

Materials and methods In this project, we are using hippocampal neurons derived from human induced pluripotent stem cells (hiPSCs) to assess the effects of a chronic treatment of BPA and substitutes at cellular and molecular levels.

Results and discussion Inhibition of WNT, TGF β and BMP signalling pathways, followed by WNT activation, induces differentiation of hiPSCs into hippocampal neural progenitors (hNPCs) within 28 days. BDNF treatment promotes neuronal maturation. RT-qPCR analyses showed that hiPSCs expressing octamer-binding transcription factor 4- (OCT-4) differentiated with high efficiency into hNPCs, expressing NESTIN and hippocampal progenitor markers prospero homeobox 1 (PROX1) and zinc finger and BTB domain containing 20 (ZBT20). Neuronal marker microtubule associated protein 2 (MAP2), and hippocampal markers ELAV like RNA binding protein 2 (ELAVL2) and glutamate ionotropic receptor kainate 4 (GRIK4) were expressed in mature neurons at day 43. hNPCs were treated chronically (14 days) with increasing concentrations (0.001, 0.01, 0.1, 1, 10, and 100 μ M) of BPA and substitutes BPAP, BPE and BPZ. All bisphenols showed a concentration-dependent decrease in cell viability, with a significant decrease at 100 μ M for BPA, BPAP and BPZ and from 10 μ M for BPE. Then, hNPCs were treated with non-toxic doses for 14 days. RNA has been extracted, and gene expression analysis of potential key gene targets is underway. Immunocytochemistry for β -III tubulin has been performed to analyze neuronal morphology. Protein levels of presynaptic and postsynaptic markers will also be quantified to measure the impact of treatments on synaptic plasticity.

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Representation of endocrine organs in TCDD physiologically-based toxicokinetics (PBTk) models

Argyro Nikolaou^{a,*}, Caroline Flora Samer^{a,b}

^a Division of Clinical Pharmacology and Toxicology, Department of acute care medicine, Geneva University Hospitals, Geneva, Switzerland

^b Department of Anaesthesiology, Pharmacology, Intensive Care and Emergency Medicine, Faculty of Medicine, University of Geneva, Geneva, Switzerland

* Corresponding author.

E-mail address: argyro.nikolaou@hug.ch (A. Nikolaou)

Introduction Endocrine disruptors (EDCs) are common environmental contaminants with concerning effects on multiple biological systems, notably the endocrine system [1]. Dioxins, a well-known class of EDCs, have been associated with thyroid and reproductive disorders in humans [2,3]. Among them, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is most toxic, characterized by its persistence and bioaccumulation due to its lipophilic nature. Understanding TCDD toxicokinetics is crucial for assessing its health risks. Given its complex metabolism [4], physiologically-based toxicokinetics (PBTk)—an extension of physiology-based pharmacokinetic (PBPK) models—provide an in silico approach to estimate xenobiotics kinetics using in vitro and in vivo data. We reviewed the existing PBTk models for TCDD, with a particular focus on the inclusion of endocrine organs.

Methods A systematic search was conducted in Pubmed, EMBASE and Google Scholar for PBTk models published up to October 2024. A total of 408 articles were identified, of which 31 met the inclusion criteria for review.

Results The majority of PBTk models did not explicitly account for endocrine tissues. Instead, they broadly categorized organs as either slowly or richly perfused. Only a few models incorporated endocrine related structures, with the placenta included in three models and the mammary gland in two.

Conclusions No PBTk models have independently assessed endocrine organs such as the thyroid, testis, or ovaries in the context of TCDD toxicokinetics. Given the mounting evidence of EDC-related health effect, integrating endocrine organs into PBTk models could enhance our understanding of EDC toxicokinetics and their adverse effects.

