SCIENTIFIC SESSION II Ongoing Experimental Studies at the Ramazzini Institute

- 1. The contribution of in vivo experimental research to the knowledge of adverse effects of RFR on human health *Fiorella Belpoggi, Italy*
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The contribution of in vivo experimental research to the knowledge of adverse effects of RFR on human health

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Background: The proliferation of cellular antennas and other radiofrequency radiation (RFR) generating devices of the last decades has led to more and more concerns about the potential health effects from RFR exposure. Since the 2011 classification as probable carcinogen by the International Agency for Research on Cancer (IARC), more experimental studies have been published that support a causal association between RFR exposure and health hazards.

Methods: We reviewed the results of both the carcinogenic and the reproductive/developmental hazards of RFR emerged from in vivo experimental studies on mammals.

Results: As regard cancer risk, two long-term experimental studies have been recently published by the US National Toxicology Program (NTP) and the Italian Ramazzini Institute (RI). Despite important experimental differences, both studies found statistically significant increases in the development of the same type of very rare glial malignant tumors. In addition to carcinogenicity, reproductive organs might be particularly exposed as well as sensitive to RFR: Seminiferous tubules, spermatozoa and Leydig cells are the main targets of this damage, and sperm count, motility and morphology represent the more frequently affected parameters.

Conclusions: According to NTP there is now clear evidence that RFR causes cancer in experimental animals. RFR re-evaluation have been also listed as a priority by IARC [101]. There is also stronger evidence that RFR exposure is responsible for causing alteration of various sperm parameters, thus affecting male fertility. Although a clear quantification of the carcinogenic and reproductive risk is still lacking, these animal findings suggest that precautionary approach should be promoted by regulatory and health agencies, specially for children and pregnant women. Caution should also be considered in the development and spread of the upcoming 5G technology, particularly in light of the proposed higher frequencies and intensities of the signal. Long-term animal studies are urgently necessary to verify the possible health effects

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New evidence on the effects of glyphosate exposure from in vivo studies and a historical agricultural cohort

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Background: The current toxicologic in vivo assessment of chronic, low level glyphosate-based herbicide (GBHs) exposure in rats represents the first phase of the Global Glyphosate Study. Additionally, to assess historical glyphosate exposure in humans, we examined urine samples from a biorepository of specimens collected from US dairy farmers between 1997 and 98.

Methods: We treated Sprague-Dawley (SD) rats with glyphosate alone or its formulation Roundup Bioflow starting from prenatal life until adulthood with a dose of glyphosate equivalent to the United States Acceptable Daily Intake (US ADI) of 1.75 mg/kg bw/day, administered orally via drinking water. Using a standardized protocol for LC-MS/MS performed on blinded samples by a certified commercial laboratory, we compared urinary concentrations of glyphosate and AMPA in urine from farmers who self-reported glyphosate application in the 8h prior to sample collection to samples from farm applicators who did not report using glyphosate (LC-MS/MS).

Results: Exposure to GBHs at doses considered safe in humans (US ADI) altered the gut microbiota of rats in early development, particularly before the onset of puberty. Exposure to GBHs was also associated with a statistically significant increase in micronuclei, statistical significant increase of anogenital distance (AGD) in males and females, delay of first estrous and increased testosterone in females.

Of 18 farmer samples tested, 39% showed detectable levels of glyphosate (mean concentration 4.04 μ g/kg; range: 1.3-12) compared to 0% detections among 17 non glyphosate applicator samples (p-value < 0.01).

Conclusions: The pilot phase of the Global Glyphosate Study revealed that GBHs were able to alter certain important biological parameters, mainly relating to sexual development, genotoxicity and the alteration of the intestinal microbiome. Whereas recent exposure assessment studies have demonstrated GBH exposure in contemporary samples of humans exposed either occupationally or environmentally, these data provide an historical perspective, showing glyphosate exposures were occurring occupationally 20 years ago.

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Effects caused by pesticides on the the historical cohort of the Patecipanza Agraria in Emilia Romagna

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The Partecipanza Agraria (Agricultural Participation) is an ancient form of collective ownership of land involved in land reclamation, which originates from the Middle Ages , still in use in Emilia-Romagna and Veneto in the Polesine di Rovigo. The genetic background of the Partecipanza Agraria of the Emilia Romagna region have been extensively studied by the University of Bologna.

Methods: The study will involve at least 100 adult male subjects over 55 years of age from the Partecipanza Agrarie of the Emilia Romagna, including Cento and Sant'Agata Bolognese. The levels in the urine of the following pesticides will be screened: Glyphosate, Boscalid, Azoxystrobin, Imidacloprid. The subjects will undergo a yearly detailed anamnestic, laboratory and imaging investigation in order to assess their health status.

Results: Now the Ramazzini Institute aims to study the burden of exposure and the effects of pesticides in the Partecipanza Agraria of the Emilia Romagna and provide, in collaboration with the University of Bologna, a comprehensive analysis of the interplay between genetics and environmental exposures in this population.

Conclusions: The Ramazzini Institute aims to establish a longitudinal study on the effects of pesticide in the historical cohort of the Partecipanza Agraria. The support form Horizon 2020 and other local and international funders will be fundamental to support the study long-term and extend the study to more individuals of the Partecipanza Agraria of the Emilia Romagna region.

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