Phase-Amplitude Coupling Between EEG Cortical Oscillations and Respiration: An Exploratory Study

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***Abstract*—Cortical oscillatory patterns are associated with a wide range of functions, including attention, motor functions, and memory. Selective modulation of different cortical oscillations is of interest in many brain-computer interface (BCI) and neurofeedback paradigms. Recent findings have suggested that respiration plays a role in modulating higher-frequency electrocortical activity. However, these previous works have mostly relied on invasive neuroimaging modalities, and the relationship between respiration and cortical oscillations recorded non-invasively though imaging techniques, including electroencephalography (EEG), remains underreported. In this study, we explore phase-amplitude coupling (PAC) between the phase of respiration signals and amplitude of EEG band power across several frequency bands. We recorded simultaneous EEG and respiration effort from nine healthy participants during an auditory task and applied a PAC algorithm to explore coupling between respiration phase and EEG band power amplitude. We observed significant PAC in at least three channels and one frequency band across all nine participants. Specifically, respiration-gamma PAC was observed in at least three channels in five of nine participants, while a similar pattern was observed in respiration-alpha PAC in four of nine participants. These findings reinforce previous observations in invasive studies of widely distributed respiration-cortical gamma PAC while suggesting that alpha band oscillations may also be modulated by respiration in some individuals. These results contribute to better understanding of the role of respiration in higher brain functions and could inform future neurofeedback paradigms that integrate respiration tracking.**

***Index Terms*—Electroencephalography (EEG), Respiration, Phase-amplitude coupling (PAC), Cortical oscillations**

I. Introduction

Electroencephalography (EEG) is a widely adopted neuroimaging modality used to explore cortical processing, identify biomarkers of disease, and develop brain-computer interfaces (BCIs) to restore function to impaired individuals. Experimental paradigms are often designed to evoke specific electrocortical responses related to processes of interest, such as attention or auditory processing. Oscillatory activity in the cortex is associated with many processes, including attention [1], memory [2], movement [3], and sensory integration [4]. In some applications, individuals can be trained to selectively modulate oscillatory activity, such as in sensorimotor rhythm BCIs [5].

Some oscillatory behavior in the cortex has been shown to be entrained by respiration. For example, nasal respiration has been shown to entrain delta-theta band oscillations in the piriform [6], parietal [7], and prefrontal [7], [8] cortices in animals. The phase of these respiration-entrained oscillations has been shown to couple with gamma band amplitude in these regions [9] previously identified phase-amplitude coupling (PAC) between other, non-respiration entrained lower and higher frequency electrocortical oscillations [10], [11]. The respiration-entrained oscillations and associated phase-amplitude coupling with gamma band amplitude were shown to be independent of previously identified cortical theta-gamma PAC, and have been identified as a potential confound in animal studies exploring PAC [9].

In addition to current findings identifying PAC between respiration and gamma band amplitude in animals, Zelano et al. (2016) found that PAC between the amplitude of gamma band power measured by intracranial EEG (iEEG) and the instantaneous phase of respiration signals has also been identified in humans in several brain structures, including the piriform cortex, hippocampus, and amygdala [12]. The same study reports significant respiration-delta, respiration-theta, and respiration-beta PAC in the piriform cortex, amygdala (excluding respiration-beta PAC), and hippocampus to varying degrees of consistency across participants. Observed PAC was found to be dependent on nasal respiration. The same study reports improved performance on cognitive tasks during nasal respiration when compared with oral respiration. A subsequent study using iEEG to explore a wider range of cortical and non-cortical locations found significant respiration-gamma PAC in greater than 40% of channels over the motor, parietal, and primary olfactory cortices along with deeper brain structures [13]. It has been posited that these respiration entrained rhythms and the oscillations coupled to them has a role in the functions associated with the regions in which the oscillations occur [14]. Previous work exploring PAC between cortical oscillations primarily reports PAC between respiration and gamma band amplitude, citing inter-subject variability in lower frequency bands [9], [13].

Here, we explore respiration-EEG PAC across several regions of the cortex and EEG frequency bands (theta, alpha, beta, and gamma). We aim to characterize individual-specific respiration-EEG PAC patterns in healthy participants and

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further investigate this under-explored phenomenon. Better understanding the relationship between respiration and cortical oscillations could have implications for future non-invasive experimental designs, as well as elucidate the role of respiration in higher brain functions. This understanding could also provide a foundation for future neurofeedback techniques involving respiration as a means to modulate higher-frequency brain activity.

