FNS PROJECT 100014_125050

Behavioral, neuro-functional and neuro-anatomical correlates of experience dependent music perception

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Co-researchers: Dimitri Van De Ville, François Lazeyras, Claude-Alain Hauert

Postdoc collaborators: Mathias Oechslin; Raoul Jenni

1. Brief summary of research plan

This research project investigated brain adaptations in correlation with changes of behavior in 60 age and sex matched young adults with 3 distinct levels of musical proficiency. The main experimental strategy relied on the perception of graded expectation violations in expressive music by musical laymen, amateur and professional pianists. During functional brain imagery we presented a comprehensive set of 120 specifically composed string quartets covering all minor and major tonalities. The endings (cadences) of these compelling pieces were manipulated hierarchically, resulting in either regular, subtly or apparently transgressed cadences. A multimodal neuroimaging approach was applied, collecting electro-encephalographic (EEG), as well as functional and structural magnetic resonance imaging (MRI) and diffusion tensor imaging (MR-DTI) data, in order to gather optimal temporal and spatial information about brain function and structure. A supplementary battery of behavioral assessments relating to the main task, including tests on working memory, fluid intelligence and musicality was applied. Furthermore, participants responded to an exhaustive questionnaire on passive and active musical experience across their lifespan. Thus our experimental design allowed studying the relationships between 1. behavioral data on lifespan musical education, musical and general cognition, 2. functional brain imagery data on music perception (fMRI, EEG) and 3. brain structure in gray (sMRI) and white matter (MR-DTI).

Additionally, an adult lesion patient passed our full battery of behavioral testing and brain imaging. Then, using the same musical material, we studied behavior and EEG responses in primary schoolchildren.

Main conclusion: Our main hypothesis anticipated gradual changes in behavior, brain functioning and brain structure with degree of musical expertise and training. Our data confirm this initial main hypothesis (James et al., 2014a; James et al., 2014b; James et al., in preparation; Oechslin et al., 2013a; Oechslin et al., 2013b; Oechslin et al., in preparation; see 2.2).

2. Summary of results

2.1 Published data and data in advanced stage of preparation

Due to our unique set of expressive ecological musical stimuli and our cutting-edge functional and structural imaging data we could reveal gradual changes in brain functioning and structure relative to music processing and general cognition with increasing musical expertise and transgression salience. As our groups were very well matched and controlled (inclusion-exclusion criteria), these results suggest that mainly nurture, not nature, rules such cerebral plasticity.

Except for the last one, in which we studied primary schoolchildren, all studies described below investigated the same 3-level-of-expertise adult groups. All functional brain imagery studies used the musical violations at closure described above.

- In the functional MRI study (**Oechslin et al., 2013a**) we could show that processing of musical expectation violations yielded gradual activation differences as a function of expertise in a fronto-temporal brain network resembling activation patterns for universal functions of working memory and attention. Additionally, the data revealed working memory advantages for musical experts outside the domain of auditory processing. Hence we concluded that the high attentional and mnesic demands of musical training and performance may yield these general cognitive advantages.

- In the EEG counterpart of this fMRI study (**James et al., in preparation**; **see Poster p.5**, Results I, II, III, IV) we could show gradual functional changes with increasing musical expertise at all levels of analysis: I. behavioral analysis, II. classical ERP waveform analysis, III. spatio-temporal/microstate analysis and IV. statistical parametric mapping (SPM) of source estimations. SPM of source estimations unveiled interaction between level of expertise and level of salience of the musical transgressions in the right middle temporal gyrus. This area also showed interaction between expertise level and transgression salience in our fMRI study, confirming partially the validity of source computation of EEG data using SPM. ***Planned submission: February 2015.***

- In the structural MRI study (**James et al., 2014a**) that applied voxel based morphometry, the gray matter differences relative to musical experience were to some extent localized in proximate brain areas compared to the fMRI data. This partially supports our original hypotheses on the relationships between functional and structural brain plasticity. Gradual differences in gray matter with expertise level occurred in brain areas linked to cognitive processing, fine motor control, working memory and relevance detection. Interestingly, gray matter increase with expertise was found in cognitive areas versus decrease in sensori-motor areas. The latter effect may be explained by increasing automation of motor skills with increasing proficiency, whereas gray matter increase in cognitive areas underpinned behavioral benefits for musical but possibly also for general cognitive abilities.

