FSM | Forschungsstiftung
Strom und Mobilkommunikation
FSM | Swiss Research Foundation for
Electricity and Mobile Communication

+41 44 632 28 15
info@emf.ethz.ch
emf.ethz.ch

Final Report

Project reference: FSM A2017-3
Applicant's name: Schürmann David, Ducray Angélique
Project title: Impact of mobile communication signals on the regulation of neural differentiation

1. State of Research.

1.1 Research activities performed, milestones and deliverables accomplished

In this explorative project, we executed mainly research activities towards objectives/tasks 1-3 of the proposal.

Objective 1: Evaluation of the impact of RF-EMF on neural differentiation.
Objective 2: Investigation of cellular signaling pathways and altered expression.
Objective 3: Analysis mitochondrial activity as indicator of neuronal aging and degeneration.
Objective 4: Exploration of epigenetic modifications of neural marker and identified target genes.

Since no indication for substantial changes of neuronal differentiation was identified on the level of morphology as well as expression of neural markers and novel target genes, we omitted extensive investigation of epigenetic modifications (objective 4) because they correlate with gene activity.

We adapted the project to compensate for the tasks related to objective 4 of our project; not only experiments with GSM-modulated RF-EMF but also with UMTS exposure were performed, and the assessment of the neural differentiation process was expanded to earlier developmental stages. These decisions and adaptations were made according the Milestones M1 and M3 of the project proposal. The reasons for these corrective actions were our findings that the confirmation of GSM exposure effects were ambivalent and signalling pathways related to differentiation/neurodegeneration were not significantly altered. In respect to the choice of model cell system for global analyses (Milestone M2), we evaluated and applied a model cell system for *in vitro* neurogenesis based on mouse embryonic stem cells since human and murine neuroblastoma cells (SH-SY5Y, N1E-115, Neuro2A,…) appeared to be little and/or not reliably responsive to RF-EMF exposure.

1.2 Findings

The detailed experimental data and conclusions of this project are provided in the publication by von Niederhäusern *et al.* 2019, in our intermediate project report in 2019, in the FSM annual report 2021 and in the attached master thesis work by Thimo Müller. Key findings/conclusions of our projects are provided narratively below, listed in relation to our project tasks:

- Task 1: Morphological and molecular analysis of neuronal differentiation under RF-EMF exposure
  - No reproducible effect of GSM exposure (1.95 GHz, 4 W/kg SAR) of N1E-115 neuroblastoma cells on neurite outgrowth
  - No impact of GSM RF-EMF exposure (935 MHz, 4 W/kg SAR) on the differentiation of SH-SY5Y neuroblastoma cells induced by retinoic acid or staurosporine
  - Absence of evident morphological effects of UMTS exposure (1.95 GHz, 5 W/kg) on neural differentiation of murine embryonic stem cells
  - No hints towards a proportional alteration of cell stages/types in differentiating cell populations (lineage commitment of embryonic stem cells, differentiating SH-SY5Y neuroblastoma cells to cholinergic and dopaminergic neurons)
- Task 2: Analyses of pathways and gene expression
  - No significant difference in signalling pathways (Erk1/2, Akt, GSK3β, β-catenin/Wnt) upon GSM exposure (935 MHz, 4 W/kg SAR) in SH-SY5Y cells, yet some trends were discernible
  - Global gene expression analysis of lineage-committing embryonic stem cells did not provide indications for altered signalling cascades/down-stream target genes of UMTS exposure (1.95 GHz, 5 W/kg SAR)
  - Little indication for impact of UMTS exposure on neural differentiation/marker gene expression
  - Some indication for temporary altered marker gene expression during lineage commitment in early phases of differentiation

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- Task 3: Mitochondrial activity
  - RF-EMF exposure (GSM, 935 MHz, 4 W/kg SAR) altered significantly mitochondrial respiration of glucose-deprived but not non-stressed undifferentiated and staurosporine-differentiated SH-SY5Y neuroblastoma cells
  - Upon GSM exposure, some trends but no statistically significant changes of mitochondrial integrity (Mfn2, OPA1) were found in differentiating SH-SY5Y cells
  - No significant effects of GSM exposure (1-4 W/kg SAR) on oxidative stress (GSH level)

Overall, we conclude that the data obtained in our project provides little evidence for a substantial impact of RF-EMF exposure on neural differentiation. Yet, there are some observations of consistent but mostly not statistically significant effects, for instance restricted to certain experimental conditions such as stress or cell type, which require further investigations.

1.3 Problems

Being aware of the risk of our explorative research project, we have previously defined alternative line of action in our milestone and could react accordingly to upcoming research and financial problem. In the end, most of our tasks could be successfully executed and finished. There was a substantial delay in the execution of the task by the project partner in Basel, partly due to issues with the initial recruitment of a suitable scientist and the pandemic situation. However, this delay did not interfere with the project's objectives as additional resources could be re-allocated.

2. Annex

2.1 Publications

A paper with the results obtained in the lab in Bern (Applicant 2) was published in 2019.

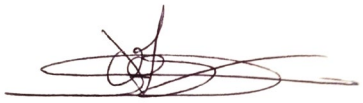
> von Niederhäusern N, Ducray A, Zielinski J, Murbach M, Mevissen M. **Effects of radiofrequency electromagnetic field exposure on neuronal differentiation and mitochondrial function in SH-SY5Y cells**. Toxicology In Vitro. 2019 Jul 24;61:104609. doi: 10.1016/j.tiv.2019.104609.

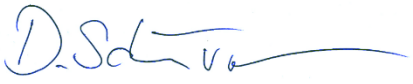
2.2 Documents

Experimental data obtained in the lab in Basel (Applicant 1) are compiled in the attached master thesis work of Thimo Müller. This work is currently for internal use only but will eventually be publically available. We intend to continue investigating some observation beyond the scope of this project and perform a more in-depth analysis of our single-cell expression data.

Date and Signature

24.09.2021





Angélique Ducray,

David Schürmann