic amplitude). The
195 amplitude threshold of the SCR was defined as 0.02 μS for both non-specific and

196 event-related SCRs. The responses to auditory stimuli were summed for Experiment
197 1.

198 For non-specific SCRs (i.e., without auditory stimuli), the total number of SCRs and
199 hence the average peak number over a one-minute time frame (mean peak/min)
200 were retrieved. For event-related SCRs (i.e., with auditory stimuli), a time window
201 relative to events between one and four seconds' duration was set up.

202 For blood pressure, arterial systolic (PAS) and diastolic (PAD) pressure were directly
203 obtained from the device, and breathing frequency from respiratory belt monitoring.

204 **Statistics**

205 Normally-distributed HRV data were analyzed using a two-way repeated measures
206 ANOVA (RM-ANOVA), followed by Bonferroni adjusted post-hoc analysis. There
207 were two factors: Stage (seven levels: Rest 1, Stim 1, Stim 2, Stim 3, Stim 4, Stim 5
208 and Rest 2) and Group (two levels: EHS and control). In Experiment 1, some non-
209 normally distributed variables were log (ln) transformed. These parameters include:
210 RR, RMSSD, SDNN, LF, HF and LF/HF ratio.

211 For Experiment 2, the two factors for the RM-ANOVA were Session (two levels: real
212 and sham) and Stage (five levels: Pre-expo, GSM 900, GSM 1800, DECT and Wi-Fi).

213 Data with non-normal distribution were analyzed using non-parametric tests for Stage
214 or Group differences (Experiment 1) and paired rank tests were performed for inter
215 sessions (i.e., Wilcoxon tests with multiple comparisons adjustment) or intra-session
216 differences (i.e., Friedman tests followed by Bonferroni adjusted post-hoc analysis if
217 significant) (Experiment 2).

218 For RED analysis under Experiment 1, a proportion of the significant responses
219 between groups was compared by using the chi-squared test. SC, tonic and phasic
220 components under auditory stimulation and the characteristics of SCRs were
221 compared using the Mann-Whitney test between the groups. Times comparison was
222 performed using the Friedman test.

223 The Wilcoxon t-test was applied to compare respiration rates and blood pressure
224 readings acquired before/after and between sessions.

225 The statistical analyses were performed and plotted using SPSS IBM Statistics
226 version 20, Graph Pad Prism version 5.0 and Excel software.

227 **RESULTS**

228 **Experiment 1**

229 **Respiratory rate**

230 Respiratory frequency was not available during the first Experiment.

231 **Blood pressure**

232 The blood pressure readings recorded during the first Experiment did not show any
233 significant difference between EHS and non EHS groups. Neither systolic (SBP: 115
234 ± 12 mmHg, SBP: 108 ± 13 mmHg, $p= 0.27$) nor diastolic pressure (DBP: 73 ± 10
235 mmHg, DBP: 71 ± 8 mmHg, $p= 0.64$) differ between groups.

236 **HRV parameters**

237 **Time-domain parameters**

238 Among all of the analyzed parameters, no significant differences between the groups
239 were found. Indeed, RR, RMSSD and SDNN did not seem to be different in the EHS
240 group when compared to the control one (Figure 4).

241 **Frequency-domain parameters**

242 LF, HF and the LF/HF ratio were not significantly different between the groups. It
243 should be noted that HF did not vary over the course of the Experiment, while LF and
244 the LF/HF ratio were modified in both groups (Figure 5). There was a trend of an
245 increase in LF/HF ratio due to LF increase. Also, the comparison of LFnu or HFnu
246 between the EHS and control groups did not show any significant difference ($p >$
247 0.05) (Figure 6).

248 **Skin conductance (SC) and SCR parameters (SCRs or RED)**

249 Statistical analysis did not show any significant differences ($p > 0.05$) between the
250 EHS and control groups for SC (3.8 ± 0.22 vs 2.93 ± 0.18 μ S), tonic (3.33 ± 0.21 vs
251 2.86 ± 0.17 μ S) and phasic activity levels (0.05 ± 0.01 vs 0.07 ± 0.01 μ S). The data
252 were expressed as a mean over a three-minute recording period \pm SD.

253 Over all recording periods, including auditory bursts (Run 2 to Run 6), there was a
254 higher percentage of responses to the auditory bursts in the EHS group compared to
255 the control group (36% of responses in the EHS group versus 29% in the control).

256 Due to the fact that the participants rapidly acclimatized to the bursts, the SCR
257 analysis presently shown was only based on the first auditory burst analysis, but not
258 on 10 bursts (significant differences between bursts). Due to the presence of non-
259 specific responses during runs, an analysis on Run 2 (the first run with bursts) was
260 considered as appropriate to compare the EHS group with the non-EHS group. The
261 results have shown no difference between the groups.

262 Other methods of analysis, including the TTP method and general methods, did not
263 show there to be any difference between the groups during Run 2 and after the first
264 stimulation.

265 **Experiment 2**

266 **Respiratory rate**

267 The statistical analysis for comparing between sessions (sham versus real) showed
268 that the respiratory rates at each stage (i.e., pre-exposure, GSM900, GSM1800,
269 DECT, Wi-Fi or post-exposure) were not significantly different. The global mean
270 values (\pm SD) calculated for all participants and for each session (sham or real) were:
271 13.05 ± 2.34 and 12.74 ± 2.18 bpm respectively.