- A very interesting phenomenon also concerning structural MRI data **(Oechslin et al., 2013a)** was found associating the results from the behavioral data on fluid intelligence (Raven's test) with the results of a manual segmentation of the hippocampus. We could show that exclusively musically trained people (amateurs and experts) showed joined increase of hippocampal volume and fluid intelligence. The intriguing fact that hippocampal volume and fluid intelligence do not simply increase as a function of musical training suggests an inhomogeneity within the musician group. Not all musicians benefit from musical training in the same way, possibly explained by different training regimens, but also genetic predispositions, and their interaction.

- In order to study the anatomical connections subserving high-level music processing and ensuing training-induced white matter adaptations, we used an innovative combined DTI-fMRI approach (**Oechslin et al., in preparation**). By means of probabilistic tractography we could designate the right hemisphere ventral stream as a hub for musical syntax processing, connecting the middle temporal gyrus (MTG) with the inferior frontal cortex (pars opercularis) via the extreme capsule. Volumetric analyses showed that musical expertise is associated to enhanced pathway integrity and moreover, that right ventral stream pathway integrity predicts the behavioral sensitivity for musical syntax violations (see **Fig. 1**). Notably, this white matter fiber bundle corresponds to the left hemisphere ventral stream, classically attributed to syntax processing in language comprehension. ***Planned submission: December 2014.***

- In another EEG study (**James et al., 2014b**), mainly non-musician primary schoolchildren discriminated the presented musical expectation violations well above chance. Previous studies involving schoolchildren rather used simple musical stimuli. We could demonstrate a specific ERP microstate/component in response to the transgressions, reminiscent of the N400, typically observed in response to semantic transgressions in language. The strength of the ERP component was positively linked to successful detection of the violations and to working memory capacity. Underlying generators could be localized in pre-motor areas, suggesting an automatic process of mimicking music to improve the processing of the musical stimuli.

2.2 Accepted publications (impact factors ResearchGate)

James, C.E., Oechslin, M.S., Van De Ville, D., Hauert, C.A., Descloux, C., Lazeyras, F., 2014a. Musical training intensity yields opposite effects on grey matter density in cognitive versus sensorimotor networks. Brain Structure & Function 219, 353-366. doi: 10.1007/s00429-013-0504-z **Impact factor 7.84**

James, C.E., Cereghetti, D.M., Roullet, E., Oechslin, M.S., 2014b. Electrophysiological evidence for a specific neural correlate of musical violation expectation in primary-school children. Neuroimage, **in press** (accepted 20.09.2014). doi: 10.1016/j.neuroimage.2014.09.047 **Impact factor 6.25**

Oechslin, M.S., Van De Ville, D., Lazeyras, F., Hauert, C.A., James, C.E., 2013a. Degree of musical expertise modulates higher order brain functioning. Cerebral Cortex 23, 2213-2224. doi: 10.1093/cercor/bhs206 **Impact factor 8.31**

Oechslin, M.S., Descloux, C., Croquelois, A., Chanal, J., Van De Ville, D., Lazeyras, F., James, C.E., 2013b Hippocampal volume predicts fluid intelligence in musically trained people. Hippocampus 23, 552-558. doi: 10.1002/hipo.22120 **Impact factor 5.49**

2.3 Publications in advanced stage of preparation

James, C.E., Oechslin, M.S., Van De Ville, D., Michel, C.M., Spatio-temporal ERP analysis and source imaging reveal progressive changes in cerebral processing of mucial syntax with level of musical expertise. In preparation. ***Planned submission: February 2015.***

Oechslin, M.S., Geschwind, M., James, C.E., Tracking training-related plasticity by combining fMRI and DTI: The right hemisphere ventral stream mediates musical syntax processing In preparation. ***Planned submission: December 2014.***

3. Realization of the original research plan

We collected the full data set as originally planned.

However, the children's' data (James et al., 2014b) do not contain a musician and a non-musician group nor different age groups as originally planned. We failed to obtain permission of the parents and of the local primary school for collecting data on sufficient children to recruit a separate group with musical training experience. However, instead of a purely behavioral study, we also collected EEG data.

In principle, we have a publication delay. However, all published results (N=4) appeared in high impact international journals, and we are far from finished publishing the data. The project was complex and we preferred taking sufficient time to prepare everything in detail and execute wide-ranging pilot studies before collecting the data. We experimented extensively with different kinds of musical expectation violation, aiming to optimally separate participants as a function of musical experience and training. These pilot data were not published. Furthermore we adapted the moment of expected hemodynamic peak resulting in different jittering for the sparse sampling fMRI study, after observing that the collected pilot data still increased in activation level at the latest moment of data collection. Our very strict inclusion and exclusion criteria for the different levels of musical expertise made recruitment of participants difficult. The result was for instance that age of beginning was identical for amateur and expert participants; age differences at beginning of musical studies between amateurs and experts are a caveat in many cross-sectional studies. Moreover we enlarged all 3 groups from 15 to 20 participants in order to increase statistical power.