II. Methods

A. Participants

Nine healthy participants (four female, age 28.3 $\pm$ 9.2) with no known history of neurological disorder or injury were recruited from the University of Rhode Island (URI). This study was approved by the institutional review board (IRB) of URI, and all participants provided informed consent before participation in the study.

B. Experimental Protocol

Participants were seated in a comfortable chair and donned an EEG cap. A pair of headphones was placed over the cap. Full details of the experimental protocol are available in our previous work [15]. Participants completed six experimental runs of an auditory oddball task, during which participants were instructed to count the number of deviant stimuli presented in a run (20 per run, 120 total). Upon hearing the n^{th} deviant stimulus, participants were instructed to mentally count from n to n+4. Deviant stimuli were 500 ms duration 40 Hz white noise click trains, while standard stimuli were 500 ms duration 1 kHz tones.

C. Signal Acquisition

EEG data were collected from 15 electrodes placed on the scalp in locations in accordance with the international 10-5 system (Fpz, AFz, F5, F6, FCz, FC3, FC4, Cz, C5, C6, TTP7h, TTP8h, TPP7h, TPP8h, and Pz) and right-ear referenced. Electrode positions were selected to cover the frontal/prefrontal region and temporal/temporoparietal cortical regions for a separate analysis exploring auditory processing. Signals were amplified using a g.USBamp biosignal amplifier (g.tec medical engineering GmbH, Austria), sampled at 256 Hz, and digitized. A respiration effort belt was fitted around the chest of the participant. Respiration signals were recorded by a second g.USBamp and synchronized with the EEG signal for further processing.

D. Signal Preprocessing

All analyses were performed using MATLAB (R2016b). The first 10 seconds and segments of data following presentation of the 18^{th} deviant stimulus were removed from the signal to avoid potential artifacts in the pre and post-stimulus periods. Signals from each run were concatenated. EEG signals were zero-phase bandpass filtered 0.5-55 Hz and independent component analysis (ICA) was applied to the signal using EEGLAB [16] as a preprocessing step to de-noise the signal. Components containing artifacts were manually identified and removed from the signal. Respiration signals were detrended and smoothed (MATLAB smooth.m) using a 10 sample window before concatenation. Signals were visually inspected, and windows containing artifacts not removed using ICA were marked for rejection with a wide margin (at least one second before and after the identified artifact). Channels Fpz and AFz were also removed from the analysis due to noise across multiple participants.

E. Data Analysis

EEG signals were further zero-phase bandpass filtered into the theta (4-7 Hz), alpha (7-14 Hz), beta (15-30 Hz), and gamma (30-55 Hz) bands using 768 point FIR bandpass filters. The Hilbert transform was applied to both the narrowband filtered EEG and respiration signal time series. Respiration signal power spectra were extracted using Welch's spectral estimate (60s windows, 50% overlap) for the purpose of visual inspection/determining general breathing rate. Instantaneous power was extracted from the EEG Hilbert time series and instantaneous phase was extracted from the respiration Hilbert time series. Previously marked windows were removed from the power and phase time series (the following PAC algorithm relies on same-sample comparisons of signal phase and amplitude; removing these samples does not otherwise affect the PAC analysis), resulting in 32.83 ± 1.28 minutes of data retained for analysis. The PAC algorithm described in Tort et al. (2010) [10] was used to calculate a modulation index value (MI) for each electrode and frequency band to quantify the observed coupling between respiration signal phase and narrowband EEG ampitude. PAC refers to the selective modulation of the amplitude of a higher frequency signal (EEG in this analysis) at different phase angles of a lower frequency signal (respiration in this analysis).

The PAC algorithm is described in the following section:

The respiration phase time series $\phi(t)$ and narrow-band amplitude time series $A(t)$ from a given frequency band/channel pair is extracted as previously stated. Phase bins of 20° width ranging from -180° to 180° are extracted ($N = 18$ bins), and samples from $A(t)$ are averaged over each bin j, where the average signal amplitude in phase bin j is denoted $\langle A \rangle_\phi(j)$. Each mean amplitude $\langle A \rangle_\phi(j)$ is normalized by the sum of mean amplitudes over the bins:

$$P(j) = \frac{\langle A \rangle_\phi(j)}{\sum_{k=1}^{N} \langle A \rangle_\phi(k)} \tag{1}$$

The Kullback-Leibler distance between the distribution $P(j)$ and the uniform distribution $D_{KL}(P, U)$ is then determined

$$D_{KL}(P, U) = log(N) - H(P) \tag{2}$$

where $H(P)$ is the Shannon entropy of the distribution P:

$$H(P) = -\sum_{j=1}^{N} P(j) log[P(j)] \tag{3}$$

The MI value is then calculated:

$$MI = \frac{D_{KL}(P,U)}{log(N)} \tag{4}$$

This process is repeated for every frequency band/channel pair. The MI value increases as the observed distribution of amplitudes over phase bins deviates from the uniform distribution.

