



Alteration of adaptive behaviors of progeny after maternal mobile phone exposure

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Abstract

Exposure of pregnant women to radiofrequency (RF) devices raises questions on their possible health consequences for their progeny. We examined the hazard threshold of gestational RF on the progeny's glial homeostasis, sensory-motor gating, emotionality, and novelty seeking and tested whether maternal immune activation would increase RF toxicity. Pregnant dams were daily restrained with loop antennas adjoining the abdomen (fetus body specific absorption rates (SAR): 0, 0.7, or 2.6 W/kg) and received three lipopolysaccharide (LPS) intra-peritoneal injections (0 or 80 µg/kg). Scores in the prepulse startle inhibition, fear conditioning, open field, and elevated plus maze were assessed at adolescence and adulthood. Glial fibrillary acidic protein (GFAP) and interleukines-1 β (ILs) were quantified. LPS induced a SAR-dependent reduction of the prepulse startle inhibition in adults. Activity in the open field was reduced at 2.6 W/kg at adolescence. GFAP and ILs, emotional memory, and anxiety-related behaviors were not modified. These data support the hypothesis that maternal immune activation increased the developmental RF exposure-induced long-term neurobiological impairments. These data support the fact that fetuses who receive combined environmental exposures with RF need special attention for protection.

Keywords Mobile phone · Radiofrequency · Neurodevelopment · Behavior · Sensori-motor processing · Locomotor activity

Introduction

Over the last several decades, radiofrequency electromagnetic field (RF-EMF) exposure has increased prominently due to the rapid development of technologies. Communication devices may adjoin the abdomen during pregnancy causing fetuses to absorb a significant amount of energy (Akimoto et al. 2010; Bellieni et al. 2012; Fiocchi et al. 2013; Varsier et al. 2014; Mortazavi et al. 2016). Previous reviews highlighted the need to investigate prenatal RF-EMF exposure on behavior

(Marino et al. 2011; Van Deventer et al. 2011). During development, the neural epithelium organizes into brain structures and determines most capabilities of the future organism to elaborate innate or acquired behaviors. Immature tissues may be particularly vulnerable to RF-EMF due to specific dielectric properties.

A link between environmental RF-EMF and early neurobiological deficits was reported by some epidemiological studies, but not all (Vrijheid et al. 2010; Guxens et al. 2016). Lower scores for verbal expression/comprehension or reduced visuomotor coordination were shown in children living in higher RF-EMF exposure areas (Calvente et al. 2015; Guxens et al. 2016). Divan et al. (2008) suggested that children's hyperactivity and emotional difficulties were linked to maternal cell phone use. Experimental studies indicated a deleterious effect of gestational exposure to Global System for Mobile Communications (GSM) signal on the trophoblast differentiation and migration and on the adolescent hippocampus, an area underlying cognition (Odaci et al. 2008; Bas et al. 2009a, b; Cervellati et al. 2009, 2013; Erdem Koc et al. 2016). Using different signals or devices, authors reported either impaired novelty processing and anxiety-related deficits or no

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measurable cognitive effect in adults (Bornhausen and Scheingraber 2000; Aldad et al. 2012; Zhang et al. 2015).

In recent studies using rodent models of neuro-inflammation, homeostasis disruption was suggested to enhance RF-EMF effects. Petitdant et al. (2016) reported that high-glial fibrillary acidic protein (GFAP) levels in the amygdala triggered a specific absorption rate (SAR)-dependent reduction of fear memory in adults. Lameth et al. (2017) showed that RF-EMF reduced the level of interleukin (IL)-1 β in lipopolysaccharide (LPS)-treated juvenile rats. Astrocytes and ILs play a determining role both in neuro-inflammation and in normal neuro-development on glia maturation and neuronal networks (Volterra and Meldolesi 2005; Bilbo et al. 2012; Bilbo and Schwarz 2012). In adults, they were shown to be affected by RF-EMF exposure (Mausset-Bonnefont et al. 2004; Bouji et al. 2012; Megha et al. 2012). Deficits in emotionality and prepulse inhibition, a process dedicated to prioritize sensory information and protect the brain against overstimulation, have been shown in individuals with schizophrenia and in progeny after maternal infection (Ornitz 1969; Rousset et al. 2006; Patterson 2009; de Souza et al. 2015). They frequently express at adolescence, a transient period for novelty seeking behaviors.