As we could consistently show gradual differences of brain and behavioral responses with expertise across our results, we gained access to prominent journals in the field of cognitive neuroscience; hence we do not regret the slow start up of the study.

Additionally we collected patient data that were not initially planned. This data set is still being analyzed. The main results are resumed below in 4. ADDITIONAL PUBLICATIONS.

M. Oechslin accepted a 70% job in Zurich from October 1 2012, and henceforth worked on a 30% basis during the final phase of the project (October 2012 till March 2013). Additionally, we engaged M. Raoul Jenni for 6 months on a 70% basis as a post-doc. He conducted a specific unplanned EEG analysis of our data that is resumed in 4. ADDITIONAL PUBLICATIONS.

4. ADDITIONAL PUBLICATIONS

Oechslin et al., in preparation (expected submission date: September 2015)

In cognitive neuroscience research lesion studies provide valuable insights into the mechanisms of structural and functional plasticity. We exposed a lesion patient (A.S.) to the same experimental paradigm as we did with the 60 subjects with three levels of musical expertise. A.S. underwent right temporal lobe ablation after discovery of a malignant astrocytoma (**Fig. 2**, upper part, right), which slowly developed in the course of her life. A.S. practiced the piano and took singing lessons from childhood to early adulthood (and still practices the piano although at present for therapeutical reasons). Consequently, A.S. can be associated to our amateur musician group. Psychoacoustic assessment revealed that her binaural hearing capacity was intact to a very high degree. A.S. passed our full battery of behavioral and brain imaging observations including structural (MRI, MR-DTI) and functional (fMRI, EEG) methods. Thus approaches to integrate case A.S. into our data set are manifold. However, irrespective of analysis methods the main question will be the following: How did her brain cope with such mass lesion?

So far, we 1) can report that A.S. detected the violations surprisingly well: she performed within the mean range of the amateur group, 2) could unveil, following a first fMRI analysis on all musical stimuli (collapsed), unaffected primary auditory activations during music processing (see **Fig. 2**). We therefore assume that higher order auditory processing functions and underlying neural circuitries (usually passing middle and inferior temporal areas that have been removed in the right hemisphere) underwent an extraordinary cerebral reorganization.

To further investigate the nature of neural plasticity in this case, our general strategy will be to fit her data (behavioral, functional and structural) into our data set of non-musicians, amateurs and experts. By this means we expect to gain insight into general principles of auditory plasticity in the clinical context of stroke and lesion rehabilitation.

Jenni et al., in preparation (expected submission date: March 2015)

Here we studied in different frequency bands, the impact of 1) levels of expertise and 2) minor versus major mode of the musical stimuli. The same EEG recordings as for James et al. (in preparation) saved as basis for this analysis.

Results of this EEG frequency analysis disclosed a decrease of theta- and gamma-frequency range activities with increasing expertise, mainly in right posterior regions. This observation may reflect increased efficiency thus decreased effort. But more importantly, minor and major compositions induced modulation of synchronized neuronal activities in high frequency ranges (beta and gamma). These effects that occurred in distributed frontal regions showed stronger activity in response to minor compositions than to major ones by musicians, and by experts in particular (see **Fig. 3**). An explanation of this observation may reside in the increased ability to bind and integrate different musical elements into a coherent percept. This binding is apparently more demanding for minor modalities, and trained musicians seem more prone to experience this increased effort.

5. RELATED PUBLICATIONS

5.1 Meanwhile, 4 publications of Clara James on closely related subjects were accepted for publication:

James, C. E., Michel, C. M., Britz, J., Vuilleumier, P., & Hauert, C. A. (2012). Rhythm evokes action: Early processing of metric deviances in expressive music by experts and laymen revealed by ERP source imaging. *Human Brain Mapping, 33*(12), 2751-2767. doi: 10.1002/hbm.21397. Impact factor 6.88.

James, C. E., Dupuis, E., Hauert, C.-A. (2012). Appraisal of musical syntax transgression by primary-school children: Effects of age and practice. *Swiss Journal of Psychology 71*(3) (161–168). doi: 10.1024/1421-0185/a000084. Impact Factor: 0.6.

