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BACKGROUND

- Research has identified two resting EEG biomarkers with potential for predicting functional outcomes in depression: theta amplitude in frontal brain regions (especially rostral anterior cingulate cortex [rACC]) using eLORETA and alpha amplitude over posterior regions using CSD-fPCA.
- Discrepant results from recent multisite studies have called into question the clinical utility of these biomarkers.
- Low signal quality, and poor discriminant and convergent validity may help explain discrepant findings.
- Potency of resting EEG oscillations, along with discriminant and convergent validity, was evaluated for these biomarkers in a sample of healthy controls.

METHODS

- Resting EEG (71-channel, 10-10 placement) was recorded from 35 healthy adults at two sessions (one-week retest).
- EEG surface potentials were converted to reference-free data with surface Laplacian (CSD) and distributed inverse transformations (exact low resolution electromagnetic tomography [eLORETA]).
- Signal strength was evaluated with signal-to-noise ratio, participant-level spectra, and frequency PCA (fPCA) covariance decomposition.
- Convergent and discriminant validity were assessed using a multitrait-multimethod (MTMM) framework.

RESULTS

- Posterior alpha was reliably identified as two spectral components, each with unique spatial patterns and condition effects (eyes open/closed; Figs 2,3), high signal quality (Fig. 1), and good convergent and discriminant validity (Table 1).
- Frontal theta was characterized by one low-variance component (Fig. 4), low signal quality (Fig. 1), lack of a distinct spectral peak (group and participant-level data), and mixed validity (Table 1).