272 **Blood pressure**

273 Under each exposure, the blood pressure readings taken before and after exposure
274 were not significantly different between the real and sham sessions for SBP ($p >$
275 0.05).

276 **HRV parameters**

277 **Time-domain parameters**

278 None of the time-domain parameters have shown any difference between sham and
279 real sessions after the Bonferroni correction was performed for multiple comparisons.
280 The corrected alpha values were obtained by taking $0.05/\text{number of comparisons}$
281 (data not shown).

282 **Frequency-domain parameters**

283 None of the frequency-domain parameters has shown any difference between sham
284 and real sessions, with or without the Bonferroni correction being performed. The
285 LF/HF ratio was not significantly different between the two sessions (Figure 7).

286 **Skin conductance (SC) and SCR parameters (SCRs)**

287 **Exposure to EMF**

288 The non-specific SCR parameters (the number of non-specific SCRs, the average
289 number of non-specific SCRs in a one-minute time frame) were not significantly
290 different between sessions and between stages of exposure. SC, as well as tonic
291 activity, was found to be time-variant after exposure for both the real and sham
292 sessions as shown in Figure 8. There is a trend towards an increase for both
293 parameters in both sessions.

294 **Exposure to auditory stimulation**

295 All activities (tonic and phasic) analyzed over a 120 second period decreased during
296 exposure to auditory sounds for both the sham and real exposures ($p < 0.0001$), but
297 not for conductance during the sham exposure. There is no significant difference
298 between runs under stimulation between SC ($p = 0.838$) or tonic activity ($p = 0.800$)
299 in both sessions.

300 Analysis was performed on the responses to the first signal and first stimulation to
301 burst, which showed a higher response to stimulation. Only five repetitions of auditory
302 stimulation were used. There are no significant differences between the sham and

303 real exposures in terms of latency, the number of SCRs and the amplitude of
304 responses ($p > 0.05$) (results not shown).

305

306 **DISCUSSION**

307 There are few reports investigating the regulatory functioning of the
308 cardiovascular and electrodermal systems in EHS patients. These studies suggested
309 possible arousal and hyper-reactivity in EHS subjects (24, 16). Most of those studies
310 were not replicated and despite an interesting hypothesis, an imbalance of the ANS
311 or hyper-reactivity in EHS subjects was not confirmed. The majority of this research
312 focused on the effects of exposure to several electromagnetic sources. The results of
313 these studies indicate that the link between exposure, symptoms and alterations to
314 the activity of the autonomic nervous system remains to be proven.

315 According to the baseline records, the HRV results do not indicate any
316 differences in autonomic cardiac control between the EHS and control (non-EHS)
317 groups. However, in response to successive auditory stimulation, the LF/HF ratio
318 seems to gradually increase over time in both populations. For both groups, a stage
319 effect is found for LF nu and HF nu. A decrease in HF nu reflects a parasympathetic
320 withdrawal, and an increase in sympathetic activity (LF nu) can explain this variation.
321 Similar findings have been reported by a study on the LF/HF ratio during sleep-
322 deprivation (19) under EMF exposure. The LF/HF ratio may also increase or
323 decrease in response to stressful situations (1). However, in this experiment, heart
324 rate monitoring did not show the presence of stress. This alteration was found for
325 both groups, and means that the responsiveness of the ANS is similar for the two
326 study groups. Indeed, this increase in the LF/HF ratio can be attributable to the
327 presence of sound stimuli, but psychological stress can increase the LF/HF ratio (11).
328 In a study on magnetic fields, in which participants were asked not to move during a
329 64-minute experiment, an increase in the LF/HF ratio (13) over the stages of the
330 experiment was found.

331 The results from the first experiment indicated that the LF/HF ratio was
332 unaffected in EHS subjects, which does not corroborate previous studies (16,17). In
333 their first study, they found differences in the heart rate, electrodermal activity
334 (latency and amplitude), diastolic pressure, critical fusion frequency and LF/HF ratio
335 of EHS volunteers in comparison to healthy subjects. These tests were significant
336 both during baseline tests and after stress induced by mathematical tasks. In their
337 second study, they used functional tests (22), including deep breathing, standing in a
338 position for one minute, followed by visual acuity and contrast sensitivity. They found
339 that the mean heart rate was different during baseline tests, whereas the LF/HF ratio
340 and the response to standing test were decreased for the EHS group. The EHS
341 group also had a faster onset and higher amplitude electrodermal response to
342 auditory tones. Moreover, in a study evaluating the effects of GSM signals, the LF/HF
343 ratio was elevated during memory tests and the critical fusion flicker threshold

344 measurement, but not in relaxed conditions (27). This discrepancy with our results
345 can be partially explained by the different tests and methodology used by the studies
346 (i.e., the absence/presence of functional or cognitive tests), but also by the difference
347 in the characteristics of the population. The nature of the challenge to the autonomic
348 nervous system leads to different neural responses. However, in our study, we did
349 not include mental tasks which can induce non-autonomic task-related influences.
350 Likewise, in the first study reported by Lyskov, participants reported to suffering from
351 skin-related symptoms, whereas in our study EHS subjects generally reported
352 symptoms related to mobile phone and/or extremely low frequency fields. In Wilén's
353 study (27), only mobile phone-related subjects were involved in the study. None of
354 the RR and HR parameters differ between our two populations. This contradicts the
355 previous studies, which reported a higher HR associated with a shorter RR in EHS
356 patients. In this study, the healthy subjects were matched for age, gender and body
357 mass index, in order to obtain comparability in the groups.