Because viral or bacterial infections leading to gestational homeostasis disruption are common, further investigations are needed on combined maternal RF-EMF exposures and inflammation. The present study aimed to test whether maternal immune activation would increase RF-EMF toxicity and looked for the hazard threshold of gestational RF-EMF on the progeny's glial homeostasis and ability for sensory-motor gating, emotionality, and novelty seeking.

High RF-EMF levels aimed to reproduce previous developmental studies (Petitdant et al. 2016). Pregnant rats were exposed to RF-EMF for the entire gestation period, to LPS on GD 15–19, or to the combined treatments. Endpoints were prepulse startle inhibition (PPI), fear conditioning (FC), open field (OF) and elevated plus maze (EPM) scores, and cerebral GFAP and IL-1 β levels.

Materials and methods

Animals

Seventy pregnant Sprague Dawley rats (Janvier, France) were single housed in the *vivarium* from GD 1 (12 h light/dark cycle, 22 °C room temperature, food and tap water ad libitum, enrichment with plastic cylinders). Weaned rats were housed two per cage. Protocols complied with the decree on vertebrate animal experiments (French State Council 1987) and were approved by the Regional Ethical Committee N. 96 (CREMEAP).

Experimental procedures

GD 1 dams were randomly assigned to one RF-EMF emission power group (0 (sham), 1 or 4 W) or to the cage control group (no daily restraint). Half of each RF-EMF group was randomly assigned to receive vehicle (saline) or LPS intraperitoneal injections (80 μ g/ml/kg, *E. coli*, serotype 055:B5, phenol extraction Sigma-Aldrich, MO) at GD 15, 17 and 19 ($n = 6$ –9/group). At birth, the number of pups per litter was recorded. At post-natal day (PND) 3, litters were adjusted to four males by reduction or adoption. Rats were randomly selected to assess cerebral markers at PND 7 and 21, fear conditioning (FC), contextual memory, elevated plus maze (EPM), open field (OF) tests, and cerebral GFAP and IL, either from PND 36 to 44 or 56 to 64 (Fig. 1).

RF-EMF exposures

A RF power source (900-64 type, generator RFPA S.A., RFS9001800-25 model, RF Power Amplifier, France) emitting a GSM 900 MHz EMF (1/8 duty factor) pulse modulated at 217 Hz was connected to a four-way divider. Each output was connected to a loop antenna (Leveque et al. 2004) that consisted of a two-metallic line circuitry printed on a dielectric substrate, which allowed four simultaneous abdomen-exposures in both the exposure and the sham anechoic chambers. A RF detector controlled incident and reflected powers. Exposures were performed daily for 45 min between 9:00 a.m. and 1:00 p.m. The rat body was restrained in cylinders (6 and 8 cm in diameter at GD 16 and GD 21) holed to minimize body temperature elevation. The head was inserted at restrainer end in a truncated cone to allow the animal to breathe. According to the finite difference time domain calculations, numerical dosimetry indicated 20 GD-averaged fetus whole body SAR of 0.7 ± 1.5 W/kg for 1 W and 2.6 ± 6 W/kg for 4 W emitting power. Data per GD and position in the uterine horn are given in Table 1.

Enzyme-linked immunosorbent assays

Standards and whole brain samples were assayed for GFAP using a sandwich ELISA assay according to Petitdant et al. (2016). IL-1 β was quantified according to the manufacturer's instructions of the commercialized kit for sandwich ELISA (Rat IL-1 β /IL-1 F2 DuoSet ELISA Development system, R&D systems).

Fear conditioning

The FC was monitored with apparatus and methods previously described by Petitdant et al. (2016) to pair a neutral conditioned stimulus (2 kHz, 100 dB sound pressure level tone) with an aversive unconditioned stimulus (0.25 mA foot

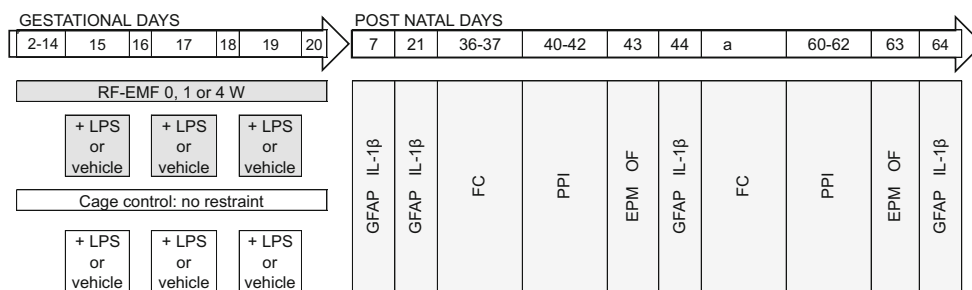


Fig. 1 Gestational treatment and post-natal test experimental design. Females received 19 RF-EMF exposures in restraint from GD 2 to GD 20 (0, 1, or 4 W) and three i.p. injections at GD 15, 17, and 19 (LPS or saline). Cage controls were not restrained. Two males per litter were

