
# Assignment 3

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Github Repository

**Neuroscience of Learning, Memory, and Cognition**

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# Contents

# Introduction to Statistical Tests

Statistical tests are methods used to analyze data, compare relationships between variables, and test hypotheses. One of the most commonly used statistical tests in scientific research is the t-test. The t-test is based on the t-statistic and is calculated as follows:

$$t = \frac{\overline{x_1} - \overline{x_2}}{\frac{s}{\sqrt{n}}}$$

where $\overline{x_1}$ and $\overline{x_2}$ are the sample means, $s$ is the standard deviation, and $n$ is the sample size. The t-test is used to determine if the difference between the two sample means is statistically significant. The null hypothesis states that there is no difference between the means of the two samples. The p-value is used to test the hypothesis. If the p-value is less than a certain threshold (usually 0.05), the null hypothesis is rejected.

There are two main types of t-tests: unpaired and paired. The unpaired t-test is used when comparing two independent groups, while the paired t-test is used when comparing two related or matched groups.

# Permutation Test

A permutation test is a non-parametric statistical test used to test the significance of an observed effect. Unlike traditional tests that rely on assumptions about the data distribution, permutation tests compare the observed data to a large number of randomly permuted datasets to determine the statistical significance. This method is particularly useful when the sample size is small or the underlying distribution is unknown. In this test, the null hypothesis assumes that there is no effect or difference between the groups.

The permutation test works by repeatedly shuffling the data and calculating the test statistic for each permuted dataset. By comparing the observed test statistic to the distribution of test statistics from the permuted datasets, the significance of the observed result can be determined.

Permutation tests are commonly used in various fields, including neuroimaging (e.g., fMRI, EEG), where the data may not follow a normal distribution. These tests are valuable for studying complex models where traditional statistical assumptions may not hold.

# Granger Causality

Granger Causality (GC) is one of the methods used to estimate causal relationships based on past values of variables. The basic idea is to check whether past values of one variable (e.g., $y(n)$) can help predict future values of another variable (e.g., $x(n)$). The model typically used is a Vector Autoregression (VAR) model, which is based on the following formulation:

$$y(n) = \sum_{p=1}^{M_y} \alpha_p y(n-p) + \epsilon_y$$

where $M_y$ is the maximum lag, and $\epsilon_y$ is the residual term. Similarly, for $x(n)$, we use the following model:

$$x(n) = \sum_{q=1}^{M_x} \beta_q x(n-q) + \epsilon_x$$

The Granger Causality test measures the ability of past values of $y(n)$ to predict future values of $x(n)$, and vice versa, by computing the relationship between $y$ and $x$. The test statistic is based on the likelihood ratio and is given by:

$$GC_{x\to y} = \log\left(\frac{\sum y_{xy}}{\sum y_{xy}}\right)$$

where $\sum y_{xy}$ refers to the sum of the residuals of the regression model. Based on the test statistic, the p-value is calculated to evaluate the statistical significance of the causal relationship.

A common criterion used to compare the fit of different models in Granger Causality testing is the AIC (Akaike Information Criterion), defined as:

$$AIC = -2\log(L) + 2k$$

where $L$ is the likelihood of the model, and $k$ is the number of parameters. Additionally, BIC (Bayesian Information Criterion) is another criterion often used to select the best model. For small datasets, AIC is typically preferred, while BIC is more suitable for larger datasets.

The number of parameters $k$ and the likelihood function for a model are crucial in the evaluation of the AR model. The relationship between BIC and likelihood can be written as:

$$BIC = -2\log(L) + k\log(n)$$

where $L$ is the likelihood of the model, and $k$ is the number of parameters.

**Note:** The software package `statsmodels` can be used to implement the AR model, and for the evaluation of Granger Causality (GC), the AIC criterion can be calculated. The AIC criterion is defined as:

$$AIC = -2\log(L) + 2k$$

The performance of the GC model can be assessed using the MSE (Mean Squared Error) and other related criteria.

**Example:** Suppose $x(t)$ and $y(t)$ are the time series data and the model is described by the following equations:

$$x(t) = A_1\cos(2\pi f_0 t) + \sigma_n n_1(t)$$
$$y(t) = A_2\cos(2\pi f_0(t-\tau)) + \sigma_n n_2(t)$$

where $\sigma_n$ represents noise in the system. Additionally, the Granger Causality (GC) test can be performed by evaluating the relationship between the variables $x(t)$ and $y(t)$.

For the parameters $A_1 = 1$, $A_2 = 0.5$, and $f_0 = 40$, the test is performed for different values of the lag $\tau$. The optimal values can be obtained by calculating the GC for different lag lengths $\tau$.