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Histomorphometric study of thyroid tissue in juvenile rats exposed to 5G electromagnetic fields

Mathilde Ramelet^{a,b,*}, Lise Ronger^{a,b}, Abdallah Al-Salameh^{a,b}, Amandine Pelletier^b, Rachel Desailoud^{a,b}, Chandreshwar Seewooruttun^b

^a Service d'endocrinologie-diabétologie-nutrition, CHU Amiens

Picardie, rue du Professeur Christian Cabrol, 80000 Amiens, France

^b Laboratoire PériTox UMR J01, Université Picardie Jules Verne, CHU Amiens-Picardie, avenue René-Laënnec, 80054 Amiens, France

* Corresponding author.

E-mail address: ramelet.mathilde@chu-amiens.fr (M. Ramelet)

Introduction 5G network deployment raises the issue of the health impact of these electromagnetic fields. Their effect on thermal regulation is of a “cold response” type. In rats exposed to 900 MHz, vasoconstriction was induced in the tail, with behavioral preference for warmer compartments. The hypothalamo-pituitary-thyroid axis is involved in thermogenesis: in response to cold, thyroid activity increases, stimulating heat production.

Objective To assess thyroid activity after 5G exposure.

Method Ten 3-week-old male Wistar rats were randomized between 2 weeks' 5G exposure at 3.5 GHz and 1.5 V/m (5G group; $n=5$) and no exposure (controls; $n=5$). After sacrifice, the thyroid gland was harvested for histomorphometry. Thyroid follicle and colloid areas were measured and the thyroid activation index (TAI: ratio of follicle to colloid area) was assessed.

Results Follicle and colloid areas were significantly greater in 5G (2729 μ m² vs 2444 μ m², $P=0.0063$; and 1317 μ m² vs 1015 μ m², $P=0.0027$ respectively) and TAI was significantly lower (5.62 vs 7.07, $P<0.001$). These results indicate thyroid hypoactivity.

Discussion There was a 5G effect, with histomorphometry demonstrating thyroid hypoactivity, suggesting mechanisms different from those underlying cold response. Impact of electromagnetic fields on thyroid function was previously reported, but results were heterogeneous and discordant depending on the type of exposure.

Conclusion TSH and thyroid hormone assays are underway to reinforce assessment of thyroid function. Further studies are needed to explore the underlying mechanisms.

Keywords Electromagnetic fields; 5G; Thyroid; Thyroid activation index

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Impact of moderate iodine deficiency on embryonic exposure to a mix of endocrine disruptors

Patricia Rannaud-Bartaire^{a,b,*}, Sébastien Le-Mével^a, Manon Bonnelle^a, Jean-Baptiste Fini^a

^a Muséum national d'histoire naturelle/CNRS laboratoire PHYMA UMR7221, Paris, France

^b Hôpital Saint-Vincent de Paul, GHICL/université catholique de Lille, boulevard de Belfort, 59000 Lille, France

* Corresponding author.

E-mail address: Bartaire.patricia@ghicl.net (P. Rannaud-Bartaire)

Objective We tested the hypothesis that moderate iodine deficiency (still frequent despite iodine supplementation of table salt since the 1970s in France) during gestation aggravates the action of endocrine disruptors (EDs) on thyroid hormone (TH) function. Some EDs interact at various levels with the thyroid system, inducing compensatory TH production, drawing on iodine reserves.

Material and method *Xenopus tropicalis* embryos were exposed from cell-stage 2 to end of neurogenesis to a mix of 14 EDs previously shown to impact TH, cell proliferation and neuron differentiation. The embryos were further exposed to sodium perchlorate 20 mg/L in the fluid, to mimic moderate iodine deficiency. We assessed cerebral gene expression on qPCR, proliferation/apoptosis ratio on brain immunohistochemistry, and behavioral impact on tadpole motion.

Results Expression of key TH axis genes was more severely inhibited under moderate iodine deficiency combined to EDs than under deficiency or EDs alone. Combined exposure also impaired tadpole motion and brain-cell proliferation.

Discussion Even moderate iodine deficiency can aggravate the effects of a pollutant mix on the thyroid axis during critical phases and notably during embryonic development. These results suggest that it is important to limit exposure to chemicals, and also to take account of all components of the exposome that are liable to aggravate impact.

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Pour en savoir plus

Fini et al. 2017.