sacrificed to assess cerebral markers at PND 7 and 21. Behaviors were assessed in fear conditioning (FC), prepulse inhibition (PPI), the elevated plus maze (EPM), and the open field (OF) in independent groups of adolescents and adults

shock). Freezing was defined as complete immobilization of the rat, except for respiration (Blanchard and Blanchard 1969). Training consisted of a habituation period and five training cycles. Contextual memory was measured in the training boxes, 3 and 24 h, respectively, after the training for the short-term and the long-term tests. Cue memory was measured in modified training boxes.

Prepulse inhibition

PPI is the reduction of the whole-body reflex response to an intense sudden stimulus by a preceding weak stimulus (Hsieh et al. 2006). PPI was assessed in the same boxes (Panlab, Spain) as for fear conditioning in horizontal plastic cylinders (diameter, 6 cm) with a background white noise (60 dB). After habituation (5 min), five pulses (120 dB, 8 KHz, 40 ms) were delivered every 30 s followed by a cycle of 40 blocks of 30 s in a pseudorandom order: ten with the pulse (120 dB, 8 KHz, 40 ms), ten with a prepulse (75, 80, or 85 dB, 10 KHz, 20 ms), ten with the prepulse followed by the pulse (inter-stimulus-

interval, 80 ms), and ten with no sound. Startle amplitude was calculated per series of ten blocks and percentage of PPI with the startle amplitude to prepulse-pulse and to pulse.

Elevated plus maze and open field

EPM and OF were tested as previously described by Petitdant et al. (2016). Rats were placed for the first time in the OF apparatus to measure their activity related to a novel environment. Adaptation to novelty was assessed using horizontal activity on the ten last minutes of the OF test.

Statistical analyses

Means $\pm$ standard error was analyzed using SPSS Statistics 19 software (IBM, IL). RF-EMF, LPS, age, and restraint were considered as between-subject factors. Time, decibel, and litters were considered as within-subject factors. Restraint effect was measured by comparing cage controls and 0 W-exposed rats, and RF-EMF effect, with the 0, 1, and 4 W-exposed

Table 1 Whole body SAR calculated in the fetuses with the 1 and 4 W emission powers (respectively, numbers at the top and the bottom). Numerical dosimetry has been performed with the finite difference time domain method. Data are given for different gestational days between

GD6 and GD14 and for five positions of the fetuses in the uterine horn. The relative sizes and positions of the antenna (red bar) and the fetuses (spheres) were schematized for GD6 and GD14.

		(W/kg)	GD6	GD8	GD10	GD12	GD14	
Position in the uterine horn	5	0.9+/-0.3		0.8+/-0.3	0.3+/-0.2	0.2+/-0.1	0.08+/-0.05	
		3.4+/-1.1		3.1+/-1.2	1.2+/-0.8	0.7+/-0.5	0.3+/-0.2	
	4	0.8+/-0.2		0.8+/-0.3	0.7+/-0.3	0.5+/-0.3	0.4+/-0.2	
		3.1+/-0.8		3.2+/-1.0	2.7+/-1.2	2.0+/-1.1	1.4+/-0.8	
	3	0.8+/-0.3		0.8+/-0.2	0.8+/-0.2	0.8+/-0.3	0.7+/-0.3	
		3.0+/-0.9		3.1+/-0.9	3.2+/-0.9	3.1+/-1.2	2.6+/-1.2	
	2	0.9+/-0.5		0.9+/-0.4	0.9+/-0.3	0.9+/-0.3	0.9+/-0.3	
		3.4+/-2.1		3.5+/-1.6	3.4+/-1.2	3.5+/-1.2	3.5+/-1.3	
	1	0.6+/-0.3		0.7+/-0.3	0.7+/-0.3	0.9+/-0.3	0.9+/-0.3	
		2.2+/-1.2		2.6+/-1.1	2.8+/-1.2	3.5+/-1.3	3.7+/-1.3	

groups. Four-way ANOVA (on RF-EMF, LPS, age, memory type or decibel or time) and three-way ANOVA (on RF-EMF, LPS, PND) were performed. When there were significant effects, factors were tested separately with three-, two-, and one-way ANOVA. Main effects were analyzed using Bonferroni's post hoc corrected *t* test. Correlation (Pearson) was calculated in Fig. 6. Significance was set at $p < 0.05$.