358 According to our findings, a globally high number of skin responses to auditory
359 stimuli are found for electrohypersensitive subjects, although the parameters of skin
360 conductance responses (amplitude and latency) were not modified. We presently
361 provided a further analysis of the skin conductance parameters using a newly
362 developed method (peak/min, extraction of skin conductance responses) which had
363 not been performed previously. Previous studies on the effects of electromagnetic
364 fields mainly focused on skin conductance levels (7), skin resistance (19), the latency
365 or onset of electrodermal activity (16) or the number of spontaneous peaks (17). Our
366 analysis provided the same parameters, but additionally the skin conductance signal
367 was decomposed, considering tonic and phasic activities to be a distinct compound.

368 An elevated number of spontaneous peaks during rest conditions or while
369 performing mathematical tasks for a 10-minute duration was reported by Lyskov and
370 colleagues (17). Combined with their previous findings on the amplitude and latency
371 of electrodermal activity, they suggest that electrohypersensitive subjects are
372 predisposed to physiological sensitivity to various physiological and psychosocial
373 stressors. A higher number of responses from EHS patients can be attributable to the
374 higher attention of electrohypersensitive individuals when compared to a control
375 group (non-electrohypersensitive individuals). Several hypotheses, such as the
376 individual difference hypothesis or the so-called 'electrodermal lability' hypothesis,
377 could explain this high number of responses. In 1958, Lacey and Lacey first used the
378 term "electrodermal lability" for subjects with high levels of non-specific responses to
379 frequency. In contrast, individuals with few electrodermal responses were called
380 "electrodermal stabiles". The related higher number of EDR has been associated with
381 the acclimatization process. Multiple individual studies have explored this difference,
382 and found that electrodermal lability is associated with neuroticism.

383 This "electrodermal lability" in the electrohypersensitive group could explain
384 the absence of the effects of EMF during Experiment 2. The response rates varied
385 significantly, as each subject represented his own control. The absence of any effects

386 of EMF exposure can be attributable to this characteristic. Indeed, it is also
387 hypothesized that exposure did not have any effect on SCRs. We can also say that
388 variability in electrodermal activity was the same during the two Experiments, and no
389 hyper-reactivity is found in response to EMF exposure.

390 Our experimental studies have some limitations. Our ECG recordings in
391 Experiment 1 were of a short duration (duration < five minutes). This makes it difficult
392 to compare between both experiments. However, in the second study, a five-minute
393 ECG recording was performed. Based on the spectral analysis of short-term HRV
394 fluctuations, a sequential time of two to five minutes is useful, as reported by the
395 literature. The recordings performed during the first experiment were also influenced
396 by auditory stimulation, resulting in a higher LF/HF ratio, whereas in Experiment 2,
397 there is a trend towards a decrease in the LF/HF ratio in the absence of such
398 stimulation. These findings support the effective sensitivity of HRV to external
399 stimulation and stress. Indeed, this could be a confounding factor for the
400 determination of the effects of EMF, and has to be taken into account for future
401 studies.

402 Secondly, we did not measure respiration rates in Experiment 1, which this
403 would have provided important information on skin conductance and heart rate
404 variability, since respiration could affect these parameters. In the context of our study,
405 the results from our SCR analysis could be affected by the absence of this data and
406 may result in an overestimation of skin conductance responses. Also, the mechanism
407 for the generation of SCRs is complex and needs further analysis. This analysis
408 should take into account respiratory effects and the results have to be confirmed. It is
409 known that breathing frequency influences the spectral powers of HRV (10, 4). As a
410 matter of fact, changes in breathing frequency (i.e., a lower or higher frequency)
411 induces a shift in sympathetic activity to adapt to the new frequency. It is known and
412 clearly established that a single deep breath can evoke an electrodermal response
413 (9) and is presently used as a control response. Here, inspiratory-related SCRs have
414 been visually inspected during Experiment 2. More generally, in order to develop a
415 clear psychophysiological inference on signals, Cacioppo and Tassinari have
416 suggested that the method of analysis should account for other physiological signals
417 or events of interest (5). Future studies, including those on skin conductance
418 responses and heart rate variability as a measure of the ANS, should take into
419 account the interaction between different signals.

420 Finally, the major limitation of our study is the small number of participants in
421 Experiment 2, as well as the absence of an additional control group, which rendered
422 the statistical power of the analyses performed relatively low. The volunteers
423 represented their own control. According to the perceived and potential invasive
424 character of exposure to electromagnetic fields for people reporting symptoms, many
425 participants declined to be exposed. Respecting the inclusion criteria (e.g., the
426 absence of chronic illness) due to the biological analysis performed in parallel also
427 contributed to the restricted number of participants.

428

429 **CONCLUSION**

430 We still reiterate that the generation of SCR is a rather complex phenomenon
431 involving cognitive and respiratory processes. Meanwhile, according to our protocol,
432 electrosensitivity is not associated with an imbalance in the regulation of the
433 autonomic nervous system. Exposure to electromagnetic fields did not have any
434 effect on those parameters. Due to the relative low number of participants, our study
435 results have to be confirmed with a higher number of participants and a comparative
436 group, which will be very interesting to support findings on the cardiovascular
437 modulation of autonomic nervous system.