A distribution of surrogate MI values was generated for each electrode and frequency band by randomly selecting a point in the middle 80% of the amplitude time series, separating the signal, and appending end of the later segment to the beginning of the earlier segment and generating a surrogate MI value. This process was repeated for 200 iterations. The observed MI value was compared with the distribution of surrogate MI values, and the ratio of surrogate MI values greater than the observed MI value was used to determine a p-value for each frequency band/channel pair.

III. Results

Fig. 1 displays the power spectra of the respiration signals of all participants. Six of the nine participants exhibited fairly regular breathing patterns throughout the course of the session, while three of the nine participants exhibited variable breathing patterns. Peak respiratory freqencies ranged from 0.08 Hz to 0.37 Hz across participants.

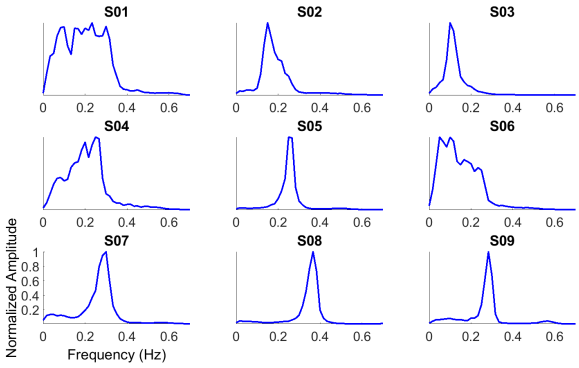

Fig. 1. Normalized power spectra of the respiration signal recorded from each subject (S).

A representation of the dynamics captured by the PAC analysis is displayed in Fig. 2. In channels where significant PAC is observed, band power amplitude of the EEG signal change depending on the phase of the respiration signal. In representative participant S03, transient increases in gamma band power are observed in the phase bins from approximately 0° to 80°. As shown in the p-value maps across the explored frequency bands and channels in Fig. 3, we observed significant respiration-EEG PAC in multiple channel/frequency band pairs across participants. As it is seen, significant respiration-gamma PAC is observed over approximately half (5/9) participants in more than three channels, while significant respiration-alpha PAC was observed in a similar (4/9) number of participants in more than three channels. A comparison between the mean

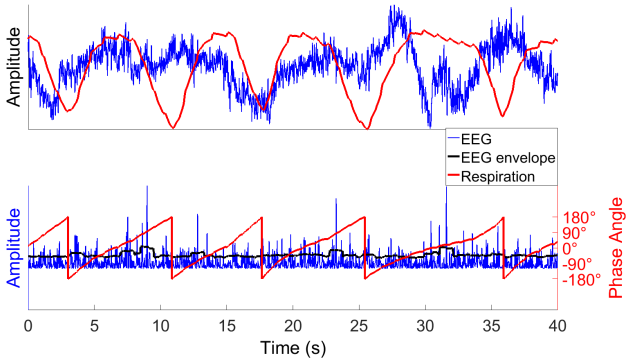

Fig. 2. Top: Raw normalized broadband filtered EEG signal from a representative participant (S03, channel FCz) is plotted in blue, while the respiration signal is plotted in red. Bottom: Gamma band amplitude from the same participant/channel is plotted against the phase of the respiration signal, plotted in red. The upper envelope of the amplitude time series is plotted in black for better visualization.

gamma amplitude distribution across phase bins over significant channel FCz $P_{Gamma,FCz}$ from a representative participant (S03) is displayed in Fig. 4. It is noted that broad signifi-