Results

Gestational LPS teratologic effects

At birth, the number of pups per litter was not affected by RF-EMF ($F_{2,54} = 1.4$, $p = 0.3$) or RF-EMF $\times$ LPS interaction, but it was reduced by gestational LPS (-28% , $F_{1,54} = 8.2$, $p = 0.006$) (Fig. 2). There was no RF-EMF effect, LPS effect or interaction on pup's weight at birth (data not shown).

Age-related increase of cerebral IL-1 β and GFAP

The three-way ANOVA (on age, LPS and RF-EMF) did not show any effect or interaction other than an age-related increase of IL-1 β ($F_3, 126 = 31.7$, $p < 0.001$) and GFAP ($F_3, 126 = 11.4$, $p = 0.001$) (Fig. 3).

Age-related reduction of fear memory

Fear memory response was not affected by gestational RF-EMF, LPS, or their interaction but rather by age ($F_1, 266 = 7.1$, $p = 0.009$) and the type of memory ($F_2, 266 = 100$, $p = 0$) (Fig. 4). Percentage of time freezing was lower in the long-term memory test compared to the sound and short-term memory ($p < 0.05$) and less in adults compared to adolescents ($p < 0.05$).

LPS and RF-EMF interaction-related reduction of PPI

The startle was not modified by RF-EMF or LPS but rather by age ($F_1, 96 = 21.7$, $p < 0.001$), with a higher amplitude in adults compared to adolescents ($p < 0.001$) (Fig. 5). There was no effect of RF-EMF ($F_2, 288 = 0.3$, $p = 0.774$) or of LPS ($F_1, 288 = 0.4$, $p = 0.6$) on the percentage of PPI (Fig. 6). There was a decibel effect ($F_2, 288 = 58.7$, $p < 0.001$), an age effect ($F_1, 288 = 4.3$, $p = 0.04$), and an interaction between RF-EMF $\times$ LPS $\times$ age ($F_2, 288 = 3.2$, $p = 0.045$). Only in the adult LPS group, inverse correlation was significant between startle PPI and RF-EMF levels ($\text{cor} = -0.42$, $p = 0.03$) (Fig. 6). In the cage control adult groups, LPS reduced PPI compared to the vehicle group.

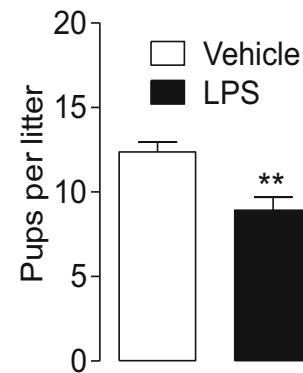


Fig. 2 Reduction of litter size by gestational LPS. Dams received LPS or vehicle at GD 15, 17, and 19. RF-EMF (antenna power 0, 1, or 4 W) and cage control groups were pooled. *** $p < 0.001$. $N = 32$ and 41

Intact anxiety-like behavior in the elevated plus maze

None of the gestational treatments (RF, LPS, and their interaction) or age and interactions affected the percentage of time spent in the open arm of the elevated plus maze ($p < 0.05$) (Fig. 7).

Effect of RF and LPS on locomotor activity

The four-way ANOVA performed on horizontal activity indicated no effect of LPS ($F_1, 78 = 0.7$, $p = 0.4$) or age ($F_1, 78 = 0.7$, $p = 0.4$) but did show significant effects of time ($F_5, 468 = 179.9$, $p < 0.001$), time $\times$ age interaction ($F_1, 468 = 5.7$, $p < 0.001$) and RF-EMF ($F_2, 78 = 5.1$, $p = 0.008$) (Fig. 8). Bonferroni post hoc indicated lower horizontal activity at 4 W emission power at 5 min compared to 1 W ($p = 0.04$) and at 20 min compared to sham ($p = 0.007$) in adolescents but not in adult rats.

There was no effect of RF-EMF or their interaction by age and LPS on adaptation (data not shown). Data were presented for restrained (all RF-EMF levels pooled) and non-restrained (cage control group) dams' progeny (Fig. 9). There was no effect of LPS, age, or their interaction on adaptation. In the progeny of non-restrained dams, there was a significant age $\times$ LPS interaction with LPS-treated adolescents which adapted more quickly (-26% horizontal activity on the 10 last minutes of the test) and LPS-treated adults, which adapted more slowly ($+29.5\%$ of activity in the 10 last minutes) compared to their respective vehicle-treated controls.