The GC test can be applied for different scenarios, and the results are dependent on the values of $\tau$ used in the calculation.

```
    def generate_signals(A1, A2, f0, sigma_n, tau, Fs, duration=2):
        """Generate signals with specified delay and noise"""
        t = np.arange(0, duration, 1/Fs)
        N = len(t)

        # Handle negative delay by time shifting
        if tau < 0:
            x_delay = int(abs(tau)*Fs)
            y_delay = 0
        else:
```

```
            x_delay = 0
            y_delay = int(tau*Fs)

        # Base signals with proper delay handling
        x_clean = A1 * np.cos(2*np.pi*f0*(t - x_delay/Fs))
        y_clean = A2 * np.cos(2*np.pi*f0*(t - y_delay/Fs))

        # Add noise
        x = x_clean + sigma_n * np.random.randn(N)
        y = y_clean + sigma_n * np.random.randn(N)

        return x, y

    def custom_granger(x, y, max_lag=5):
        """Custom Granger causality implementation for both directions"""
        def make_lags(data, lag):
            return np.array([data[i:-lag+i] for i in range(lag)]).T

        n = len(x)
        results = {}

        for direction in ['x->y', 'y->x']:
            if direction == 'x->y':
                target, source = y, x
            else:
                target, source = x, y

            # Create lag matrices
            lags_target = make_lags(target, max_lag)
            lags_source = make_lags(source, max_lag)

            # Restricted model (only target history)
            X_restricted = np.hstack([lags_target, np.ones((n-max_lag, 1))])
            y_target = target[max_lag:]

            # Unrestricted model (target + source history)
            X_unrestricted = np.hstack([lags_target, lags_source, np.ones((n-
max_lag, 1))])

            # Solve OLS
            try:
                beta_restricted = np.linalg.lstsq(X_restricted, y_target,
rcond=None)[0]
                beta_unrestricted = np.linalg.lstsq(X_unrestricted, y_target,
rcond=None)[0]
            except:
                results[direction] = np.nan
                continue

            # Calculate residuals
            res_restricted = y_target - X_restricted @ beta_restricted
            res_unrestricted = y_target - X_unrestricted @ beta_unrestricted

            # Compute F-statistic
            RSS_r = np.sum(res_restricted**2)
            RSS_ur = np.sum(res_unrestricted**2)
            df_num = max_lag
            df_den = X_unrestricted.shape[0] - X_unrestricted.shape[1]
```

```
            F = ((RSS_r - RSS_ur)/df_num) / (RSS_ur/df_den)
            results[direction] = F

        return results

    # Parameters
    A1 = 1
    A2 = 0.5
    f0 = 5          # Changed to 5Hz
    Fs = 500        # Changed to 500Hz
    taus = [-0.01, 0, 0.01]
    sigma_n_values = np.linspace(0, 5, 128)
    max_lag = 5

    # Results storage
    results = {tau: {'x->y': [], 'y->x': []} for tau in taus}

    # Main computation loop
    for tau in taus:
        print(f"Processing  = {tau:.3f}s...")
        for sigma_n in sigma_n_values:
            x, y = generate_signals(A1, A2, f0, sigma_n, tau, Fs)
            gc = custom_granger(x, y, max_lag)
            results[tau]['x->y'].append(gc['x->y'])
            results[tau]['y->x'].append(gc['y->x'])

    # Plotting
    plt.figure(figsize=(15, 5))
    for idx, tau in enumerate(taus, 1):
        plt.subplot(1, 3, idx)
        plt.plot(sigma_n_values, results[tau]['x->y'], 'b', label='→XY')
        plt.plot(sigma_n_values, results[tau]['y->x'], 'r--', label='→YX')
        plt.title(f' = {tau:.3f}s (Delay: {tau*Fs:.1f} samples)')
        plt.xlabel('Noise Power  ()')
        plt.ylabel('Granger F-statistic')
        plt.grid(True)
        plt.legend()

    plt.tight_layout()
    plt.show()
```

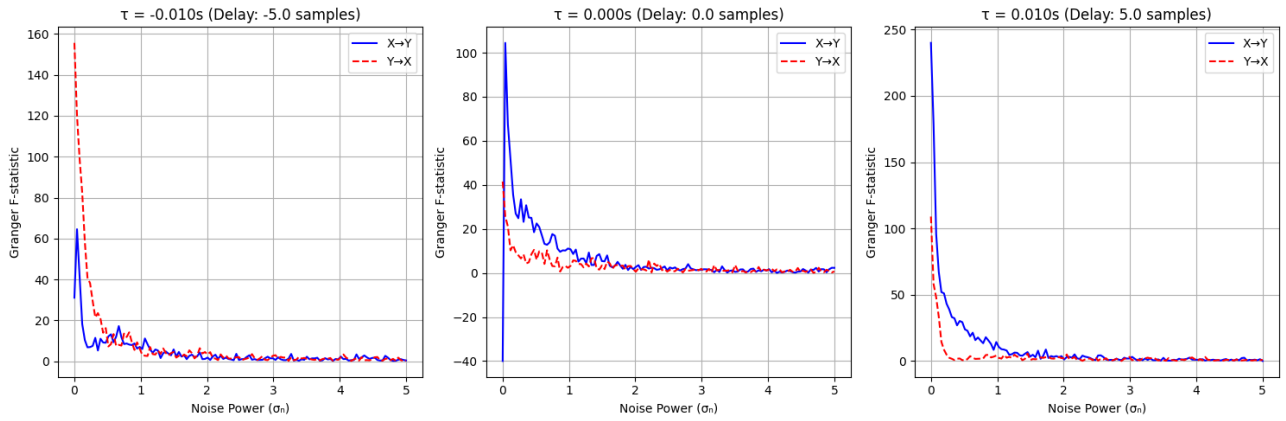


Figure 1: Granger Causality with different amounts of $\tau$

Soloution

The figure shows the relationship between Granger Causality F-statistics and noise power ($\sigma_n$) for different values of the time delay parameter ($\tau$).