James, C. E. (2012). Music and language processing share behavioral and cerebral features. *Frontiers in Psychology, 3*, 52. doi: 10.3389/fpsyg.2012.00052. Impact Factor: 2.80.

James, C. E. (2012). La musicalité humaine au travers du cycle de vie; Perspectives comportementales et neuroscientifiques. *Le Bulletin de L'AmiRéSoL*. ISSN 1634-6750. ***This publication was not peer-reviewed and appeared in a journal for professional musicians.***

5.2 Meanwhile, 6 publications of Mathias Oechslin on closely related subjects were accepted for publication:

Oechslin, M.S., Läge, D., Vitouch O. (2012), Training of tonal similarity ratings in non-musicians: a rapid learning approach, *Frontiers in Psychology, Cognitive Science*, 3:142, 2012. Impact factor: 2.8.

Oechslin, M.S. (2012), Impact of musical expertise on cerebral language processing. In: Altenmüller E., Demorest S.M., Fujioka T., Halpern A.R., Hannon E.E., Loui P., Majno M., Oechslin M.S., Osborne N., Overy K., Palmer C., Peretz I., Pfordresher P.Q., Särkämö T., Wan C.Y., Zatorre R.J., Introduction to The Neurosciences and Music IV: Learning and Memory, *Annals of the New York Academy of Sciences*, 1252(1): 1-16. Impact factor: 4.36

Ott, C., Langer N., **Oechslin, M.S.,** Meyer, M., Jäncke, L. (2011), Processing of voiced and unvoiced acoustic stimuli in musicians, Frontiers in Psychology, *Auditory Cognitive Neuroscience*, 2:195. Impact factor: 2.8

Meyer, M., Elmer S., Ringli, M., **Oechslin, M.S.,** Baumann, S., Jäncke L. (2011), Long-term exposure to music enhances sensitivity of the auditory system in children, *European Journal of Neuroscience*, 34(5): 755-65. Impact factor: 3.75

Oechslin, M.S., Imfeld, A., Loenneker, T., Meyer, M., Jäncke (2010), The plasticity of the superior longitudinal fasciculus as a function of musical expertise: a diffusion tensor imaging study. *Frontiers in Human Neuroscience*, 3:76. Impact factor: 2.91

Oechslin, M.S., Meyer, M., Jäncke L. (2010), Absolute pitch - functional evidence for speech-relevant auditory acuity. *Cerebral Cortex,* 20(2): 447-55. Impact factor: 8.31

6. CONTRIBUTIONS

I (principal investigator, undersigned) consider the investment of Mathias Oechslin and myself for all aspects concerning the execution of this study as equivalent and complementary.

Co-researchers Dimitri Van De Ville and François Lazeyras importantly contributed to the data analyses and publications. Claude-Alain Hauert importantly contributed to the project as a consultant, but retired in 2012.

7. MASTER'S THESES

Three Master students were involved in the project. Clara James was director and co-director of these Master theses. The studies were published (James et al., 2014b; Oechslin et al., 2013b).

- Co-direction of Master's thesis in Medicine, University of Lausanne. Céline Decloux (June 2012). *Hippocampus size predicts fluid intelligence in musically trained people.*
- Direction of Master's thesis in cognitive psychology. Elodie Roullet (September 2012). *Potentiels évoqués de la perception musicale et capacités cognitives chez l'enfant tout-venant.* Faculty of Psychology and Educational Sciences, University of Geneva.
- Direction of Master's thesis in cognitive psychology. Donato Cereghetti (January 2013). *La perception musicale chez l'enfant: neuroimagerie électrique et fonctionnement cognitif.* Faculty of Psychology and Educational Sciences, University of Geneva.

8. PERSPECTIVES

Clara James occupies at present (engagement May 2012) a fixed position as Dean of Research and Professor at the *University of Applied Sciences and Arts, Western Switzerland, School of Health Sciences* (HES-SO). Moreover August 1 2013 she was nominated Privat Docent at the *Faculty of Psychology and Educational Sciences of the Geneva University*. October 1 2014 she submitted a revision of an FNS project based partially on the data of the here reported project, proposing a study on possible benefits on cognitive aging by means of musical and physical training, using behavioral and neuroscientific approaches, again together with D. Van De Ville and François Lazeyras.