There was no RF-EMF effect, but a significant age effect ($F_1, 122 = 21.2$, $p < 0.001$) and LPS $\times$ age interaction ($F_1, 122 = 6.4$, $p = 0.02$) on vertical activity which was significantly increased in all adults compared to adolescents ($p < 0.05$) (Fig. 9a, b). Progeny of non-restrained LPS-treated dams showed a higher adult vertical activity by 48% compared to the vehicle-treated controls.

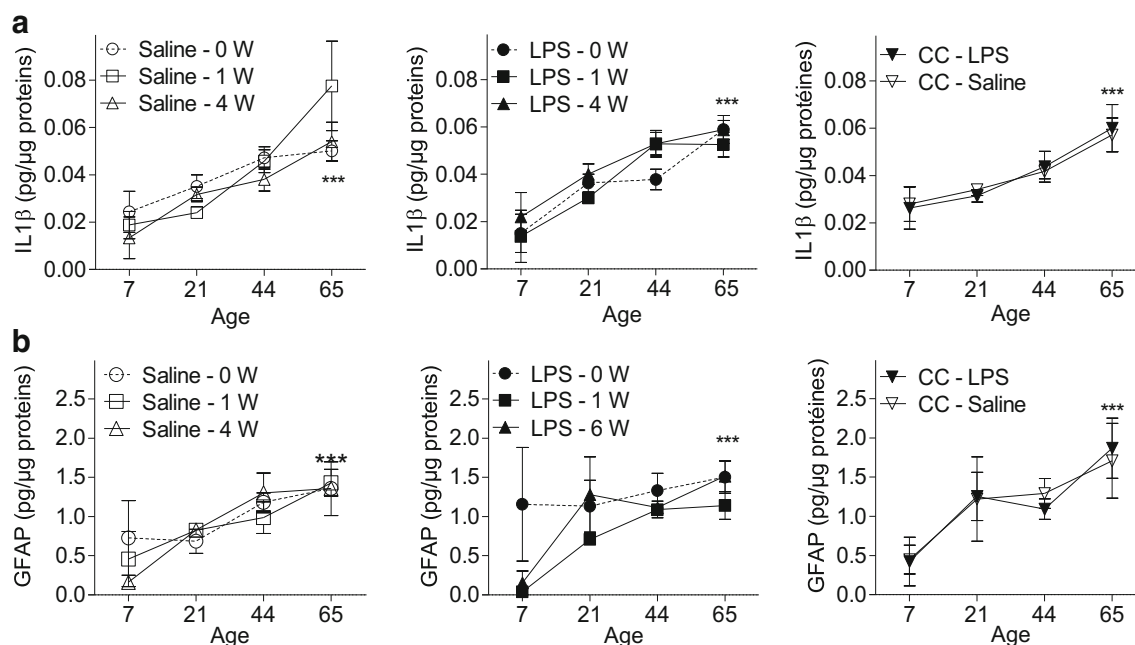


Fig. 3 Absence of effect of gestational treatments on cerebral IL-1 β (a) and GFAP (b). Dams received LPS or vehicle at GD 15, 17, and 19. They were exposed to GSM 900 MHz with restraint during the entire gestation period (antenna power 0, 1, or 4 W). Cage controls (CC) were not

restrained. Both markers increased from the juvenile period (PND 7) until adulthood (PND 65) but were not modified by gestational GSM, LPS, or restraint. *** $p < 0.001$ higher than PND7. $N = 5-9$ /group

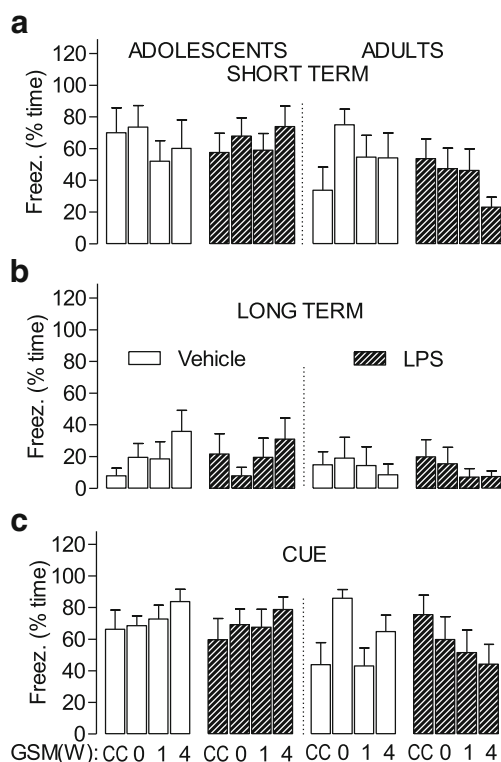


Fig. 4 a Short-term, b long-term, and c cue memory to fear conditioning. Dams received LPS or vehicle at GD 15, 17, and 19. They were exposed to GSM 900 MHz with restraint during the entire period of gestation (antenna power 0, 1, or 4 W). Cage controls were not restrained. $N = 6-9$ /group