- **X-axis (Noise Power)**: This represents the noise power ($\sigma_n$) applied to the time series data.
- **Y-axis (Granger F-statistic)**: The F-statistic is used to test the Granger causality between the two time series (X and Y). A higher F-statistic indicates stronger causality from one series to the other.
- **Curves for X $\rightarrow$ Y and Y $\rightarrow$ X**: These two lines represent the direction of causality being tested. The solid blue line (X $\rightarrow$ Y) shows the Granger causality from X to Y, and the dashed red line (Y $\rightarrow$ X) shows the Granger causality from Y to X.

The figure is divided into three panels that represent different values of the time delay parameter ($\tau$):

1. **Left panel ($\tau = -0.010s$)**: A delay of -5 samples. This shows a strong peak in the F-statistic for low noise power, with a rapid decline as noise power increases.
2. **Middle panel ($\tau = 0.000s$)**: No delay (0 samples). The F-statistic here behaves similarly but with a different rate of decline compared to the other panels.
3. **Right panel ($\tau = 0.010s$)**: A delay of 5 samples. The F-statistic is significantly higher at low noise power compared to the other panels and shows a similar decline with increasing noise.

Soloution

1. **What change in Granger Causality value occurs due to the increase in noise power?**

   As noise power ($\sigma_n$) increases, the Granger F-statistic declines sharply for both directions of causality (X $\rightarrow$ Y and Y $\rightarrow$ X). This suggests that increasing noise reduces the strength of the Granger causality between the two time series. At low noise power, the Granger F-statistic is much higher, indicating a strong causality, but this relationship weakens as the noise power increases.

2. **What relationship does Granger Causality have with the symbol $\tau$?**

   The symbol $\tau$ represents the time delay between the two time series. The figure shows that the value of $\tau$ influences the strength of Granger causality, especially at low noise power. With $\tau = 0.010s$ (right panel), there is a higher F-statistic compared to the case where $\tau = -0.010s$ (left panel). In general, the time delay affects the peak and the rate at which the F-statistic decays as noise power increases.

# Receiving Pre-processed Data

- First, download the pre-processed data along with the relevant information. Make sure the data corresponds to the correct criteria such as punishment and reward. Pay attention to the detailed instructions on how to use the data in the file `DataSetDescriptions.docx`.

- The data should be standardized using the z-score method.

- From each dataset, select the most recent samples (e.g., for 20 samples) and match them by selecting data at equivalent time points.

- After pre-processing, the data can be used for various analysis methods. Make sure to check the data structure before proceeding with the analysis.

```
    reward_data = sio.loadmat('Reward.mat')
    reward_trials = reward_data['All_data_Pos']
    punishment_data = sio.loadmat('Punishment.mat')
    punishment_trials = punishment_data['All_data_Neg']

    datalengths = sio.loadmat('DataLengths.mat')
    trial_lengths = datalengths['data_lengths']

    num_subjects, num_electrodes, num_trials, num_time_samples = reward_trials
    .shape

    num_selected_trials = 20
    normalized_reward_trials = np.zeros((num_subjects, num_electrodes,
    num_selected_trials, num_time_samples))
    normalized_punishment_trials = np.zeros((num_subjects, num_electrodes,
    num_selected_trials, num_time_samples))

    electrode_labels = ['FPz', 'F7', 'F3', 'Fz', 'F4', 'F8', 'T7', 'C3', 'Cz',
    'C4', 'T8', 'P7', 'P3', 'Pz', 'P4', 'P8', 'Oz']

    for subject_idx in range(num_subjects):
        max_reward_trials = min(trial_lengths[subject_idx][0], 200)
        reward_random_indices = np.random.choice(max_reward_trials,
    num_selected_trials, replace=False)
        for trial_num, trial_idx in enumerate(reward_random_indices):
            reward_trial_data = reward_trials[subject_idx, :, trial_idx, :]
            normalized_reward = (reward_trial_data - np.mean(reward_trial_data
    , axis=-1, keepdims=True)) / np.std(reward_trial_data, axis=-1, keepdims=
    True)
            normalized_reward_trials[subject_idx, :, trial_num, :] =
    normalized_reward


        max_punishment_trials = min (trial_lengths[subject_idx][1], 200)
        punishment_random_indices = np.random.choice(max_punishment_trials,
    num_selected_trials, replace=False)
        for trial_num, trial_idx in enumerate(punishment_random_indices):
            punishment_trial_data = punishment_trials[subject_idx, :,
    trial_idx, :]
            normalized_punishment = (punishment_trial_data - np.mean(
    punishment_trial_data, axis=-1, keepdims=True)) / np.std(
    punishment_trial_data, axis=-1, keepdims=True)
            normalized_punishment_trials[subject_idx, :, trial_num, :] =
    normalized_punishment

        normalized_reward_trials_healthy = normalized_reward_trials
    [[11,13,15,18,19,20,21,22,23,24,25,26,27,28,29]]
```

```
        normalized_reward_trials_AD = normalized_reward_trials
    [[0,1,2,3,4,5,6,7,8,9,10,12,14,16,17]]

        normalized_punishment_trials_healthy = normalized_punishment_trials
    [[11,13,15,18,19,20,21,22,23,24,25,26,27,28,29]]
        normalized_punishment_trials_AD = normalized_punishment_trials
    [[0,1,2,3,4,5,6,7,8,9,10,12,14,16,17]]
```

# Data processing using GC

For groups of 2 individuals

# Evaluating Data Using PAC Criterion in Different Frequency Bands

## *PAC Computation and Comparison of Values*

1. In this section, we compute the PAC (Phase-Amplitude Coupling) for different frequency bands to assess the relationships between the different variables. We focus on the analysis of how the PAC interacts with individuals based on punishment and reward, as described in the `DataSetDescriptions.docx` file.

