

ABNORMAL RESTING-STATE INTER-NETWORK COUPLING IN PATIENTS WITH NON-NEUROGENIC OVERACTIVE BLADDER

Hypothesis / aims of study

Recent functional magnetic resonance imaging (fMRI) studies using urinary bladder filling tasks demonstrated alterations in the supraspinal bladder control network in women with impaired bladder function and urinary incontinence, particularly regarding network connectivity and white matter changes [1]. However, it is still unclear if patients with overactive bladder (OAB) show altered supraspinal responses during empty bladder conditions. Especially, it is not known if resting-state (RS) activity is altered by catheterization usually require for bladder filling tasks. Thus, we applied a functionally-motivated network approach, using RS functional network connectivity (RS-FNC) analysis [2], to examine RS related network interactions in age-matched controls and patients with OAB during the conditions "empty bladder without catheter" and "empty bladder with catheter". Based on previous publications we hypothesize lower FNC in OAB patients.

Study design, materials and methods

We examined 10 healthy age- and handedness matched females (age 37.4 (SD=9.2)) and 10 females with NNOAB (38.1 (SD=8.9)). Prior to fMRI, urodynamics was performed to verify detrusor overactivity in NNOAB patients. Ethics approval and written subject consents were obtained prior to this fMRI study. For the RS-fMRI (7 min duration, awake, and eyes closed), 34 axial slices covering the whole brain were acquired on a 3.0 T Philips Ingenia scanner with a multi-slice EPI sequence (voxel size = 3 x 3 x 3 mm; 1 mm gap; TR: 2 s; TE: 16 ms; flip angle: 80°; acquisition matrix: 80 x 80; FOV: 240 mm) using a 15-channel head coil. After preprocessing of the fMRI data using SPM8 (involving exclusion of dummy scans, temporal filtering, realignment, spatial normalization to the MNI template, and spatial smoothing (6 mm)), we estimated the RS networks using GIFT [3] and independent component analysis (ICA) across all subjects. IC dimension estimation was performed using the minimum description length criteria, modified to account for spatial correlation. All non-neuronal ICs (e.g. cardiac-induced pulsatile artifact, CSF, and head motion) were removed, resulting in a total of 9 neuronal ICs (including the default mode network, DMN). Prior to FNC analysis, IC time courses were bandpass (0.013 Hz and 0.24 Hz). Next, group differences in FNC strength were calculated using the FNC toolbox [2] for the both experimental conditions. Additionally, the temporal lags between ICA-derived networks were computed to gain directed FNC. Significant between-group FNC (and lag) results are shown at $p < 0.05$ (corrected for multiple comparisons using FDR correction).

Results

Fig. 1 shows a representative RS network (DMN) across all subjects. RS FNC for the conditions "without" and "with-catheter" within groups did not reveal significant differences ($p > 0.05$). The condition "with-catheter" revealed significant group differences (Fig. 2A). Controls showed significantly higher (directed) FNC for: DMN (left-dominant) -> DMN (right-dominant) and fronto-parietal attention network -> DMN (left-dominant). In addition, we observed significant FNC lag differences, as indicated by the arrows in Fig 2A. Group differences are additionally highlighted on Fig 2B on an axial view.

Interpretation of results

The interplay between neuronal networks appears to be altered in OAB patients compared to healthy subjects already during RS. Especially aberrant coupling of the fronto-parietal attention network might indicate a general neuronal deficit that impairs adequate bladder control, i.e. suppression of premature micturition reflex, consequently resulting in OAB and urinary incontinence. These novel findings can be an important link to the underlying pathophysiology of OAB in otherwise neurological unimpaired patients.

Fig 1. Default mode network connectivity across controls and NNOAB patients

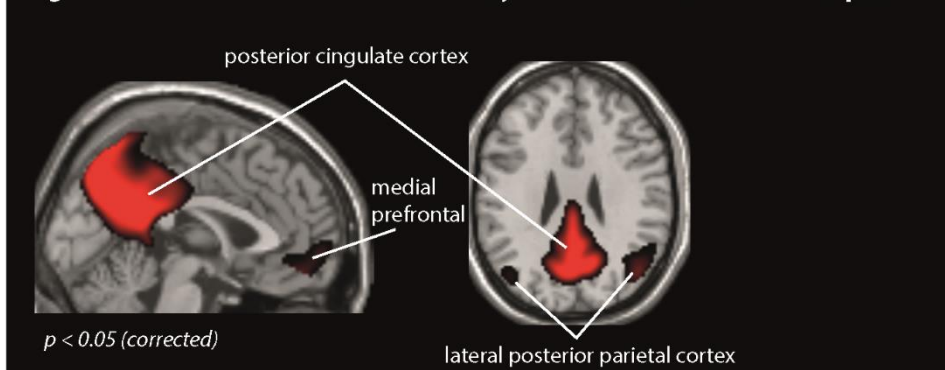
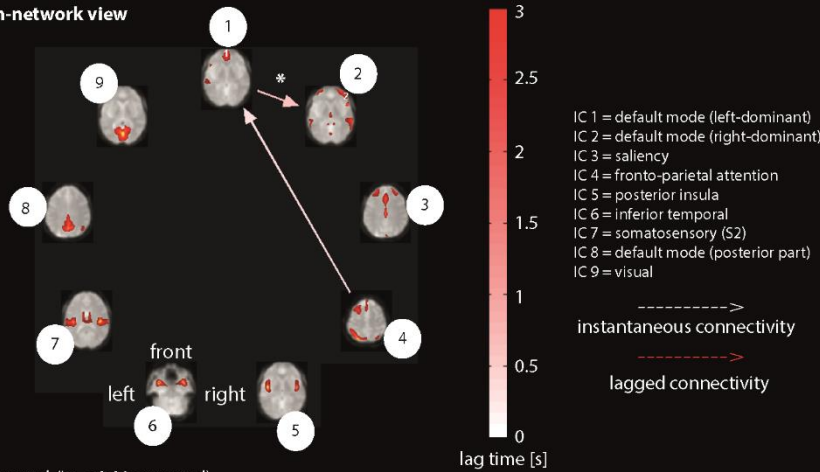


Fig 2. Between group functional network connectivity (with catheter)

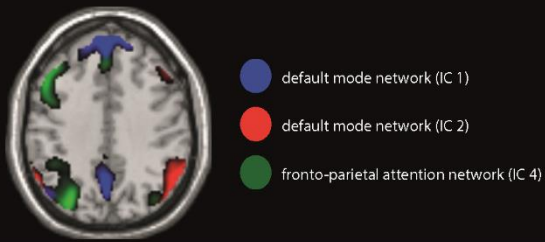
Controls > NNOB patients

(A) Between-network view



($p < 0.05$, corrected, * $p < 0.01$ corrected)

(B) Axial view



Concluding message

OAB patients demonstrate significant differences in supraspinal functional connectivity compared to healthy controls which might be part of the still poorly understood pathomechanism of OAB. Functional neuroimaging is a powerful tool to visualize and assess such neural correlates of bladder dysfunction.

References

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2. 2 Jafri MJ, Pearlson GD, Stevens M, Calhoun VD. (2008): A method for functional network connectivity among spatially independent resting-state components in schizophrenia. *Neuroimage* 39(4):1666-81.
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Disclosures

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