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Introduction

- A complete understanding of the **mechanisms of action of VNS** is still lacking, preventing an appropriate selection of patients.
- Vagal afferents** terminate densely (bilaterally) in the **nucleus of the solitary tract (NTS)**, which in turn projects to the **Locus Coeruleus (LC)** – main source of **norepinephrine (NE)**.
- LC-NE system is known to **prevent seizure development** and induce **long-term plastic changes**, particularly with the **release of norepinephrine in the hippocampus**^{1,2}.

This study aims at exploring functional characteristics of the LC and microstructural properties of LC-hippocampus connections in VNS patients and compare them between responders and non-responders.

Results

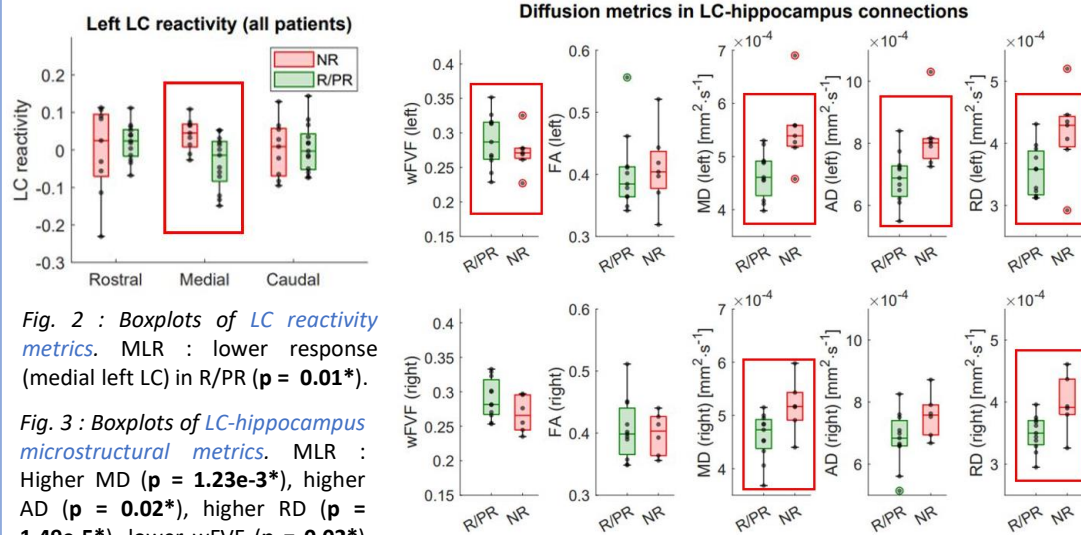


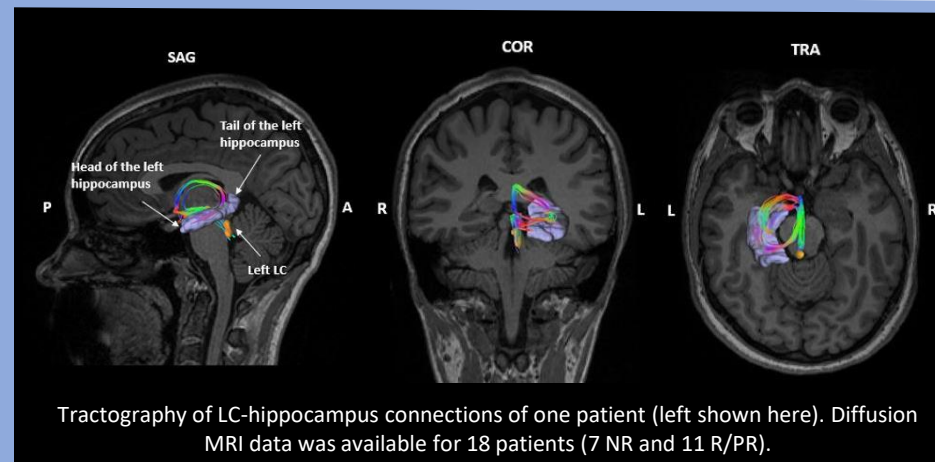
Fig. 2 : Boxplots of LC reactivity metrics. MLR : lower response (medial left LC) in R/PR ($p = 0.01^*$).

Fig. 3 : Boxplots of LC-hippocampus microstructural metrics. MLR : Higher MD ($p = 1.23e-3^*$), higher AD ($p = 0.02^*$), higher RD ($p = 1.49e-5^*$), lower wFVF ($p = 0.02^*$) in left LC-hippo tracts in NR. Higher MD ($p = 0.01^*$) and higher RD ($p = 0.003^*$) in right LC-hippo tracts in NR.

Methods

- 23 implanted patients : 10 NR (6 F, 4 M, age : 35.1 ± 15.19 y) - 13 R/PR (7 F, 6 M, age : 38.92 ± 11.22 y)
- SIGNA™ Premier 3T MRI system (GE Healthcare, Milwaukee, WI, USA) was used.
- Anatomical images were acquired with a **MPRAGE sequence** (voxel size : $1 \times 1 \times 1$ mm³).
- MT-TFL sequence** (neuromelanin-sensitive MRI sequence) was **optimized** and used to **localize the LC** (28 slices centered perpendicularly to the rhomboid fossa - voxel size : $0.39 \times 0.39 \times 1.7$ mm³).
- BOLD functional MRI** data were acquired with a multiband EPI sequence during an **auditory oddball task** – a task known to recruit the LC (voxel size : $1.7 \times 1.7 \times 2$ mm³).
- Multi-shell diffusion MRI** data acquired with a PGSE sequence (2-mm isotropic voxels)
- Tractography of LC-hippocampus connections** (Q-sampling Imaging – QA tracking index).
- Microstructural features : **DTI metrics** and **Microstructure Fingerprinting metrics**³ (based on Monte Carlo simulation of the random walk of water molecules).
- Multivariate Linear Regression (MLR) :

$$fMRI/dMRI \text{ metrics} \sim VNS \text{ response} + \text{age} + \text{sex} + AEDs + \text{benzo} + \text{epilepsy duration}$$



Conclusion

- DRE patients may show **different functional and structural states of the vagal afferent network** - **particularly in the LC-NE system**.
- The LC features investigated could define a **subgroup of DRE patients** with **higher seizure suppressing effects with VNS**.

References

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