2. For each frequency band ($500\,\text{Hz} \leq f_z \leq 1000\,\text{Hz}$), we compute the PAC using different frequency points and amplitude frequency points. Specifically, we compute PAC for a range of phase frequency points and amplitude frequency points.

3. The data set should be pre-processed using z-score normalization for each variable.

4. For this experiment, we use the MVL method to compute PAC values across frequency ranges.

5. A t-test is performed across the different frequency points, and the PAC values are analyzed using Python's scipy library.

6. The final computed PAC values will be used to understand the relationship between the reward/punishment criteria.

```
def calculate_PAC_Main(normalized_trials, start_timestep, end_timestep):

    subject_count = normalized_trials.shape[0]
    channel_1 = 3  # 4th channel Fz
    channel_2 = 13  # 14th channel Pz
    trial_count = normalized_trials.shape[2]

    # Initialize PAC object with specified frequency ranges
    p_obj = Pac(idpac=(6, 0, 0), f_pha=(4, 9, 1, 1), f_amp=(20, 51, 1, 1))

    # List to store PAC values (2D arrays for each trial and subject)
    pac_values = []

    # Loop over each subject and trial to compute PAC
    for subject in range(subject_count):
        subject_data = normalized_trials[subject, :, :, :]  # Shape: (17, 20,
    800)

```

```
        for trial in range(trial_count):
            # Extract the data for the 4th and 14th channels
            data_channel_1 = subject_data[channel_1, trial, start_timestep:end_timestep]  # Shape: (250,)
            data_channel_2 = subject_data[channel_2, trial, start_timestep:end_timestep]  # Shape: (250,)

            # Check if data contains NaN values
            if np.any(np.isnan(data_channel_1)) or np.any(np.isnan(data_channel_2)):
                continue

            # Compute phase and amplitude for the selected channels
            pha_p = p_obj.filter(500, data_channel_2, ftype='phase')
            amp_p = p_obj.filter(500, data_channel_1, ftype='amplitude')

            # Check if phase or amplitude signals contain NaN
            if np.any(np.isnan(pha_p)) or np.any(np.isnan(amp_p)):
                continue

            # Compute PAC using mean_vector_length
            pac_result = mean_vector_length(pha_p, amp_p)

            # Check if PAC result is NaN
            if np.any(np.isnan(pac_result)):
                continue

            # Append the 2D PAC result (shape: [num_phase_freqs, num_amp_freqs])
            pac_values.append(pac_result)

    # Convert the list of PAC values to a numpy array (shape: 600, 30, 4, 1)
    pac_values = np.array(pac_values)

    # Average over the first dimension (axis=0: averaging across trials/subjects)
    pac_values_avg = np.mean(pac_values, axis=0)

    # Remove the last singleton dimension (axis=-1)
    PAC_main = pac_values_avg.squeeze()

    return (p_obj, PAC_main)

def main():
    p_obj_reward_first_h, PAC_main_reward_first_h = calculate_PAC_Main(normalized_reward_trials_healthy, 200, 450)
    p_obj_punishment_first_h, PAC_main_punishment_first_h = calculate_PAC_Main(normalized_punishment_trials_healthy, 200, 450)
    p_obj_reward_first_a, PAC_main_reward_first_a = calculate_PAC_Main(normalized_reward_trials_AD, 200, 450)
    p_obj_punishment_first_a, PAC_main_punishment_first_a = calculate_PAC_Main(normalized_punishment_trials_AD, 200, 450)

    p_obj_reward_second_h, PAC_main_reward_second_h = calculate_PAC_Main(normalized_reward_trials_healthy, 450, 700)
    p_obj_punishment_second_h, PAC_main_punishment_second_h = calculate_PAC_Main(normalized_punishment_trials_healthy, 450, 700)
    p_obj_reward_second_a, PAC_main_reward_second_a = calculate_PAC_Main(
```

```
    normalized_reward_trials_AD, 450, 700)
    p_obj_punishment_second_a, PAC_main_punishment_second_a =
    calculate_PAC_Main(normalized_punishment_trials_AD, 450, 700)

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_reward_first_h.comodulogram(PAC_main_reward_first_h, title="Averaged
     PAC Comodulogram Reward First Interval Healthy", cmap='viridis', vmax=0.1,
     vmin=0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_punishment_first_h.comodulogram(PAC_main_punishment_first_h, title="
    Averaged PAC Comodulogram Punishment First Interval Healthy", cmap='viridis
    ', vmax=0.1, vmin=0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_reward_first_a.comodulogram(PAC_main_reward_first_a, title="Averaged
     PAC Comodulogram Reward First Interval AD", cmap='viridis', vmax=0.1, vmin
    =0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_punishment_first_a.comodulogram(PAC_main_punishment_first_a, title="
    Averaged PAC Comodulogram Punishment First Interval AD", cmap='viridis',
    vmax=0.1, vmin=0)
    plt.tight_layout()
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    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_reward_second_h.comodulogram(PAC_main_reward_second_h, title="
    Averaged PAC Comodulogram Reward Second Interval Healthy", cmap='viridis',
    vmax=0.1, vmin=0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_punishment_second_h.comodulogram(PAC_main_punishment_second_h, title
    ="Averaged PAC Comodulogram Punisgment Second Interval Healthy", cmap='
    viridis', vmax=0.1, vmin=0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_reward_second_h.comodulogram(PAC_main_reward_second_a, title="
    Averaged PAC Comodulogram Reward Second Interval AD", cmap='viridis', vmax
    =0.1, vmin=0)
    plt.tight_layout()
```

```
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_punishment_second_h.comodulogram(PAC_main_punishment_second_a, title
    ="Averaged PAC Comodulogram Punisgment Second Interval AD", cmap='viridis',
     vmax=0.1, vmin=0)
    plt.tight_layout()
    plt.show()
```