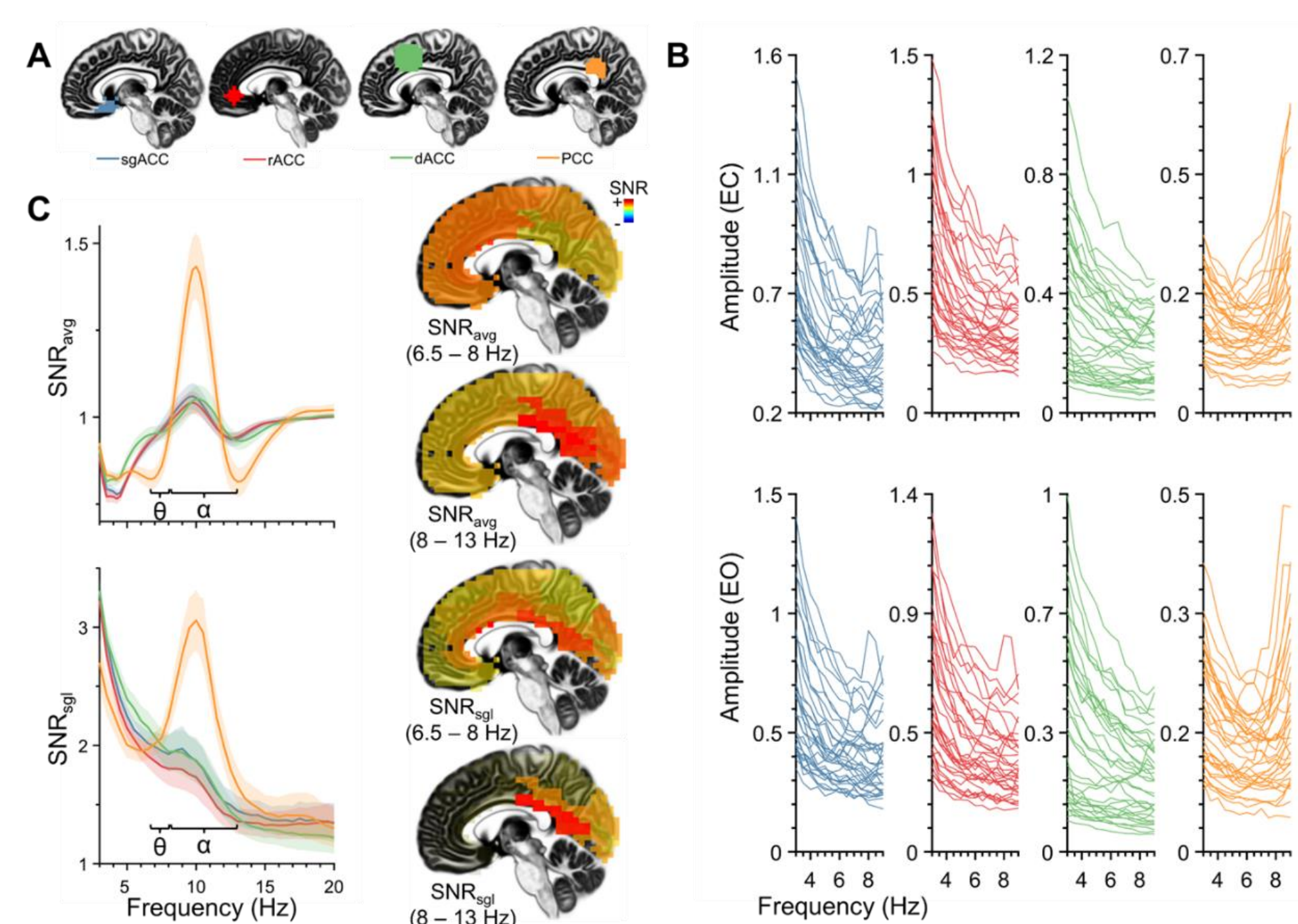


Fig. 1: Measurement quality of resting EEG (A) ACC ROIs. (B) Mean amplitude spectra for each participant, for eyes closed (EC, top panel) and eyes open (EO, bottom panel). Most spectra did not reveal a theta peak. (C) Two different SNR metrics both demonstrating low SNR for theta and high SNR for alpha in resting EEG.

Candidate Biomarkers	CSD				eLORETA			
	MF θ	MF α	5 Hz	9 Hz	rACC θ	rACC α	6 Hz	9 Hz
MF θ	0.76				0.87			
MF α w/ spatial normalization	0.22	0.42			-0.26	0.89		
5 Hz Comp.	0.67	0.43	0.91		0.11	-0.15	0.89	
9 Hz Comp.	0.37	-0.52	-0.06	0.91	0.40	0.03	-0.10	0.82
10.5 Hz Comp.	0.41	0.21	0.28	-0.14	0.91			
rACC θ	0.45	-0.33	0.20	0.48	0.01			
rACC α w/ spatial normalization	-0.43	0.25	-0.15	-0.17	-0.40			
6 Hz Comp.	0.58	0.41	0.82	0.04	0.15			
9 Hz Comp.	0.09	-0.54	-0.26	0.89	-0.44			
10.5 Hz Comp.	0.48	-0.08	0.22	0.24	0.69			

Table 1: Multitrait-multimethod matrix (MTMM). Blue cells indicate test-retest reliability. Green cells with coefficients larger than red and yellow cells reflect good discriminant and convergent validity. Principal components (peak frequency at 5, 6, 9, or 10.5 Hz) demonstrated good convergent validity, good discriminant validity, and good test-retest reliability. Theta activity calculated with conventional FFT analyses (MF θ , rACC θ) demonstrated poor validity.

CONCLUSIONS

- Correlations between candidate biomarkers suggest that posterior alpha components constitute reliable, convergent, and discriminant biometrics in healthy adults.
- Component-based identification of spectral activity (CSD/eLORETA-fPCA) was superior to fixed, a priori frequency bands.
- Improved quantification and conceptualization of frontal theta is necessary to determine clinical utility.



Background: Resting frontal theta (rACC LORETA) and posterior alpha (CSD-fPCA) are candidate biomarkers of depression outcome.

Objective: Examine biomarker validity in healthy adults.

Results: Unlike theta, two distinct alpha components were reliable and valid.

Conclusion: Improve methods for measuring resting rACC theta.