There was no effect of LPS, RF-EMF, age, or their interaction on central activity ($p < 0.05$) (Fig. 9).

Discussion

In the present study, maternal immune activation triggered a SAR-dependent reduction of sensory-motor gating. Both maternal treatments induced a biphasic modification of novelty-related activity. Maternal RF-EMF reduced horizontal activity

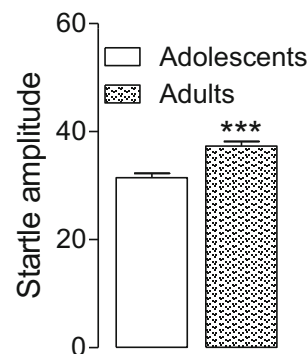


Fig. 5 Age effect on the startle reflex amplitude. Dams received LPS or vehicle at GD 15, 17, and 19. They were exposed to GSM 900 MHz with repeated restraint during gestation (antenna power 0, 1, or 4 W). Cage controls were not restrained. RF-EMF (antenna power 0, 1, or 4 W), LPS, and cage control groups were pooled. *** $p < 0.05$ higher in adults than adolescents. $N = 61-62$ /group

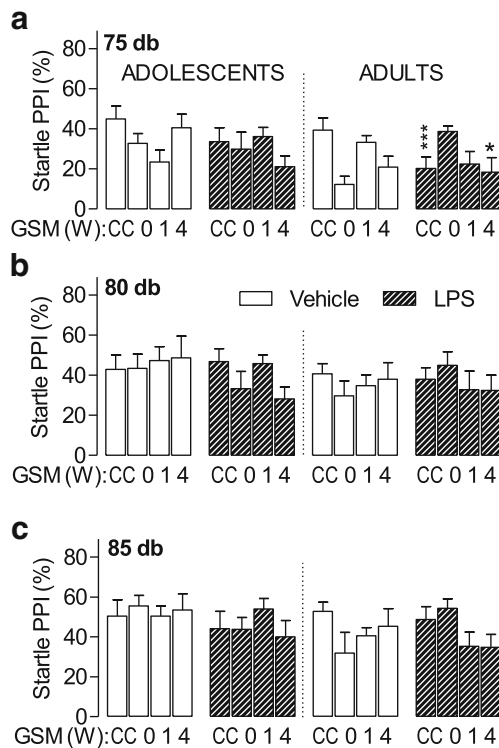


Fig. 6 **a** 75, **b** 80, and **c** 85 dB prepulse inhibition of the startle reflex in adolescent and adults after gestational exposure to GSM and LPS. Dams received LPS or vehicle at GD 15, 17, and 19. They were exposed to GSM 900 MHz with restraint during the entire period of gestation (antenna power 0, 1, or 4 W). Cage controls were not restrained. * $p < 0.05$ compared to sham controls. *** $p < 0.001$ compared to adolescents. $N = 6-9/\text{group}$

in adolescents while it did not affect adult scores. Activity after maternal immune activation without restraint was reduced in adolescents and increased in adults.

Here, antennas were placed on the body during the entire gestation period to mimic cell phone use with a hands free kit and its carriage in bags or pockets. litter-averaged SAR peaked in the first half of gestation confirming previous data in rats and humans (Aït-Aïssa et al. 2010; Varsier et al. 2014). With the higher emission power, SAR averaged on the entire