438

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443

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447

448 **Disclosures**

449 No conflicts of interest, financial or otherwise, are declared by the author(s).

450

451 **Author contributions**

452 B.S. conceived and designed research

453 S.A. and L.H. performed experiments

454 S.A. and JG performed statistics and prepared figures

455 B.S., S.A., J.G., E.S.B and F.T. interpreted results

456 B.S. And S.A. drafted manuscript

457 B.S., S.A., F.T. edited and revised manuscript

458 B.S., E.S.B and F.T. approved final version of manuscript.

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552 Figures

553

554 Figure 1. Experimental procedures for measuring physiological changes during Experiment
555 1. SC: skin conductance, no auditory stimulation; HRV: heart rate variability; RED:
556 electrodermal response to auditory stimulation.

557

558 Figure 2. Experimental procedures for measuring physiological changes during Experiment 2
559 (sham or real sessions). SC: skin conductance, no auditory stimulation; HRV: heart rate
560 variability; RESP: measurement of breathing frequency.

561

562 Figure 3. Procedures during the post-exposure period (Experiment 2). SC: skin conductance,
563 no auditory stimulation; RED: electrodermal response to auditory stimulation; HRV: heart rate
564 variability; RESP: measurement of breathing frequency.

565

566 Figure 4. Time-domain parameters of heart rate variability during Experiment 1. Data are
567 presented as mean \pm SEM, RM-ANOVA: No significant effect on groups for RR, SDNN and
568 RMSSD.

569

570 Figure 5. Frequency-domain parameters of heart rate variability during Experiment 1. Data
571 are presented as mean \pm SEM, RM-ANOVA: No significant effect on groups for LF, HF and
572 LF/HF ratio.

573

574 Figure 6. Variations of LF nu and HF nu during Experiment 1. Data are presented as Mean \pm
575 SEM. No significant effect on groups.

576

577 Figure 7. Inter-session comparisons of LF/HF ratio (a) and HR (b) in EHS participants
578 exposed to different radiofrequency signals during Experiment 2. Data are presented as
579 mean \pm SEM.

580

581 Figure 8. Inter-session comparisons of skin conductance (a) and tonic activity (b) in EHS
582 participants exposed to different radiofrequency signals during Experiment 2. Data are
583 presented as mean \pm SEM.

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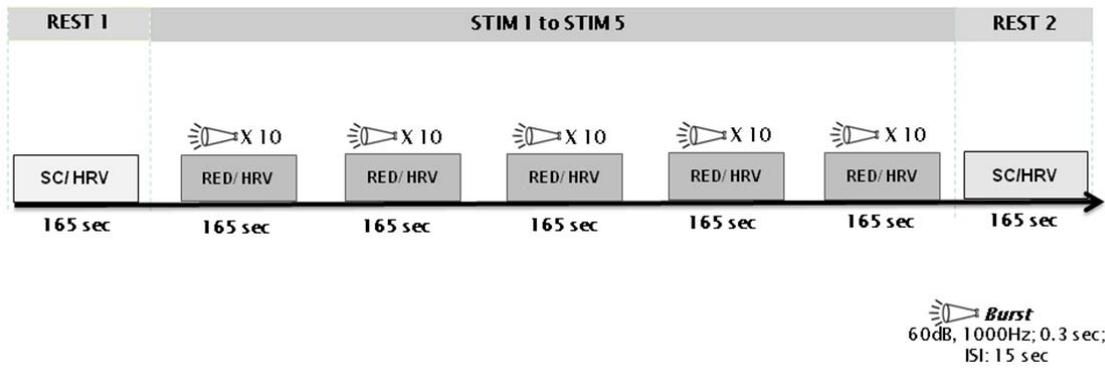