Mathias Oechslin is currently working as a postdoctoral research fellow (PI) at the *International Normal Aging and Plasticity Imaging Center (INAPIC), University of Zurich*. In parallel he is holding a position as a senior research associate at the *Department of Neuropsychology, University of Zurich*.

31.10.2014, Geneva, Clara James

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Spatio-temporal ERP analysis and source imaging reveal progressive changes in cerebral processing of musical syntax with level of musical expertise.

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Aim

Study the impact of level of musical expertise on cerebral processing of musical expectation transgression.

Introduction

■ This EEG experiment is part of a multi-modal brain imaging project entitled: «Behavioral, neuro-functional and neuro-anatomical correlates of experience dependent music perception» (SNF grant 100014-125050). fMRI data from this project, using similar stimuli and identical participants, also showed gradual changes in cerebral processing with increasing expertise [1]; VBM data demonstrated gradual changes in gray matter density [2].

■ The main experimental strategy relies on the perception of graded expectation transgressions in expressive music by musical laymen, amateur and professional pianists.

■ **Spatio-temporal ERP analysis**: reduces high density ERP time series into a series of functional microstates based on their voltage topographies. This approach is opportune to analyze processing stages of acoustic musical stimuli, due to its high temporal resolution, and to study their underlying generators in the brain by means of source localization algorithms.

Main Hypothesis

We anticipate gradual changes in behavior and brain functioning with degree of musical aptitude that show progressive functional brain plasticity as a function of training intensity.

Methods & Stimuli

Stimuli: 90 original expressive compositions for string quartet (composer: Bruno Pietri).

Syntactic transgression of harmony at musical closure, 3 levels (all in-key) (**Figure 1**):

1. Regular (**R**), I = 1rst degree: tonic, root position
2. Subtle transgression (**T1**), I⁶ = 1rst degree, 1rst inversion
3. Apparent transgression (**T2**), IV⁶ = 4th degree, 1rst inversion

Task description: closure correct? YES/NO (right-hand button presses).

Figure 1: Examples of stimuli

Explanatory variables

1. Expertise (EX) (cf. Table 1)

1. Non-musicians, n=19 (**N**; 24.9 ± 4.5 years,10F)
2. Amateurs, n=20 (**A**; 22.2 ± 3.1 years, 9F)
3. Experts, n=20 (**E**; 24.5 ± 4.5 years, 10F)

Age (y)	A (h/w)	E (h/w)	t-values
6 to 8	3.0 (± 1.9)	3.1 (± 1.7)	t_{26} 1.1
8 to 10	3.5 (± 0.5)	4.2 (± 0.5)	t_{38} 1.1
10 to 12	4.0 (± 2.3)	6.5 (± 4.3)	t_{38} 2.7*
12 to 14	4.7 (± 2.6)	9.0 (± 5.3)	t_{38} 3.3**
14 to 16	5.3 (± 3.2)	14.8 (± 7.7)	t_{38} 5.1***
16 to 18	4.7 (± 2.2)	19.9 (± 9.3)	t_{38} 7.1***
18 to 25	4.8 (± 2.6)	30.7 (± 8.5)	t_{38} 12.4***

* p < .05, ** p < .01, *** p < .001; h/w: hours per week; y: years

Table 1: Training intensity of musicians

2. Syntactic Transgression (T)

1. Regular (**R**, n=90)
2. Transgression 1 (subtle, **T1**, n=90)
3. Transgression 2 (apparent, **T2**, n=90)

EEG acquisition and Raw Data Processing: 204 electrodes;1000 Hz; average referenced; band-pass filtered (0.25-30 Hz); artefact free epochs averaged to Event-Related Potentials (ERPs) up to 750 ms after stimulus onset (= onset of terminal chord).

Spatio-Temporal ERP analyses: k-means clustering of scalp potential topographies over time into an optimal number (cross validation criteria) of **functional microstates** [3].

Inverse Space: Localization of putative ERP sources in the brain by means of computation of **LORETA** (Laplacian weighted Minimum Norm) distributed linear inverse solutions [4]; solution space: 3005 nodes.

Results I, Behavior

H: Hits (NO to T1 or T2)
FA: False Alarms (NO to R)

d-prime : z-score (H) - z-score (FA) measure of sensitivity [5] for T1 and T2 (**Figure 2 & Table 2**).