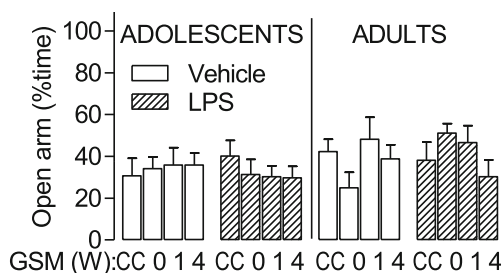
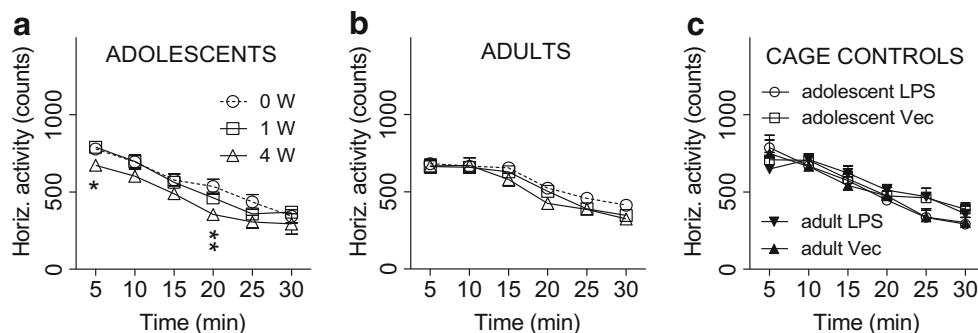


Fig. 7 Anxiety-related behavior in adolescents and adults after gestational exposure to GSM and LPS. Dams received LPS or vehicle at GD 15, 17, and 19. They were exposed to GSM 900 MHz with restraint during the entire gestation period (antenna power 0, 1, or 4 W). Cage controls were not restrained. $N = 6-9/\text{group}$

gestation period was equivalent to the International Commission for Non-ionization Radiation Protection limits for local exposures set at 2 W/kg.

Gestational LPS, which cannot cross the blood-placental barrier, is known to induce the systemic activation of the maternal immune system involving production of pro-inflammatory cytokines, toxic for the developing fetal brain (Dammann and Leviton 2000; Ashdown et al. 2006; Meyer and Feldon 2009; Boksa 2010; Oskvig et al. 2012). In comparison to the literature, a lower LPS dose was used to avoid dam's death, which probably explains negative results in several behavioral outcomes. Indeed, sensorimotor gating deficits highly differ with timing, dose, and route of LPS administration (Borrell et al. 2002; Romero et al. 2007, 2010). In our immune-activated maternal model, PPI was not disturbed because of a sub-threshold LPS dose. PPI was not impacted by gestational GSM alone either but showed a SAR-dependent reduction selectively in the immune activated model. Capacity to detect the auditory stimulus and ability to elaborate the motor response were probably not impaired as the cochlear function was previously shown not to be affected by intra-uterine RF-EMF (Budak et al. 2009) and as the startle reflex generated by motor neurons was similar in all groups. Sensory information filtration involves the caudal pontine reticular nucleus (PnC), which receives both the pulse and the prepulse signals from distinct neural circuitries. The prepulse information is transmitted through the inferior and superior colliculi and the pedunculopontine tegmental nucleus (Li et al. 2009). Efficiency of this circuitry may rely on neurodevelopment processes which were impaired by the combined maternal LPS and RF-EMF exposures. One may hypothesize that behavioral deficits may result from less effective glutamatergic or GABA neurotransmissions, previously shown after RF-EMF (Mausset et al. 2001; Mausset-Bonnefont et al. 2004; Aldad et al. 2012; Zhao et al. 2012) and after LPS (Kentner et al. 2016; Batinic et al. 2017). It may involve abnormal myelination or synaptic plasticity. One possible developmental mechanism may implicate fetus temperature increase described with both maternal fever and RF-EMF exposure (Hart and Faber 1965; Fiocchi et al. 2013). Moreover, embryonic stem cells and cellular events in newborn are sensitive to physical and environmental factors (Kaplan et al. 2016). RF-EMF effects were described on several mechanisms underlying brain structure and function integrity. Previous studies report RF-EMF effects on neuronal and glial cell proliferation and differentiation, neurogenesis, and apoptosis, as well as cell cytoskeleton, calcium homeostasis, reactive oxygen species production, and inflammatory cytokine system (Çelik et al. 2016; Dasdag and Akdag 2016; Altunkaynak et al. 2016; Kaplan et al. 2016). Impaired sensory filtration may predict health impact and social inadaptation in adults with disturbed abilities to generate adapted responses to the environment. This deficit is common in schizophrenia.

Fig. 8 Horizontal activity in the open field in **a** adolescents, **b** adults, and **c** cage controls. Dams were exposed to GSM 900 MHz (antenna power 0, 1, or 4 W) with repeated gestational restraint. LPS and vehicle groups were pooled. * $p < 0.05$, ** $p < 0.01$ lower in 4 W compared to other levels. $N = 12$ –18/group



Accordingly, previous studies reported structural alteration and loss of function in the frontal cortex, brain stem, and cerebellum after RF-EMF exposures and reduced neurocognitive performances linked to heavy cell phone use in young people (Altunkaynak et al. 2016; Deniz et al. 2017).