Fig.1

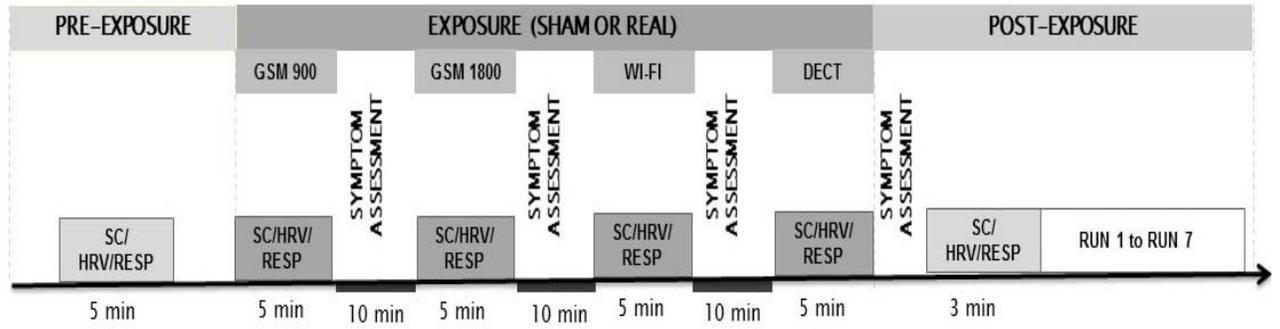


Fig. 2

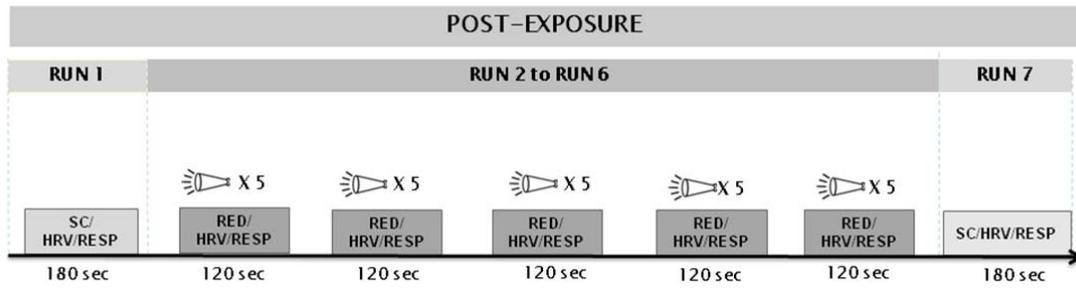


Fig.3

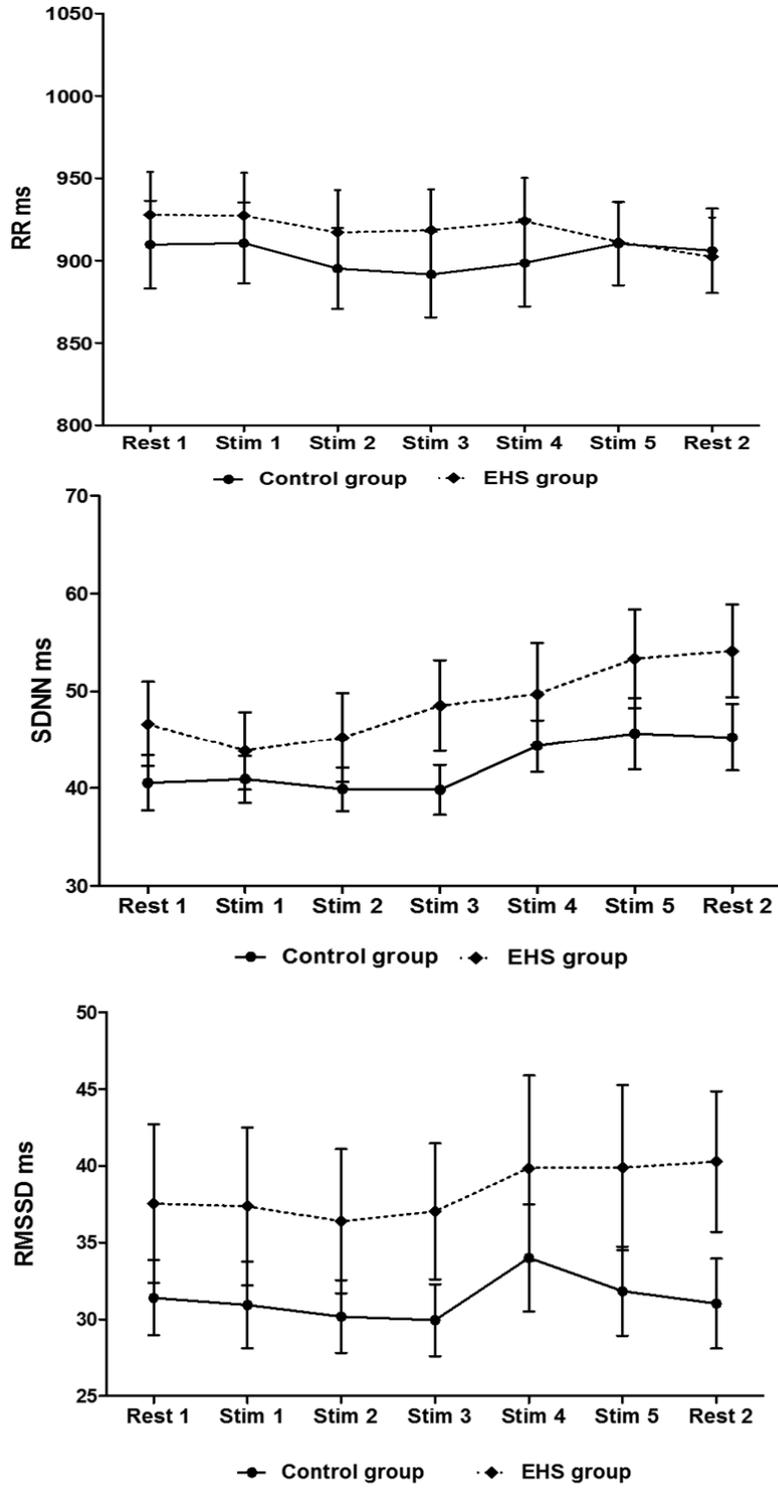