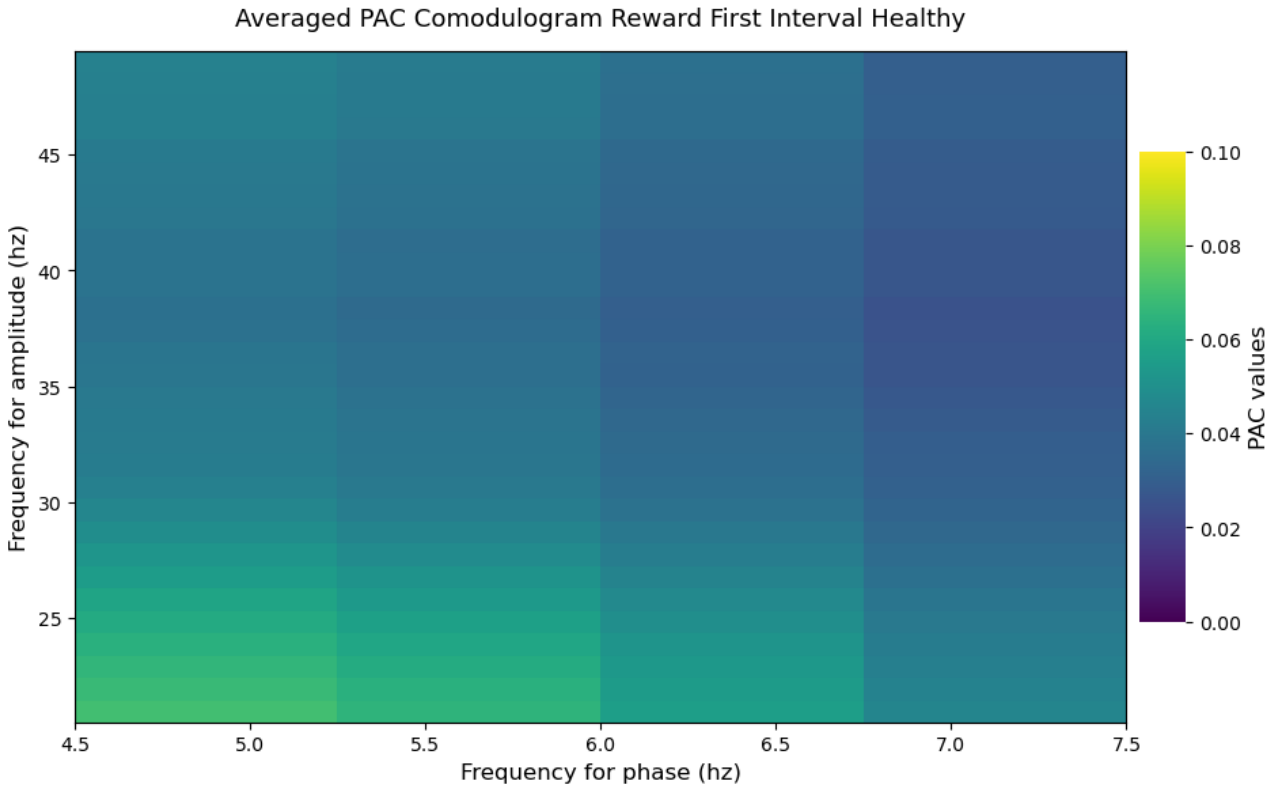


Figure 2: Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for Healthy Subjects