Maternal RF-EMF induced a SAR-dependent reduction of horizontal activity to the presentation of the novel environment in adolescents. This effect was absent in adults, which may suggest an impairment of adolescent-typical novelty-seeking behavior through maturing midbrain systems. Two previous studies did not indicate any impairment probably because of their different sequence of repeated behavioral tests (Cobb et al. 2000; Zhang et al. 2015).

Further OF responses were observed only in the progeny of cage control dams, suggesting that daily restraint-related gestational stress probably affected pup's scores. The biphasic alteration on adaptation to novelty, which was faster in adolescents and slower in adults, may indicate that gestational LPS impaired mature and maturing prefrontal retro-control mechanisms. Adult increased interest for vertical exploration suggested repetitive behaviors or impulsivity, mediated through abnormal dopaminergic systems. One may hypothesize subtle manifestation of a stereotypy as previously shown by autistic behaviors (including grooming and stereotypies) after maternal LPS injection (Kirsten and Bernardi 2017).

Impaired emotionality was previously reported in mice at higher frequencies (9 GHz) (Zhang et al. 2015) or using high-LPS doses (Bilbo et al. 2005; Paintlia et al. 2008). Probably due to different LPS doses and EMF signals, none of the maternal treatments impacted emotionality, in concordance with our previous study (Petitdant et al. 2016).

In the same way, long-term GFAP reactivity was reported in specific brain areas using high-LPS doses (Bilbo et al. 2005; Paintlia et al. 2008; De Souza et al. 2015). Here, none of the maternal treatments modified over time IL and GFAP increases from birth until adulthood, confirming the absence of a long-lasting effect of developmental RF-EMF (Watilliaux et al. 2011; Lameth et al. 2017) or LPS (Petitdant et al. 2016).

This study also afforded evidence for teratotoxicity induced by gestational LPS as previously shown by Petitdant et al. (2016), while gestational RF-EMF had no effect. It confirmed previous studies (Klug et al. 1997; Poulietier de Gannes et al. 2012) and may suggest confounding factors in the epidemiological association between early spontaneous abortions and mobile phone use during pregnancy (Mahmoudabadi et al. 2015).

To conclude, our study is the first to highlight gestational inflammation-induced vulnerability towards RF-EMF exposure on the ability to filtrate sensory information. Cerebral impairments were SAR-dependent supporting the causal relationship between EMF-RF exposure and deficits. RF-EMF levels tested in this study may surround the possible toxic threshold for gestational RF-EMF. These data with those of other studies support the fact that special attention should be

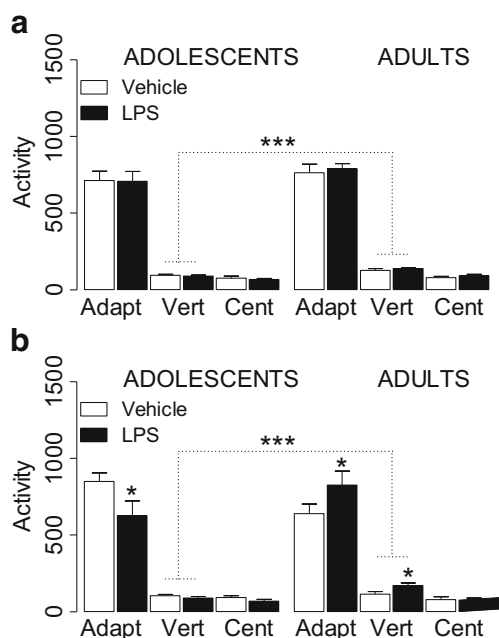


Fig. 9 LPS effect on adaptation to a novel environment, vertical activity, and central activity in the progeny of **a** restrained and **b** non-restrained pregnant rats. Dams received LPS or vehicle at GD 15, 17, and 19. Exposed groups with antenna powers set at 0, 1, or 4 W were pooled. In non-restrained rats, gestational LPS increased adaptation of the progeny at adolescence. Adults showed slower adaptation and increased vertical activity. * $p < 0.05$ compared to the vehicle group. *** $p < 0.001$ age-effect. $N = 6$ –9/group

devoted to the protection of embryos and fetuses that can be co-exposed to environmental factors and EMFs at diverse frequencies and intensities.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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