Fig.4

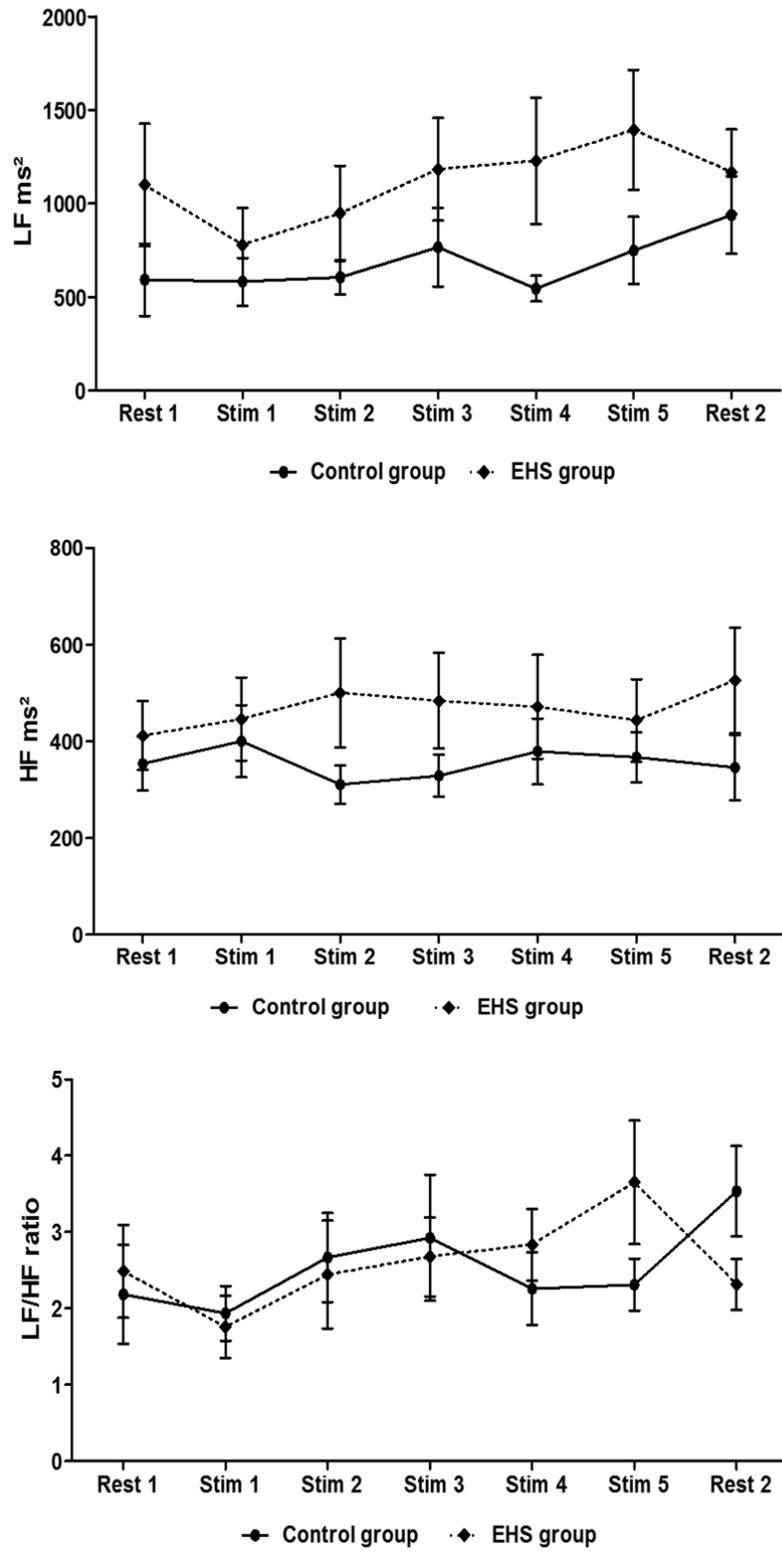


Fig.5

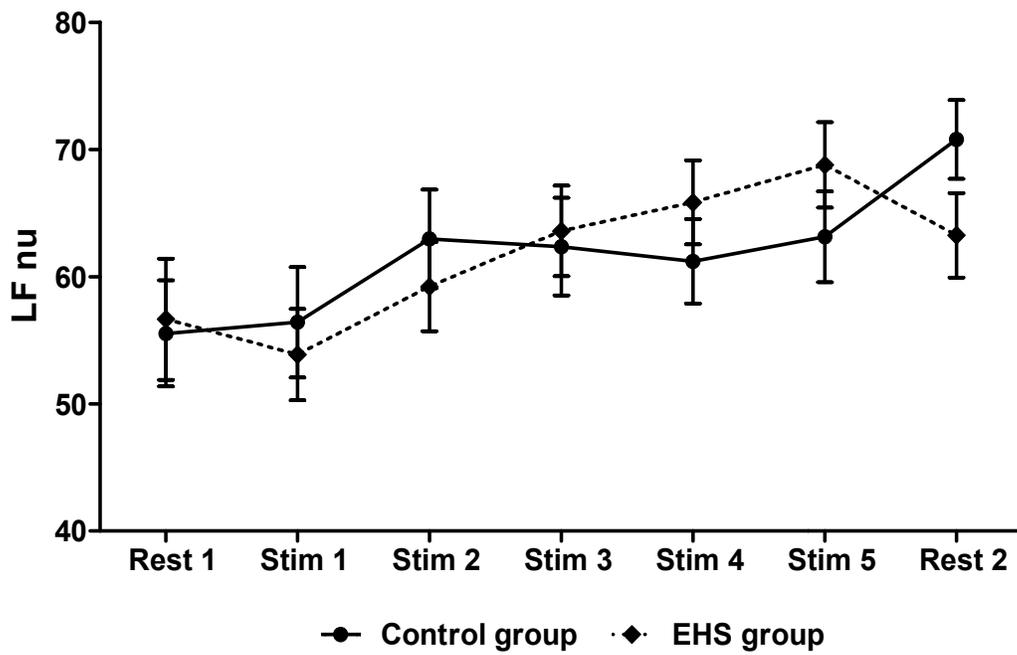
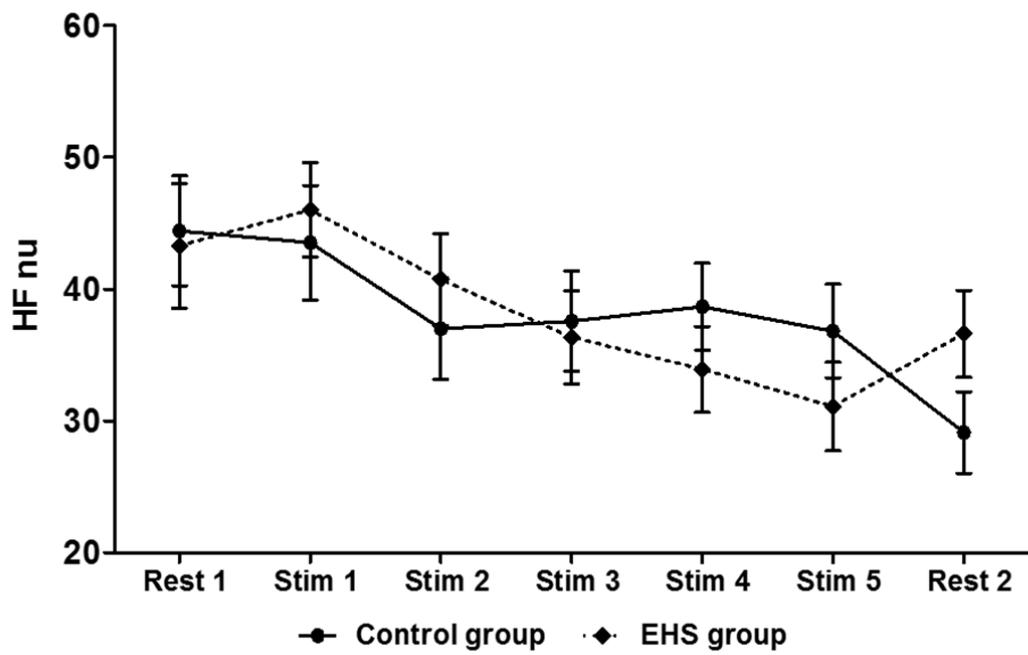