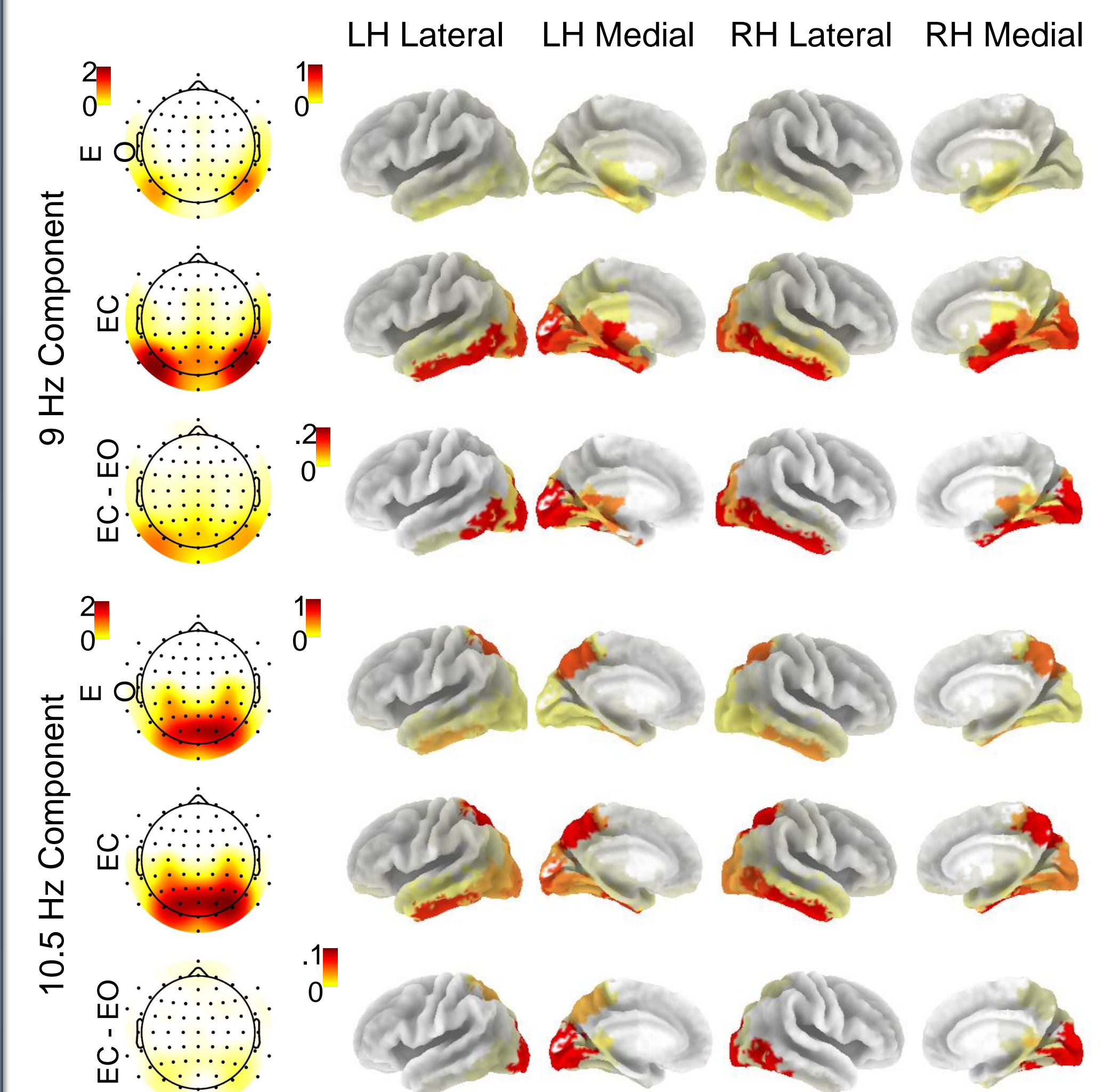