EFFECT ▼	df	partial eta²	F-values
EX	2	0.77	94.7****
T	1	0.74	155.8****
T x EX	2	0.53	31.2****

* p < .05, ** p < .01, *** p < .001, **** p < .0001
EX: Expertise; T: Transgression

Table 2: Anova results on d-prime: [EX (3, inter) x T (2, intra)]

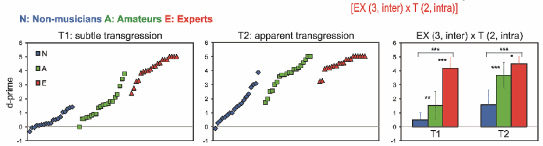

Figure 2: Behavioral Results. The left 2 panels show individual d-prime scores, the right panel depicts mean d-prime scores, asterisks indicate Bonferroni corrected contrasts; * p < .05, ** p < .01, *** p < .001.

Results II, ERPs

■ **ERPs**: An Anova [EX (3, inter) x T (3, intra) x Electrode (204, intra)], over the full time window, p < .01, time constraint > 20 ms, yielded significant Expertise x Transgression interaction. **Figure 3** shows these effects at Cz and Fz.

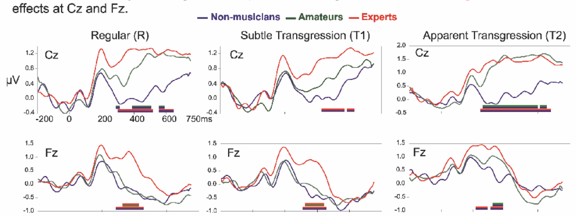

Figure 3: ERP Results shown at 2 exemplar electrodes Cz and Fz; color coded bars indicate significant Bonferroni corrected contrasts over time between grand average ERPs of Non-musicians, Amateurs and Experts with a minimum time constraint of 20 consecutive ms; E vs. N: ; E vs. A: ; A vs. N:

Results IV, Inverse Space

■ **Inverse Space** : An Anova [EX (3, inter) x T (3, intra) x Node (3005, intra)], on mean current density, p <.01, cluster size > 10, over the 295-480ms period resulting from the spatio-temporal ERP analysis, allowed localization of putative sources in the brain for this time period. Significant interaction Expertise x Transgression occurred in Right Middle Temporal gyrus, Right Inferior Temporal gyrus, Right Angular gyrus, and bilateral Middle Occipital Gyrus. Effects were strongest in the Temporal areas (**Figure 6**).

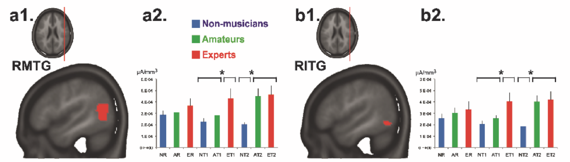

Figure 6: Significant Expertise x Transgression interaction in the Right Middle Gyrus (a., RMTG) and Inferior Temporal Gyrus (b., RITG) over the 295-480 ms period. a1.-b1. Significant voxels superimposed on slices of MNI 152 template brain. **a2.-b2.** Mean current density (µA/mm3) for each group and condition. Vertical bars represent standard errors. Asterisks indicate significant contrasts.

Selected References

1. Oechslin, M.S., Van De Ville, D., Lazeyras, F., Hauert, C.A., James, C.E., 2013. Degree of musical expertise modulates higher order brain functioning. Cereb Cortex 23, 2213-2224.
2. James, C.E., Oechslin, M.S., Van De Ville, D., Hauert, C.A., Descloux, C., Lazeyras, F., 2013. Musical training intensity yields opposite effects on grey matter density in cognitive versus sensorimotor networks. Brain Struct Funct.
3. Murray, M.M., Brunet, D., Michel, C.M., 2008. Topographic ERP Analyses: A Step-by-Step Tutorial Review. Brain Topogr 20, 249-264.
4. Michel, C.M., Murray, M.M., Lantz, G., Gonzalez, S., Spinelli, L., Grave de Peralta, R., 2004. EEG source imaging. Clin Neurophysiol 115, 2195-2222.
5. MacMillan, N.A., Creelman, C.D., 1991. Detection theory: a user's guide. Cambridge University Press, Cambridge.
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Conclusions

■ We observed progressive changes in behavioral responses and electrophysiological brain responses to musical syntax transgression as a function of musical expertise, suggesting that degree of training intensity drives such behavioral and cerebral plasticity at least partially.

■ Between 300 and 500 ms after stimulus onset, each level of expertise showed typical microstates, of which durations differed with transgression salience. Putative brain sources in right middle and inferior temporal areas showed enhanced responses with increasing expertise possibly reflecting more effective second order music processing [6], and representation of auditory complex features respectively.