Fig. 6

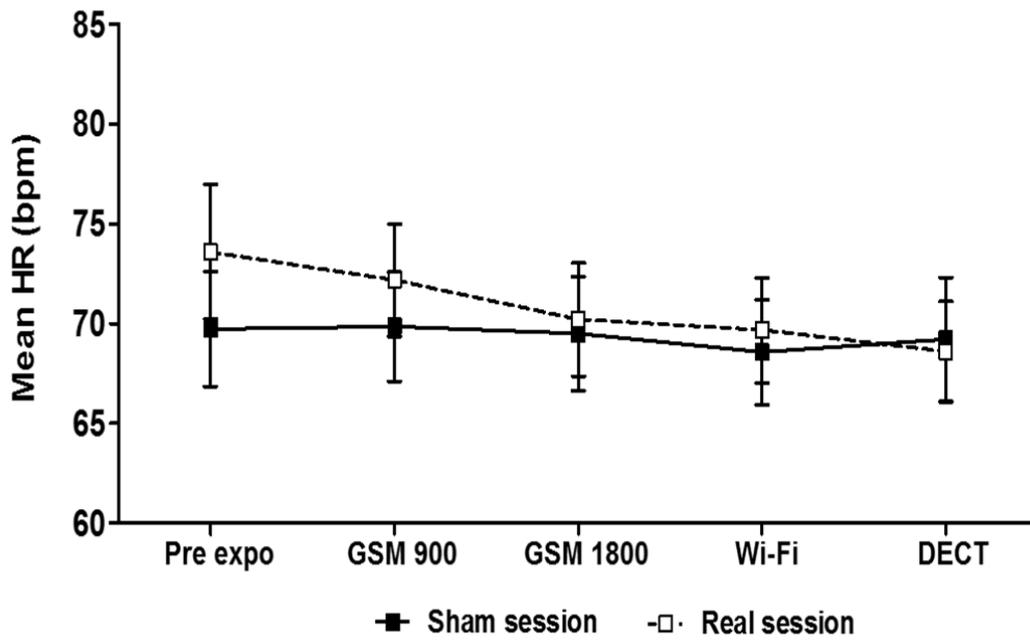
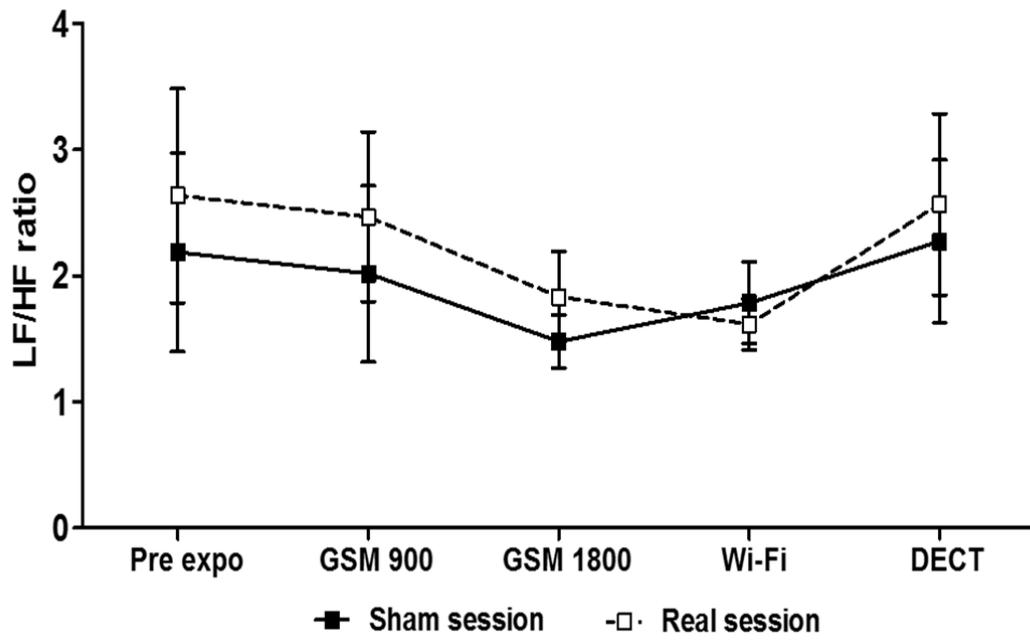