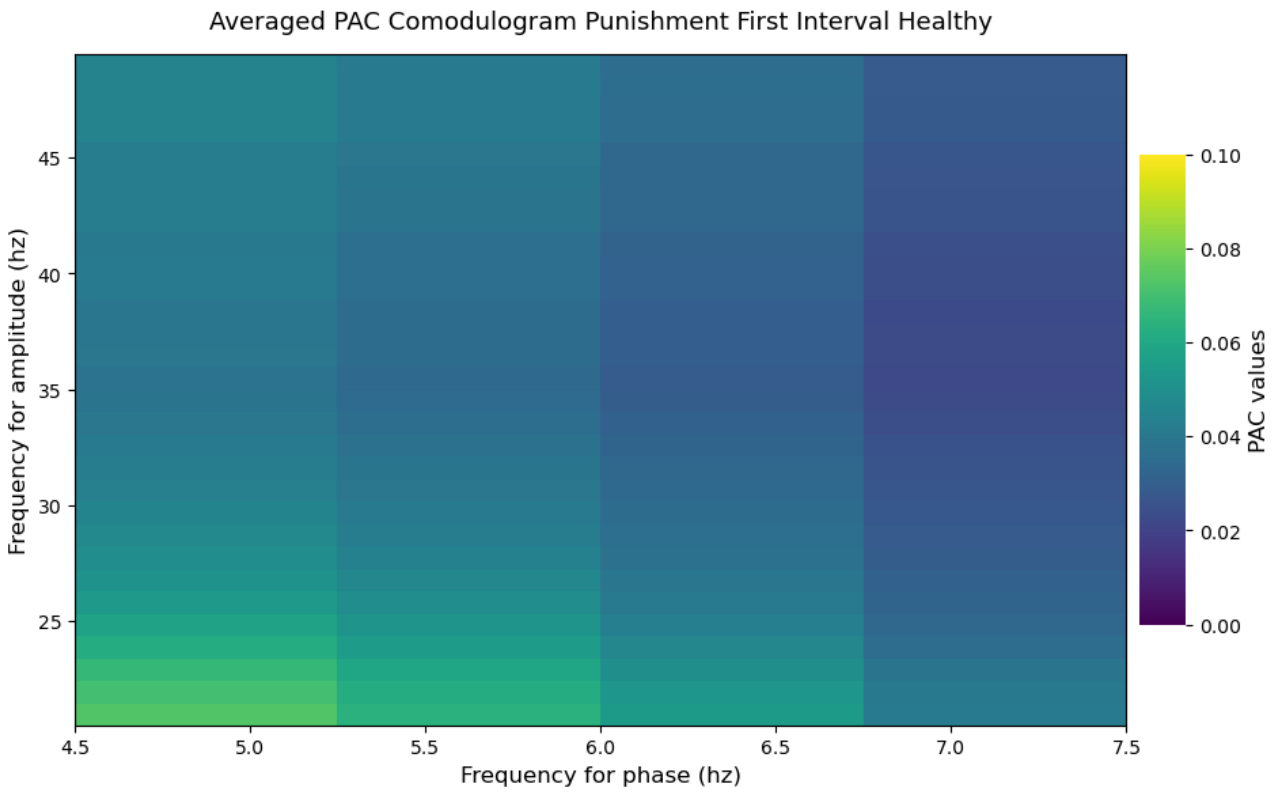


Figure 3: Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for Healthy Subjects