Results III, Functional microstates (stages1-2)

■ **Stage 1**, **Figure 4**: a k-means clustering analysis yielded 7 ERP microstates optimally representing data variance of all groups and conditions.

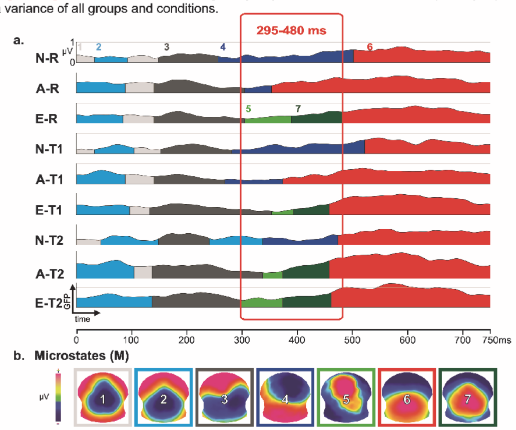

Figure 4: Results of Spatio-temporal ERP analysis: functional microstates. a. Color coded segments below the GFP curves represent time periods of strongest occurence of the microstates in the grand means. **b.** Scalp potential topographies of ERP microstates, framed in corresponding color code.

■ **Stage 2**, **Figure 5**: mean duration (in ms) of presence of ERP microstates resulting from individual subject fitting for all experimental groups and conditions for the 295-480 ms time period highlighted in **Figure 4a**. Fitted Microstates (M): 2 to 7. **Table 3**, corresponding Anova Results *[EX (3, inter) x T (3, intra) x M (6, intra)]*. Some pertinent significant contrasts (uncorrected) are provided in **Table 4**.

N: Non-musicians, A: Amateurs, E: Experts, R: Regular, T1: subtle transgression, T2: apparent transgression

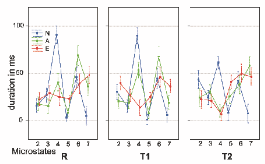

Figure 5: Mean duration of presence (ms) of functional microstates 2-7; 295-480 ms period

EFFECT ▼	df	partial eta²	F-values
EX	2	0.23	8.3***
T	2	0.16	10.9****
T x EX	4	n/a	n/a
M	5	0.16	10.9****
M x EX	10	0.22	8.0****
T x M	10	0.08	4.8****
T x M x EX	20	0.06	1.8*

* p < .05, ** p < .01, *** p < .001, **** p < .0001
EX: Expertise; T: Transgression; M: Microstate
n/a: not applicable; total duration of all microstates always 185ms

Table 3: Anova results on mean duration of Microstates (M) 2-7; 295-480 ms period: [EX (3, inter) x T (3, intra) x M (6, intra)]

Table 4: Pertinent contrasts

EX	T	M	df	F-values
N vs A/E	R/T1/T2	4	1	72.2******
A/E vs N	R/T1/T2	7	1	16.8***
E vs N/A	R/T1/T2	5	1	15.1***
N vs E & A vs E	T1	4	2	20.6******
E vs A/N	R/T1	5	2	17.3***

* p < .05; ** p < .01; *** p < .001; **** p < .0001
***** p < .00001; ****** p < .000001

Figure 1. A. Mean tract volumes of MTG_POp (light grey) and MTG_INS (dark grey) are plotted (±SEM) for each group (E: experts; A: amateurs; N: non-musicians). B. The proximal relation of the two tracts is outlined by here-combined 3d renderings (yellow: MTG_POp; green: MTG_INS). C. Scatterplots (including all participants, n=59) and regression lines indicate the negative relationship between sensitivity (d-prime) for harmonic violations in musical pieces and MTG_POp volume; on the left side for subtle (T1) and on the right side for apparent (T2) harmonic transgressions. MTG: Middle Temporal Gyrus; POp: Pars Opercularis; INS anterior Insula.