Fig.7

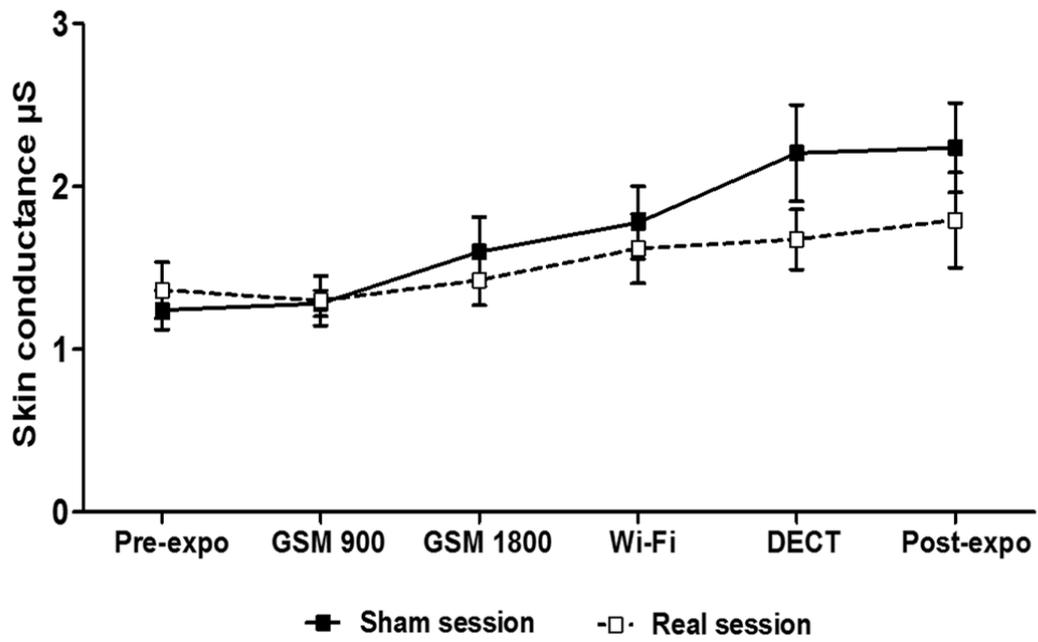
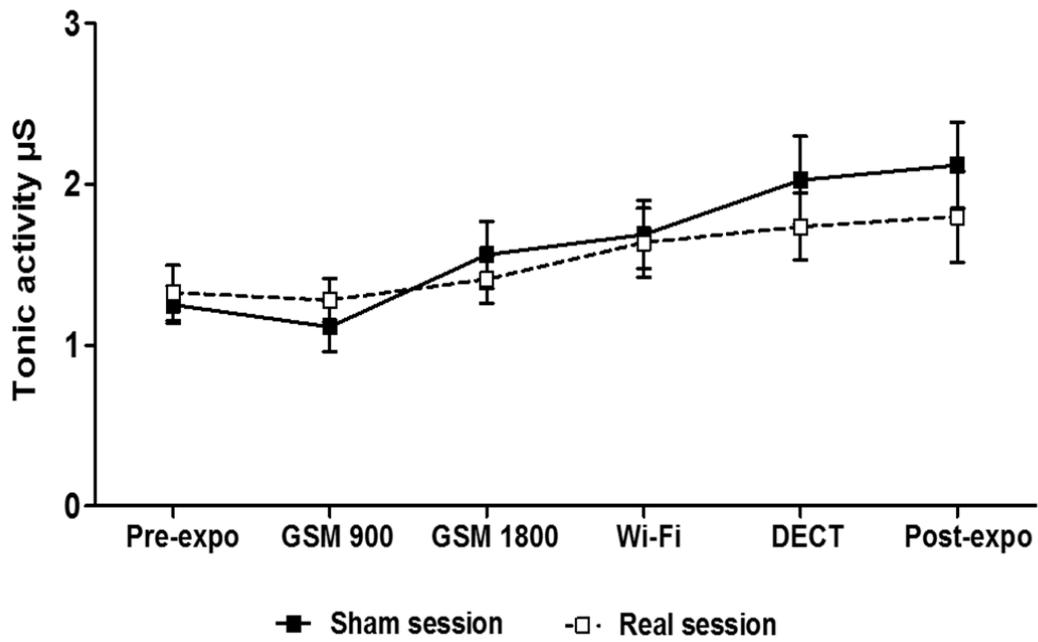


Fig.8