Magnetic vestibular stimulation (MVS) influences fMRI resting-state fluctuations: The modulation of the default-mode network as an exemplary case

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Background: Dizziness in the presence of strong magnetic fields (>1 tesla) has been noticed ever since the first magnetic resonance experiments have been conducted[1]. Recently, Roberts and co-workers[2] showed that healthy subjects at rest, who are kept in total darkness and exposed to the static magnetic field of a MR machine developed a persistent nystagmus, while patients with bilateral peripheral vestibular failure did not show this effect. Furthermore, the nystagmus' slow phase velocity was modulated systematically depending on the subject's head orientation relative to the field. The authors argued that the ionic fluids in the inner ear, which are constantly flowing as cells maintain resting activity, will be diverted by a (magnetic) Lorentz-force. This creates a pressure onto the cupula "the rotatory motion sensor" in the inner ear, thus leading to the nystagmus eye-movement akin to a constant (accelerating) rotatory stimulation. This model was further supported by a simulation study[3] and a study of patients with unilateral labyrinthine disorders[4]. It was speculated that this magnetic vestibular stimulation (MVS) effect might influence fMRI results, because a nystagmus is indicative of an imbalance of the vestibular system, potentially influencing other systems that connect with it.

Purpose: The aim of the current study was to investigate if MVS does indeed modulate BOLD signal fluctuations. Here we present results from experiments conducted at 1.5 tesla & 3 tesla focusing on the case of MVS disproportionately influencing vestibular subparts of the default mode resting-state network (DMN).

Methods: We measured spontaneous nystagmus eye-movements and resting-state fMRI of 29 subjects resting in total darkness. Measurements were done in a 1.5 tesla MRI (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany) as well as in a 3 tesla MRI (GE Signa Hdx, GE Healthcare, Waukesha, WI, USA). We used FSL-MELODIC (http://fsl.fmrib.ox.ac.uk/) to estimated resting-state networks and noise components for the combined resting-state fMRI data of all subjects in both MRIs. The individual responses and weightings for each component per subject and MRI were estimated from the ICA results using dual regression (also part of FSL). These were analysed for significant changes of modulation between field strengths as well as additional regression of covariates determined from the recorded nystagmus. The DMN was selected manually as one component of the group ICA. The parts of the DMN that did not modulate significantly (dual regression analysis) between field strength and those that did modulate significantly were separated and all voxels were assigned to regions of interest taken from the AAL atlas. The signal-scaling behavior Λ in all regions of interest was evaluated as the magnitude of the fraction of the amplitudes at 3 tesla divided by the amplitudes at 1.5 tesla. This should thus reveal if there was an additional linear increase with field strength due to MVS or if there is only a square root BOLD signal increase as expected from theory[5].

Results & Discussion: We found that those subparts of the default mode network that were significantly (i.e. $p<.05$FWE) modulated between field strengths are commonly associated with vestibular function. The signal-scaling behavior of the other parts of the DMN that were not significantly modulated (figure 1 A_2-C_2) showed a scaling behavior as expected simply from considering a constant effect, i.e. no MVS modulation and only BOLD signal increase approximately with square root of field strength, in accordance with theory[5]. In contradistinction, those subparts that were significantly modulated showed signal-scaling behavior beyond the square root increase (figure 1 A_1-C_1), that roughly fell into two categories, which can be interpreted as follows. (i) Those parts commonly assumed (e.g. see [6]) to be closely connected to the vestibular peripheral sense-organs (e.g. Cerebellar Vermis) did modulate in accordance with the Lorentz-model prediction (i.e. linear increase of the effect due to linear increase of MVS with field strength). (ii) The other significantly modulated subparts shown in figure 1 (A_1-C_1), which only showed intermediate modulation, i.e. modulation that is less than expected from the Lorentz-model prediction[2], but still significantly above the expected "square root" increase alone[5], are commonly assumed[6] to be further removed, in terms of connectivity, from the vestibular peripheral sense-organs, (i.e. connected to the periphery via intermediary areas), and are therefore modulated less strongly by MVS than those that are more closely connected to the periphery.

Conclusion: Magnetic vestibular stimulation (MVS) significantly affects BOLD signal fluctuations at rest, particularly those of the DMN. The modulated areas are associated with vestibular function and modulation was strongest in areas closest (in terms of connectivity) to the vestibular peripheral sense-organs.

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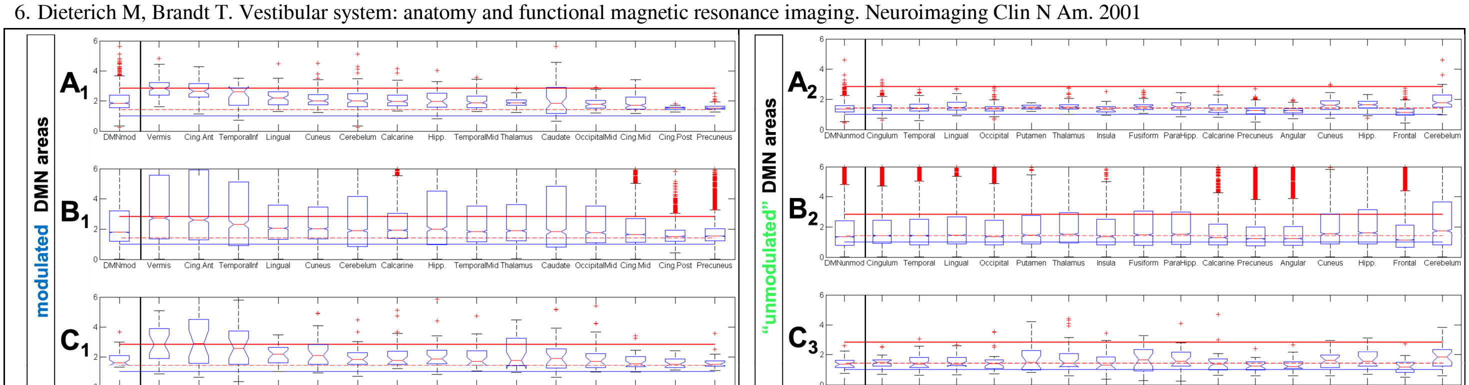

Figure 1: The scaling behavior Λ per ROI as boxplots. Left(A_1-C_1) are significantly modulated subparts and right(A_2-C_2) are "unmodulated" subparts of the DMN. The red (full)line marks $\Lambda=2\sqrt{2}$ ($=3T/1.5T*\sqrt{(3T/1.5T)}$), i.e. linear scaling of MVS and square root BOLD signal increase with field strength. The red dashed-line marks the constant effect, i.e. only square root BOLD signal increase[5], ($\Lambda=\sqrt{2}=\sqrt{(3T/1.5T)}$). $A_{1/2}$ shows the voxel-wise distribution of Λ for the median-subject, $B_{1/2}$ shows aggregate-data distribution (all voxels of all subjects collected) and $C_{1/2}$ shows subject-wise Λ for the median-voxel of the region of interest.