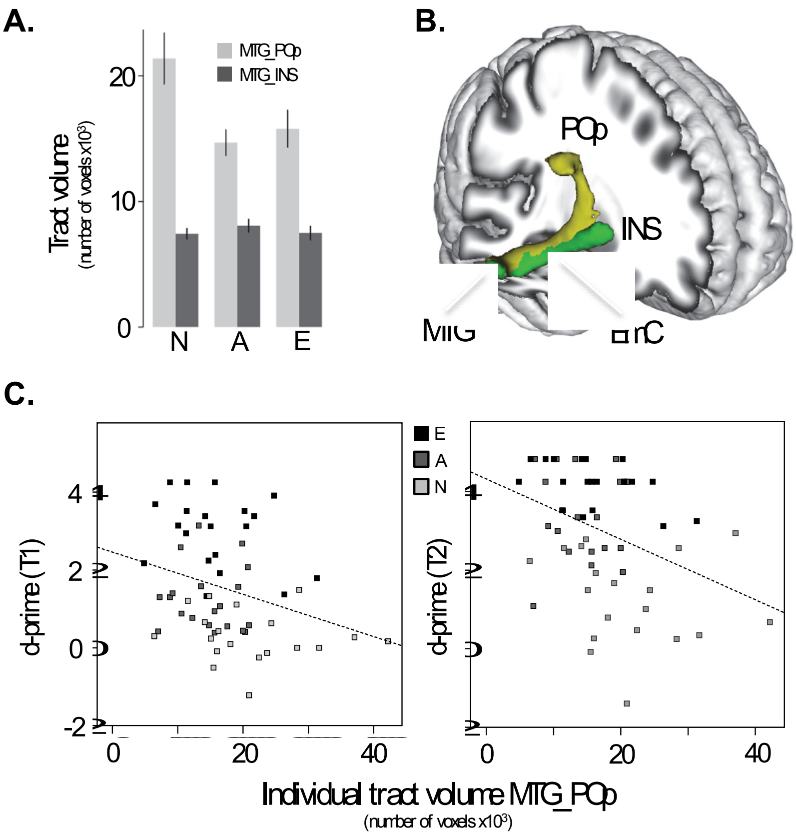

Figure 2: *Coronal (-12) and sagittal (62) section of patient A.S. (spatially normalized brain) showing brain activations (effects of interest) in left and right primary and secondary auditory areas during musical processing. Dashed zones approximately delineate the temporal lesion.*

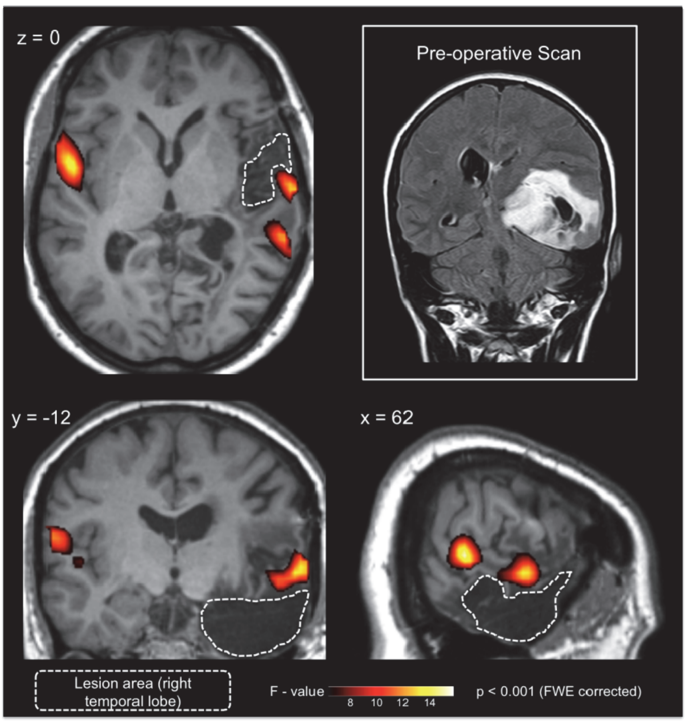

Figure 3: *Distributions of the power amplitudes observed in each of the 9 Regions of Interest (ROIs; upper right panel: FL = frontal left, CL = central left, PL = posterior left, FC = frontal center, CC = central center, PC = posterior center, FR = frontal right, CR = central right, PR = posterior righ). For all panels, scales of power amplitude are defined for each line, from top to bottom frontal, central, and posterior), and for each frequency band (theta [4-7Hz], alpha low [8-10.5Hz], alpha high [10.5-14Hz], beta low [14-20Hz] beta high [20-30Hz], gamma low [30-45Hz] gamma high [60-90 Hz]), in response to minor and major stimuli. All plots summarize repeated measures ANOVA for Expertise (Non-musicians – Amateurs – Experts) x Tonality (minor in blue – major in red); whiskers indicate standard error, asterisks indicate level of significance: *P < 0.05, **P < 0.01, ***P < 0.005 (corresponding to a Bonferroni-correction for multiple tests: 9 ROIs).*