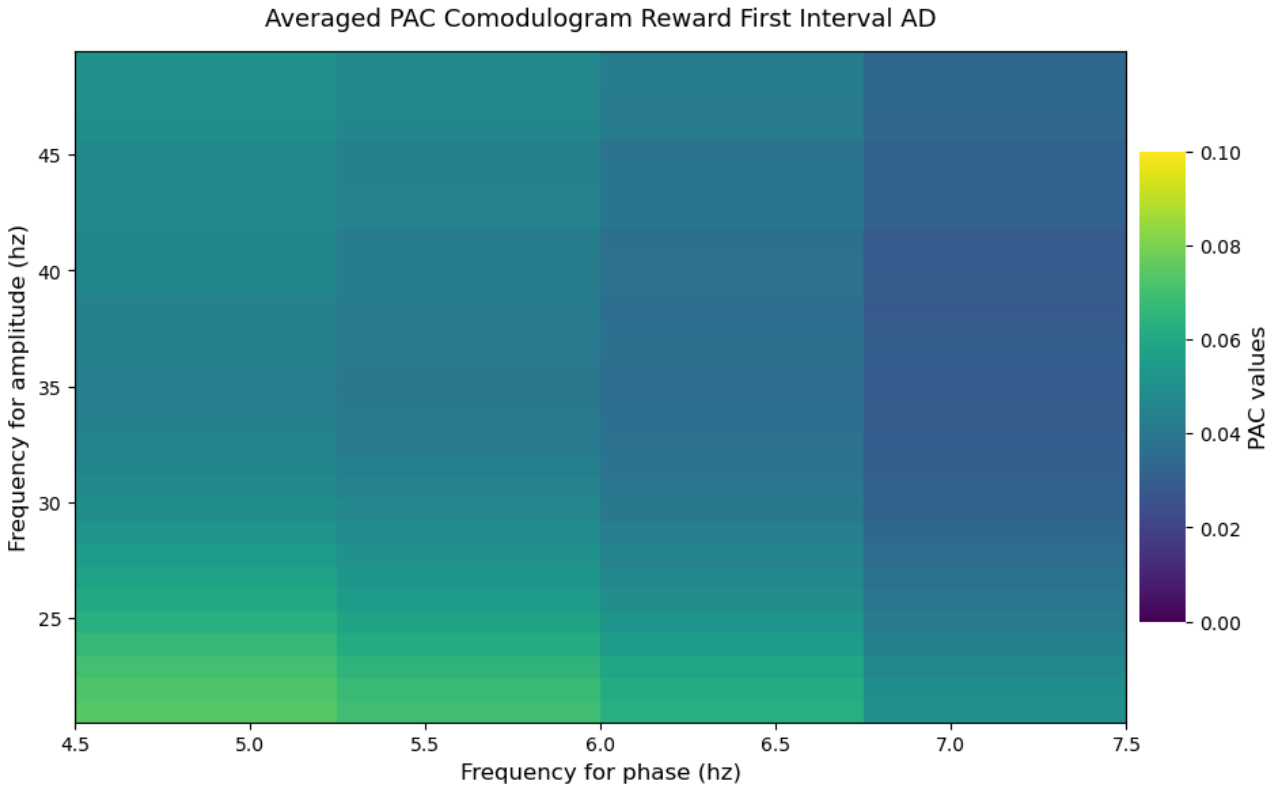


Figure 4: Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for AD Subjects

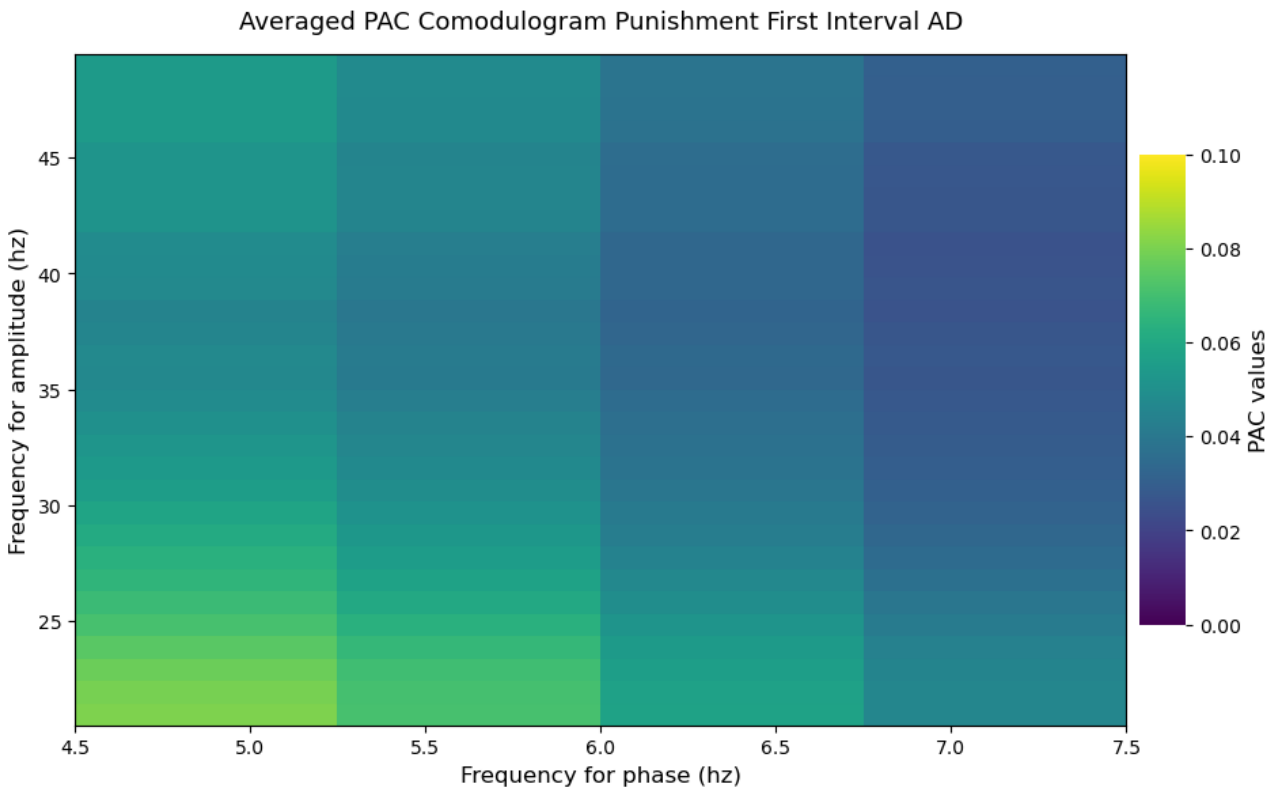


Figure 5: Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for AD Subjects