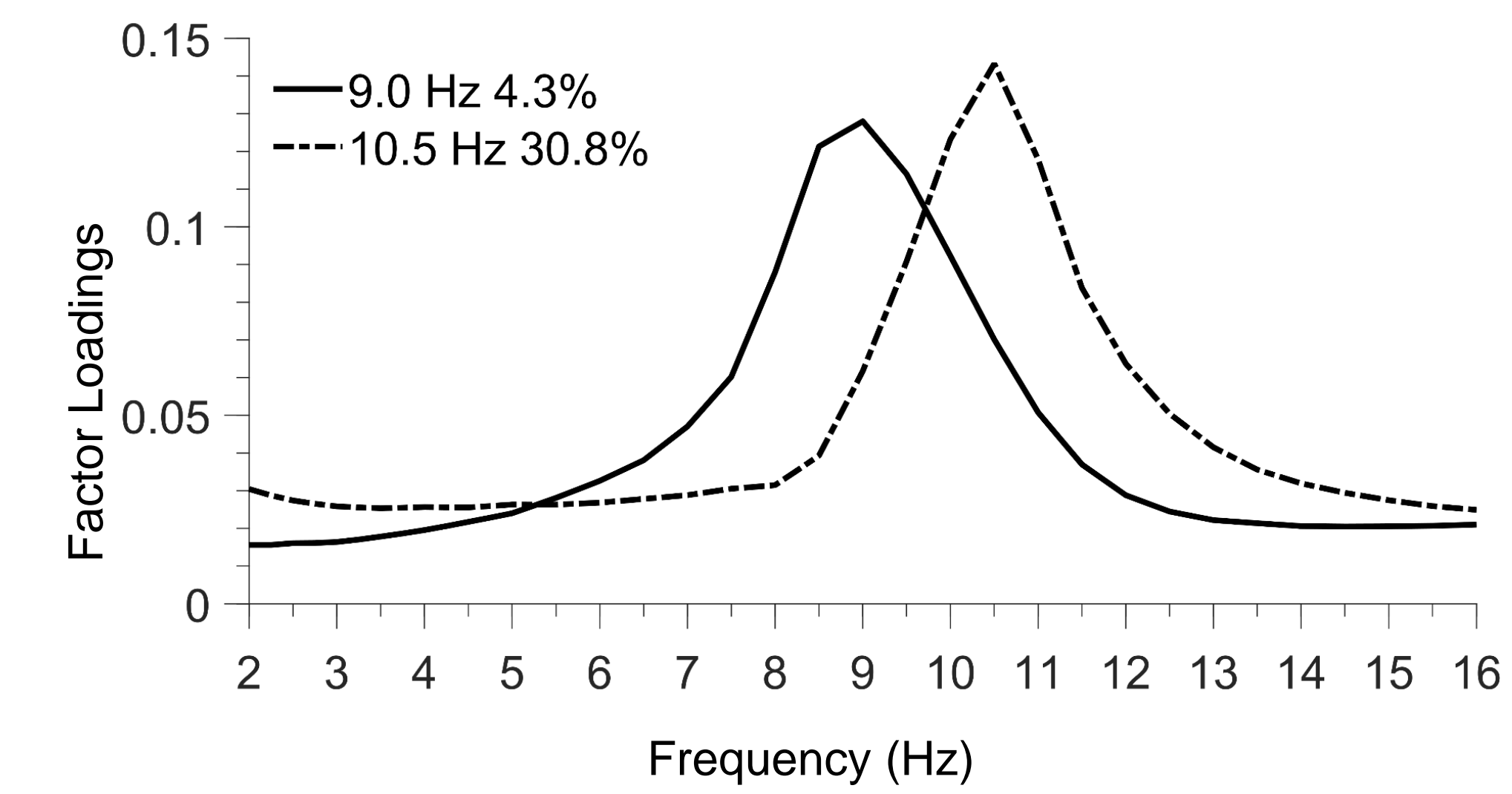


