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Report on the Short Term Scientific Mission ""Time-series and panel data analysis applied to the Tinnitus Database" (COST-STSM-BM1306-30328) of Jan Bulla
BMBS COST Action BM1306

1. Purpose of your mission

The STSM had two main purposes. First, the application of appropriate statistical methods to the Tinnitus Database (a large database of clinical tinnitus data, maintained at Regensburg, see Landgrebe et al. 2010). Secondly, the training of colleagues from Regensburg in statistical analysis methods. In the following, we illustrate these two scopes more detailed.

1. **Primary aim** of the STSM was the application of statistical methods belonging to the field of time-series and panel data analysis to the tinnitus database. Focus was the selection and application of appropriate statistical methods which permit the identification of factors mediating and/or moderating the relief of tinnitus. Additional focus was lying on a specific data set, gained from a study on repetitive transcranial magnetic stimulation (rTMS) stimulation combined with relaxation techniques.
   Furthermore, we aimed to discover potential shortcomings of existing statistical methods, and determine possible future paths. This could, inter alia, lead to the development of suitable statistical approaches tailor-made for the particular tinnitus data analysed.
2. **Secondary aim** of the STSM was the promotion of interdisciplinary exchange by joint work on various data sets. This was supposed to be carried out during a small workshop on time-series and panel data analysis in the medical domain. During the workshop, the colleagues from Regensburg were supposed to receive training in statistical analysis via the software package R (R Development Core Team 2015).

Landgrebe M., Zeman F., Koller M., Eberl Y., Mohr M., Reiter J., Staudinger S., Hajak G., Langguth B. (2010), 'The Tinnitus Research Initiative (TRI) database: A new approach for delineation of tinnitus subtypes and generation of predictors for treatment outcome', *BMC Medical Informatics and Decision Making* 10, 42–7.

R Development Core Team (2015), 'R: A language and environment for statistical computing', *R Foundation for Statistical Computing*, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org.

2. Description of the work carried out during a mission

- The following colleagues from Regensburg received the training in advanced statistical methods described within the secondary aim described above (see Section 1.): Martin Schecklmann, Astrid Lehner, Winfried Schlee. The works were carried out in form of several small joint sessions, but also on individual basis.
- We analysed of a data set on combined treatment approach integrating rTMS and a variety of relaxation techniques in patients with chronic tinnitus showed a positive effect of this approach. During the analysis, we paid particular attention on the comparison of previously utilized statistical approaches and more suitable alternatives, and investigated potential advantages and disadvantages.
- Winfried Schlee and I started with the analysis of a data set extracted from the Tinnitus Database. Main focus was the impact of the perceived tinnitus frequency on TQ (Tinnitus Questionnaire) score with the goal to identify different tinnitus subtypes.
- We started a workgroup with colleagues Thomas Probst and Michael Pfaffer for advancing the analysis of the Tinnitus Database. The two colleagues have already started working on the subject, but need to extend their statistical analysis methods in order to capture the particular features of longitudinal data.
- Winfried Schlee received special training in mixture regression models. These models are going to serve for exploratory analyses of the Tinnitus Database.

3. Description of the main results obtained

The list below contains the main results, ordered by progress in decreasing order.

1. A treatment approach integrating rTMS and a variety of relaxation techniques for patients with chronic tinnitus showed promising results, in particular in comparison to patients receiving only rTMS treatement. Within this study, we also carried out a comparison of mixed effects models with classical repeated ANOVA type analyses subject to missing value imputation.
2. Analysis of a data set extracted from the Tinnitus Database showed a significant impact of the perceived tinnitus frequency on TQ score. Moreover, age shows a significant effect, in particular in interaction with the perceived tinnitus frequency. The data are fully prepared for further analyses.
3. Mixture models showed a promising performance as exploratory tool for the Tinnitus Database. We were able to perform a couple of preliminary analyses, and could verify stability of the estimation algorithms and consistency of the estimation results.

4. Future collaboration with the host institution

The collaboration with the research group in Regensburg will be continued. We intend to carry out a second STSM in spring or summer 2016 for concluding our currently ongoing analysis of the Tinnitus Database, and evaluating future perspectives.

5. Foreseen publications/articles resulting from a mission

1. The results of our joint work on rTMS and relaxation techniques has been submitted (Kreuzer et al. 2015).
2. A smaller project on the relationship between tinnitus frequency and TQ score is ongoing. We intend to present first results at the *TRI 2016 Conference*, as well as submitting them in spring 2016.
3. Analysis of the Tinnitus Database is the largest project with highest complexity. Therefore, prediction of the outcome is difficult, and no time-frame for submitting articles can be determined yet.

Kreuzer P., Poeppl T., Bulla J., Schlee W., Lehner A., Langguth B., Schecklmann M. (2015), 'A proof-of-concept study on the combination of repetitive transcranial magnetic stimulation and relaxation techniques in chronic tinnitus', submitted to the *Journal of Neural Transmission*

6. Confirmation by the host institution of the successful execution of your mission

The confirmation is going to be sent by email directly.