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The effects of sacral neuromodulation on brainstem functional connectivity patterns in overactivity bladder patients: An ultra-high field neuroimaging study

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Background

The lower urinary tract (LUT) relies on continuous communication with the central nervous system (CNS) to maintain optimal storage and voiding functions. Studies indicate that the sacral spinal cord sends sensory signals from the LUT directly to the periaqueductal gray (PAG), which acts as a relay, determining when this input requires conscious awareness and decision-making for voiding[1]. In overactive bladder (OAB), this system may malfunction, with altered PAG activity potentially leading to incorrect processing of LUT signals. Treatment of OAB through sacral neuromodulation (SNM) may restore sensory processing in the PAG[2], although exact PAG changes induced by SNM remain unclear.

Objectives

Understanding SNM mechanisms is essential for predicting patient response, which could help avoid unnecessary surgeries and enable timely treatment for those likely to benefit. This study aims to identify differences in PAG functional organization between healthy individuals and OAB patients, before and after SNM treatment. We hypothesize that OAB affects the consistency of PAG's organization and that SNM restores it to a healthy baseline.

Design, Setting and Participants

The study included six healthy women and five women diagnosed with OAB, all of whom provided informed consent. Two OAB patients were additionally scanned post-SNM treatment. All participants underwent a 7 Tesla fMRI scan, with 420 multiband echo planar imaging (mb-EPI) volumes collected per participant (acceleration factor=2, MB-factor=2, TR=1400ms, TE=22ms, resolution=1.1x1.1x1.1mm).

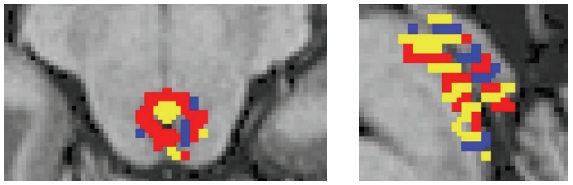

Figure 1: Example of functional organization of the periaqueductal gray in one of the participants in our study. Voxels with the same color belong to one functional subregion.

Statistics

The PAG of each participant was subdivided into clusters using the Louvain module detection algorithm, previously validated for analyzing PAG organization by our group[3] (figure 1). The 420 fMRI volumes were divided into six segments of 70 volumes each and independently parcellated to assess PAG organization variability over time. Correlations between each segment and the last segment measured variability, which was statistically compared between healthy and OAB participants.

Results

Our findings show significantly higher variability in PAG organization among healthy adults compared to OAB patients ($p \leq 0.05$). In the two OAB patients treated with SNM, PAG variability was restored similar to those in healthy controls (figure 2).

Conclusion

Our study suggests that PAG functional organization consistency, as measured by fMRI, can distinguish healthy individuals from OAB patients. Preliminary data show that SNM restores PAG organization in OAB patients to a healthy state, offering insights into SNM's role in LUT sensory processing. These findings are crucial for identifying predictors of SNM success and establishing objective measures for therapeutic response.

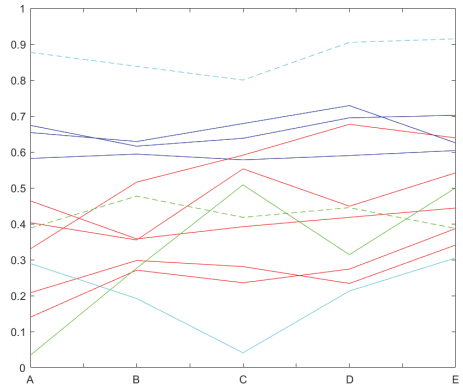

Figure 2: Correlation values for healthy controls (red) and overactive bladder (OAB) patients (blue). Two OAB patients that underwent scanning before and after treatment with sacral neuromodulation (SNM) are included (green and light blue). Dotted lines represent baseline measurement and solid lines the post SNM measurement. Difference between healthy adults and OAB patients was statistically significant ($p \leq 0.05$).

References

1. Blok BF, De Weerd H, Holstege G. Ultrastructural evidence for a paucity of projections from the lumbosacral cord to the pontine micturition center or M-region in the cat: a new concept for the organization of the micturition reflex with the periaqueductal gray as central relay. Journal of comparative neurology. 1995;359(2):300-309.
2. Gill BC, Pizarro-Berdichevsky J, Bhattacharyya PK, et al. Real-time changes in brain activity during sacral neuromodulation for overactive bladder. The Journal of urology. 2017;198(6):1379-1385.
3. de Rijk MM, van den Hurk J, Rahnama'i MS, van Koeveringe GA. Parcellation of human periaqueductal gray at 7-T fMRI in full and empty bladder state: The foundation to study dynamic connectivity changes related to lower urinary tract functioning. Neurourology and Urodynamics. 2021;40(2):616-623.

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