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The effect of a therapeutic dose of folic acid after bariatric surgery and its impact on mental well-being

Natia Romashvili*, Nino Chochidze

Department of bariatric and metabolic surgery, L.T.D AVERSI CLINIC, Tbilisi 0160, Georgia

* Corresponding author.

E-mail address: natiaromashvili@yahoo.com (N. Romashvili)

Objective This study will examine the role of folic acid in bariatric patients and its impact on psychological health. A mixed methods approach will be used to gain a deeper understanding of how this B9 regulation affects individuals' attitudes, mental states, and behaviors. The results of this study aim to raise awareness of the value of B9 in long-term weight-related challenges and provide valuable information on health.

Methods The study will utilize a mixed-methods approach, combining quantitative surveys with qualitative interviews to assess quality. The study was conducted in the bariatric surgery depart-

ment of Aversi Clinic in 2021–2024. Sixty patients were divided into two groups. In the first group, folate levels were determined before surgery and during shortages treatment was started at 800 mcg per day. In the second group, B9 was not prescribed before surgery, so they did not take in a therapeutic dose for the first month.

Results As a result of observation and data analysis, it was revealed that, in the first group of patients, 76%, who received therapeutic doses of B9, the postoperative period was calm, anxiety was not detected at a high rate; also, depression was detected in only four patients, and adherence to the post-bariatric diet and recommendations was high. In the group that did not receive folic acid, 63%, relatively high anxiety and depression were observed. As for the result, it was more or less satisfactory.

Conclusion This study aspires to identify sustainable strategies for maintaining how B9 can play an important role in enhancing both physical and mental health, ultimately contributing to successful and enduring weight loss during surgery. Therefore, based on the data obtained, it can be assumed that the research design, which aimed to determine B9's role, was evident even in a small study; which also increased the achievement of treatment results and patient compliance.

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Transcriptomic study of adrenal stress genes in rats exposed to 5G electromagnetic fields

Lise Ronger^{a,b}, Mathilde Ramelet^{a,b}, Amandine Pelletier^b, Rachel Desailoud^{a,b}, Abdallah Al-Salameh^{a,b}, Chandreshwar Seewooruttun^{b,*}

^a Service d'endocrinologie-diabétologie-nutrition, CHU Amiens-Picardie, rue du Professeur Christian Cabrol, 80000 Amiens, France

^b Laboratoire PériTox UMR_I01, université Picardie Jules Verne, CHU Amiens-Picardie, avenue René-Laënnec, 80054 Amiens, France

* Corresponding author.

E-mail address: chandreshwar.seewooruttun@u-picardie.fr (C. Seewooruttun)

Introduction The biological effects of 5G electromagnetic fields on living organisms are poorly understood. Studies suggested that exposure to radio frequencies, and notably 2G fields (900 MHz), may alter the structure and function of the adrenal glands, impacting hormonal response to stress. The effect of 5G fields (3.5 GHz) on these mechanisms, however, is not known.

Objective To assess the impact of exposure to 2G and 5G electromagnetic fields on the expression of genes involved in the adrenal stress response in rats at different developmental stages.

Material and methods Male Wistar rats were divided into 2 age groups: juveniles (3 weeks) and young adults (8 weeks). They were exposed to 900 MHz (2G) and 3.5 GHz (5G) electromagnetic fields at an intensity of 1.5 V/m in 2 daily 1-hour sessions, for 2 weeks. Expression of adrenal stress genes (CH25H and StAR) and corticosteroidogenic enzymatic cofactors (CYP-11a1, CYP-21a1 and HSD-3b1) was assessed on RT-qPCR.

Results No significant changes in transcriptomic expression were observed, whatever the developmental stage or exposure intensity. Grouping the animals by exposure condition revealed no significant effect of electromagnetic fields on the adrenal markers studied (Figure 1).

Discussion and conclusion Contrary to some studies suggesting an effect of radio frequencies on adrenal function, in the present study 2-week exposure to 5G or 2G fields did not alter the expression of stress genes. It would be useful to explore longer exposure and higher intensity to assess possible long-term effects and reproduce real-life conditions of exposure to electromagnetic fields.