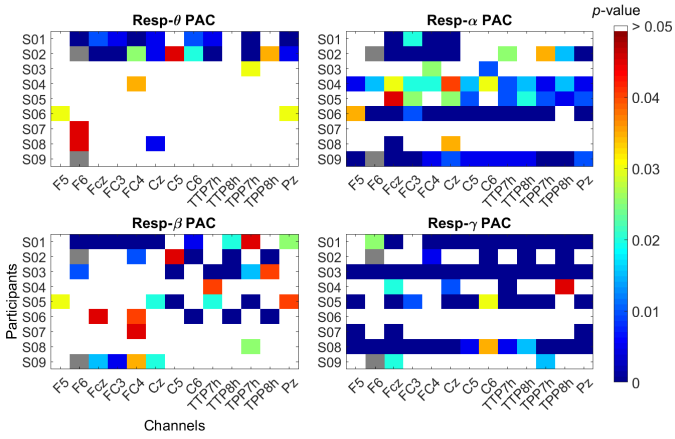

Fig. 3. p-value maps generated by the PAC analysis between respiration and EEG theta, alpha, beta, and gamma frequency band power amplitude. p-values greater than 0.05 are displayed as white cells, while channels excluded from the analysis are displayed as gray cells.

cant respiration-alpha PAC is observed in two participants that do not demonstrate significant respiration-gamma PAC (S06 and S09). The spatial distribution of significant respiration-gamma and respiration-alpha PAC appears inconsistent; some participants exhibit broadly distributed PAC (S01, S03, S05, S06, S08), while others demonstrate localized respiration-EEG PAC (S02 demonstrates right-lateralized respiration-gamma PAC and frontocentral respiration-alpha PAC). Respiration-theta and respiration-beta PAC is less consistent across participants. Significant respiration-theta PAC is only observed in two participants (S01 and S02), while significant respiration-beta PAC is observed in more than three channels in 4/9 participants (S01, S02, S03, S06). This respiration-beta PAC is right lateralized in participants S02 and S06.

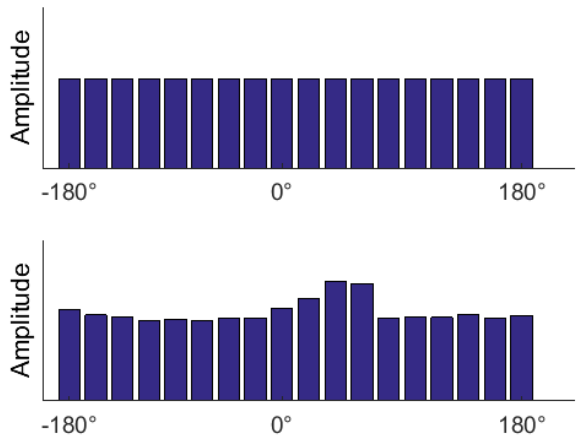

Fig. 4. Top: Uniform distribution of amplitude values in phase bins. Bottom: Observed distribution of gamma amplitude values across phase bins in channel FCz ($P_{Gamma,FCz}$) from a representative subject (S03) demonstrating significant respiration-gamma PAC.

IV. Conclusions

Overall, we observed widespread respiration-gamma and respiration-alpha PAC across participants, with substantial inter-participant differences in significant frequency bands and electrode locations. Specifically, we observed respiration-gamma PAC across the frontal, frontocentral, central, temporoparietal, and parietal regions in several subjects. The observation of widespread but inconsistent respiration-gamma PAC follows and reinforces previous iEEG findings [13]. The observation of respiration-alpha PAC is also notable. Among the many processes associated with cortical alpha band activity, changes in alpha band power have been related to attention [1], as well as changes in respiration [17]. Further research investigating this finding and possible relationship between respiration-alpha PAC and attention may be warranted. Overall, the performed analysis suggests the presence of frequency-band specific coupling between respiration signal phase and EEG cortical oscillations.

There are several limitations to this study and the strength of conclusions drawn. The respiration signal used in this analysis was collected with a respiration effort belt, which cannot differentiate between nasal and oral respiration. Respiration-EEG PAC has been shown to be dependent on breathing route [12]. This limitation could partially explain the inconsistencies across participants in observed PAC patterns. Future studies should be conducted with a more appropriate respiration signal, such as nasal airflow pressure sensor. The use of EEG as a neuroimaging modality could also be considered a constraint in this study when compared with previous works due to the lower spatial resolution of surface EEG compared with invasive methods [18] and susceptibility to muscle artifacts.

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References

[1] S. Itthipuripat, T. C. Sprague, and J. T. Serences, "Functional MRI and EEG index complementary attentional modulations," *J. Neurosci.*, vol. 39, no. 31, pp. 6162–6179, Jul. 2019.

[2] W. Klimesch, "EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis," *Brain Res. Brain Res. Rev.*, vol. 29, no. 2-3, pp. 169–195, Apr. 1999.

[3] S. L. Norman, D. J. McFarland, A. Miner, S. C. Cramer, E. T. Wolbrecht, J. R. Wolpaw, and D. J. Reinkensmeyer, "Controlling pre-movement sensorimotor rhythm can improve finger extension after stroke," *J. Neural Eng.*, vol. 15, no. 5, p. 056026, Oct. 2018.