Fig. 2: Low and high alpha components from a simultaneous CSD/eLORETA-fPCA solution. (A) Factor loadings revealed peak frequencies at 9 and 10.5 Hz (low and high alpha, respectively). (B) Topographies (column 1) and tomographies (columns 2-5) of corresponding factor scores for eyes open (EO) and eyes closed (EC) conditions, and for net alpha amplitude (EC-minus-EO). Across CSD and eLORETA data, low alpha showed posterior-lateral maxima, whereas high alpha had a posterior-medial maximum. LH / RH = Left / Right Hemisphere.

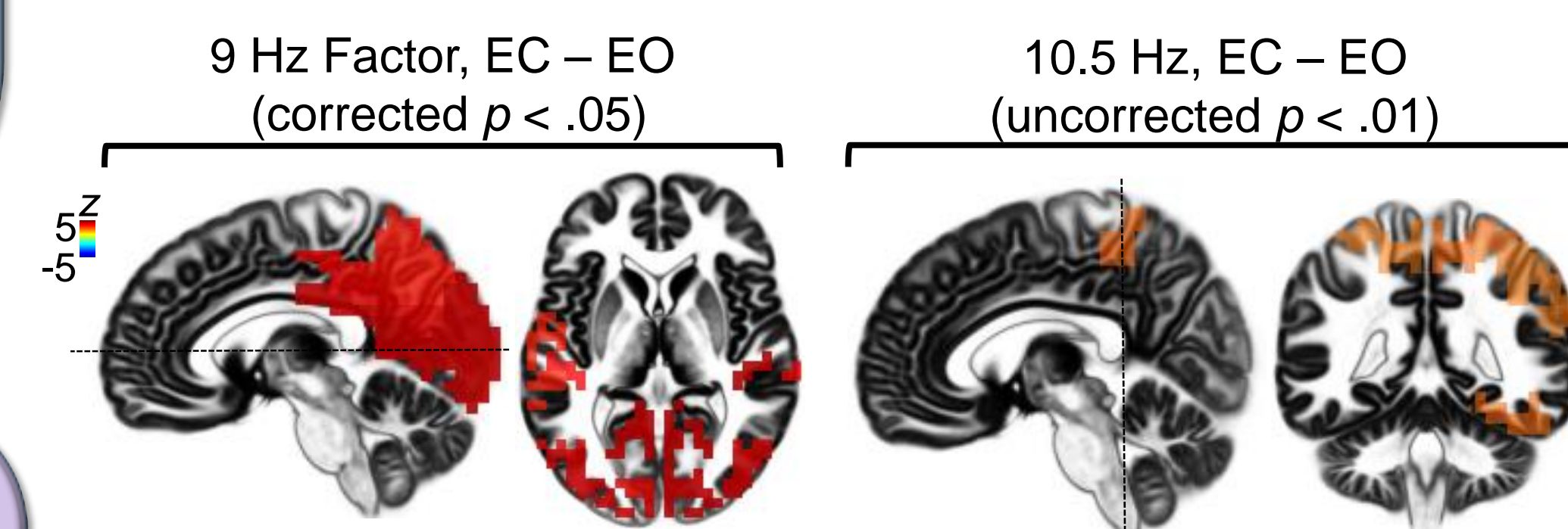


Fig. 3: Statistical evaluation of net alpha (EC-EO) tomographies stemming from the combined CSD/eLORETA fPCA solution shown in Fig. 2. Hot colors (reds and oranges) indicate greater alpha for EC than EO. Low alpha showed robust condition differences (thresholded at corrected $p < .05$); by comparison, condition differences for high alpha did not survive multiple comparisons correction and are presented with a more liberal threshold (uncorrected $p < .01$).

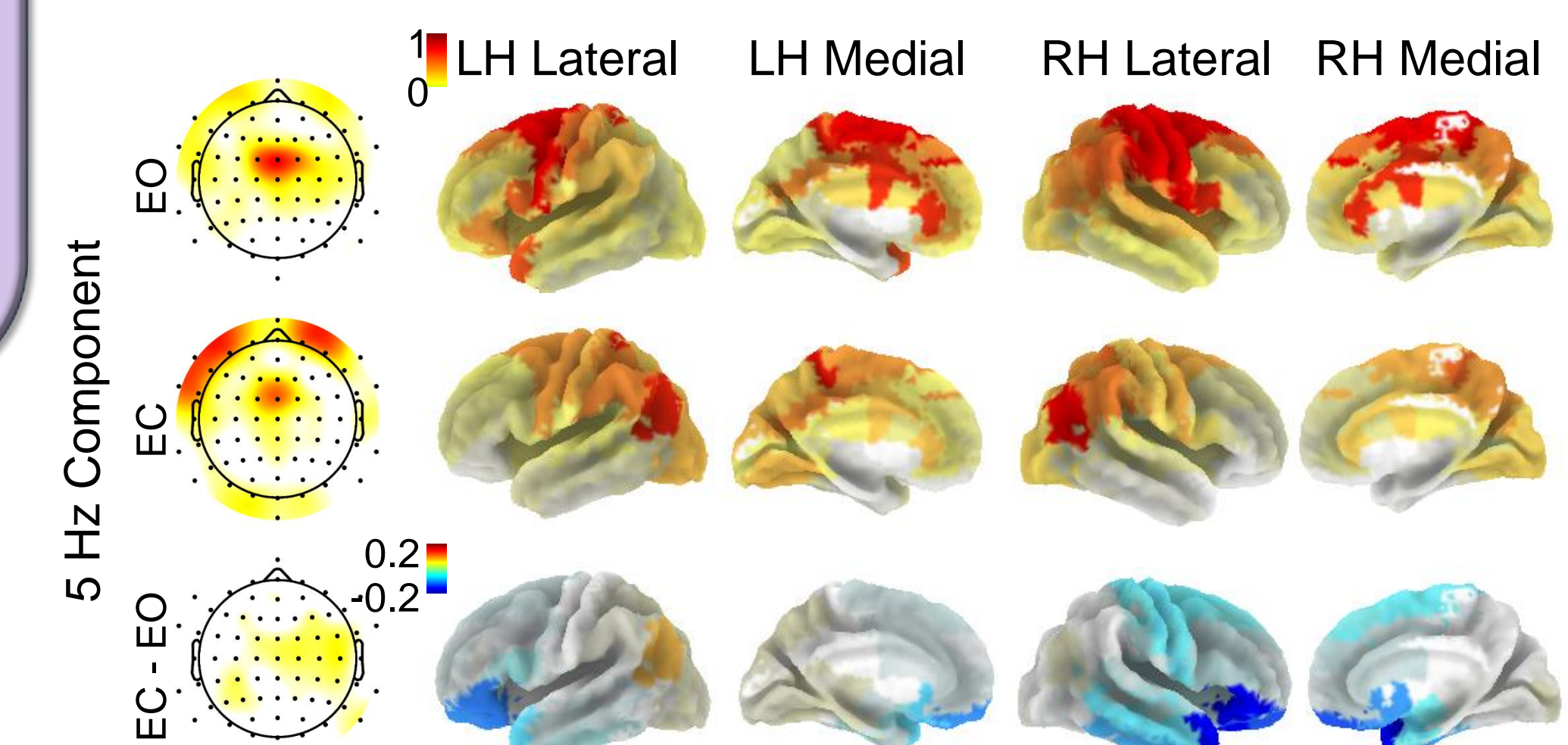
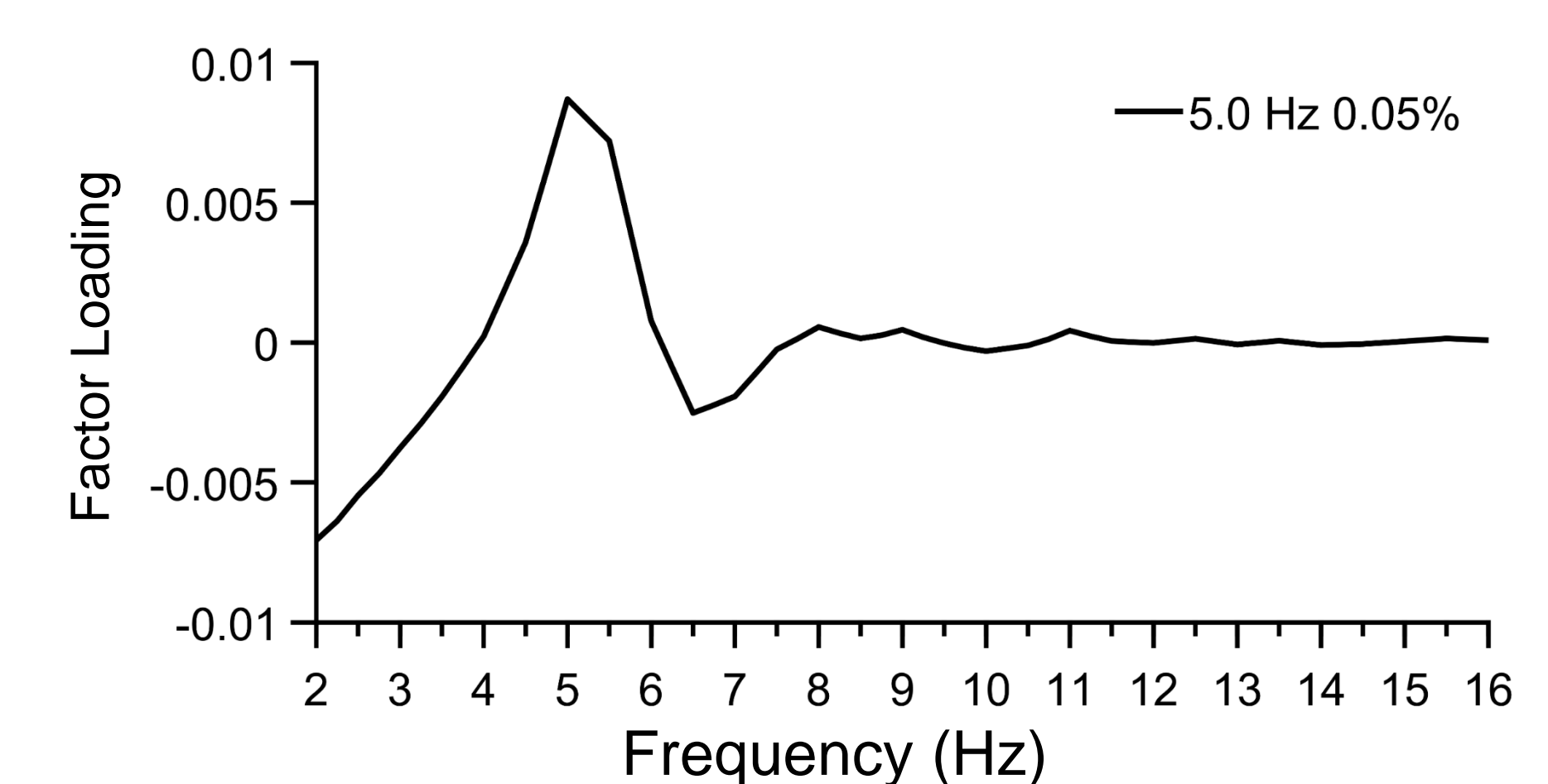