[4] C. S. Herrmann, D. Strüber, R. F. Helfrich, and A. K. Engel, "EEG oscillations: From correlation to causality," *Int. J. Psychophysiol.*, vol. 103, pp. 12–21, May 2016.

[5] C. I. Penaloza, M. Alimardani, and S. Nishio, "Android feedback-based training modulates sensorimotor rhythms during motor imagery," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 26, no. 3, pp. 666–674, Mar. 2018.

[6] A. Fontanini and J. M. Bower, "Variable coupling between olfactory system activity and respiration in ketamine/xylazine anesthetized rats," *J. Neurophysiol.*, vol. 93, no. 6, pp. 3573–3581, Jun. 2005.

[7] W. Zhong, M. Ciatipis, T. Wolfenstetter, J. Jessberger, C. Müller, S. Ponsel, Y. Yanovsky, J. Brankačk, A. B. L. Tort, and A. Draguhn, "Selective entrainment of gamma subbands by different slow network oscillations," *Proc. Natl. Acad. Sci. U. S. A.*, vol. 114, no. 17, pp. 4519–4524, Apr. 2017.

[8] J. Biskamp, M. Bartos, and J.-F. Sauer, "Organization of prefrontal network activity by respiration-related oscillations," *Sci. Rep.*, vol. 7, p. 45508, Mar. 2017.

[9] A. B. L. Tort, J. Brankačk, and A. Draguhn, "Respiration-entrained brain rhythms are global but often overlooked," *Trends Neurosci.*, vol. 41, no. 4, pp. 186–197, Apr. 2018.

[10] A. B. L. Tort, R. Komorowski, H. Eichenbaum, and N. Kopell, "Measuring phase-amplitude coupling between neuronal oscillations of different frequencies," *J. Neurophysiol.*, vol. 104, no. 2, pp. 1195–1210, Aug. 2010.

[11] F. Jung, V. Witte, Y. Yanovsky, M. Klumpp, J. Brankačk, A. B. L. Tort, and A. Draguhn, "Differential modulation of parietal cortex activity by respiration and ϑ oscillations," *J. Neurophysiol.*, vol. 127, no. 3, pp. 801–817, Mar. 2022.

[12] C. Zelano, H. Jiang, G. Zhou, N. Arora, S. Schuele, J. Rosenow, and J. A. Gottfried, "Nasal respiration entrains human limbic oscillations and modulates cognitive function," *J. Neurosci.*, vol. 36, no. 49, pp. 12 448–12 467, Dec. 2016.

[13] J. L. Herrero, S. Khuvis, E. Yeagle, M. Cerf, and A. D. Mehta, "Breathing above the brain stem: volitional control and attentional modulation in humans," *J. Neurophysiol.*, vol. 119, no. 1, pp. 145–159, Jan. 2018.

[14] D. H. Heck, S. S. McAfee, Y. Liu, A. Babajani-Feremi, R. Rezaie, W. J. Freeman, J. W. Wheless, A. C. Papanicolaou, M. Ruszinkó, Y. Sokolov, and R. Kozma, "Breathing as a fundamental rhythm of brain function," *Front. Neural Circuits*, vol. 10, p. 115, 2016.

[15] J. McLinden, S. B. Borgheai, S. Hosni, C. Kumar, N. Rahimi, M. Shao, K. M. Spencer, and Y. Shahriari, "Individual-specific characterization of event-related hemodynamic responses during an auditory task: An exploratory study," *Behav. Brain Res.*, vol. 436, no. 114074, p. 114074, Jan. 2023.

[16] A. Delorme and S. Makeig, "EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis," *J. Neurosci. Methods*, vol. 134, no. 1, pp. 9–21, Mar. 2004.

[17] P. Gomez, S. Shafy, and B. Danuser, "Respiration, metabolic balance, and attention in affective picture processing," *Biol. Psychol.*, vol. 78, no. 2, pp. 138–149, May 2008.

[18] Q. Wang, P. A. Valdés-Hernández, D. Paz-Linares, J. Bosch-Bayard, N. Oosugi, M. Komatsu, N. Fujii, and P. A. Valdés-Sosa, "EECoG-Comp: An open source platform for concurrent EEG/ECoG comparisons-applications to connectivity studies," *Brain Topogr.*, vol. 32, no. 4, pp. 550–568, Jul. 2019.