Fig. 4: Midfrontal theta component extracted by combined CSD/eLORETA-fPCA. A. Factor loadings revealed a peak frequency at 5 Hz. B. The overall component topography was consistent with previous work investigating midfrontal theta. Component tomography suggests sources in premotor areas, including the dACC. There were no significant condition differences (EC vs EO) for the theta component after multiple comparisons correction (corrected $ps > .3$). LH / RH = Left / Right Hemisphere.

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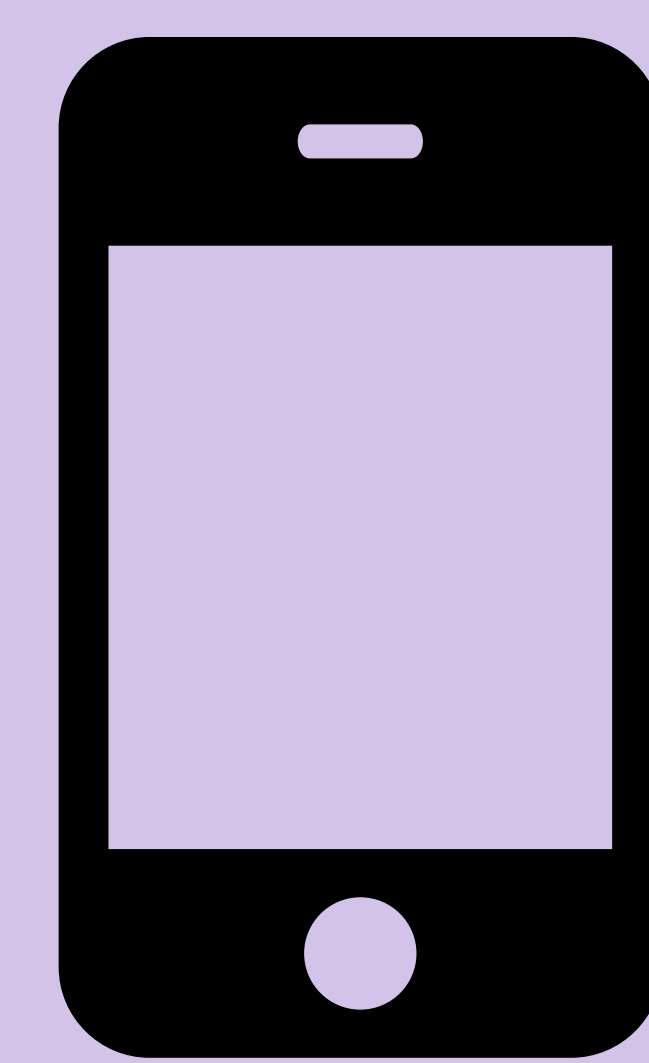


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