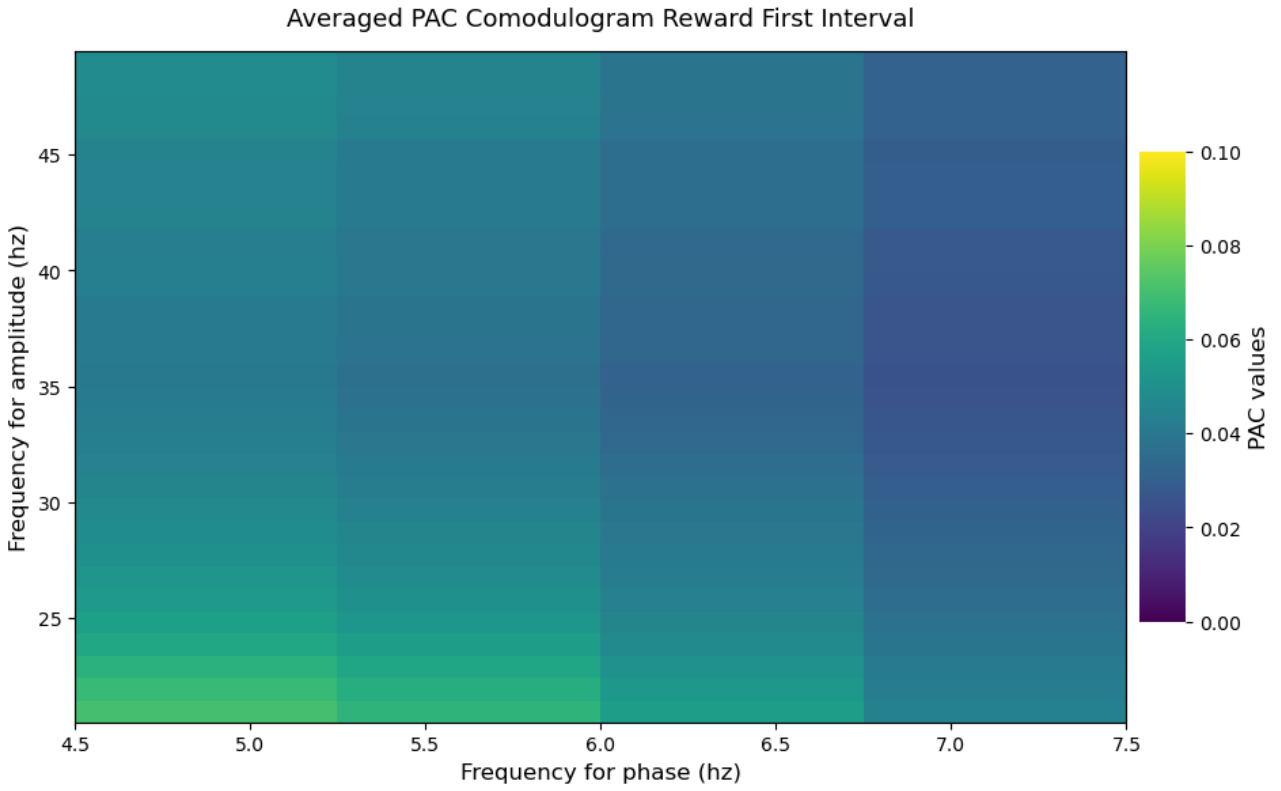


Figure 6: Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for Healthy Subjects

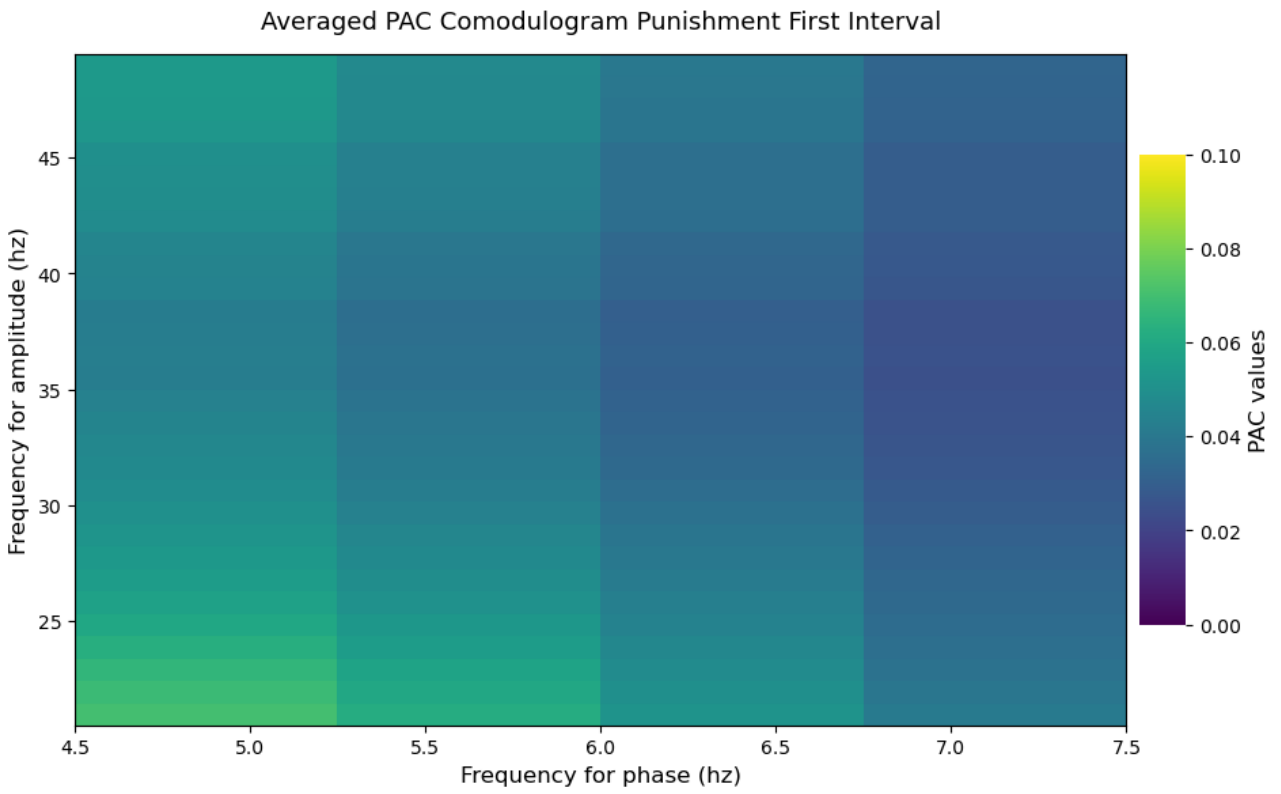


Figure 7: Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for Healthy Subjects

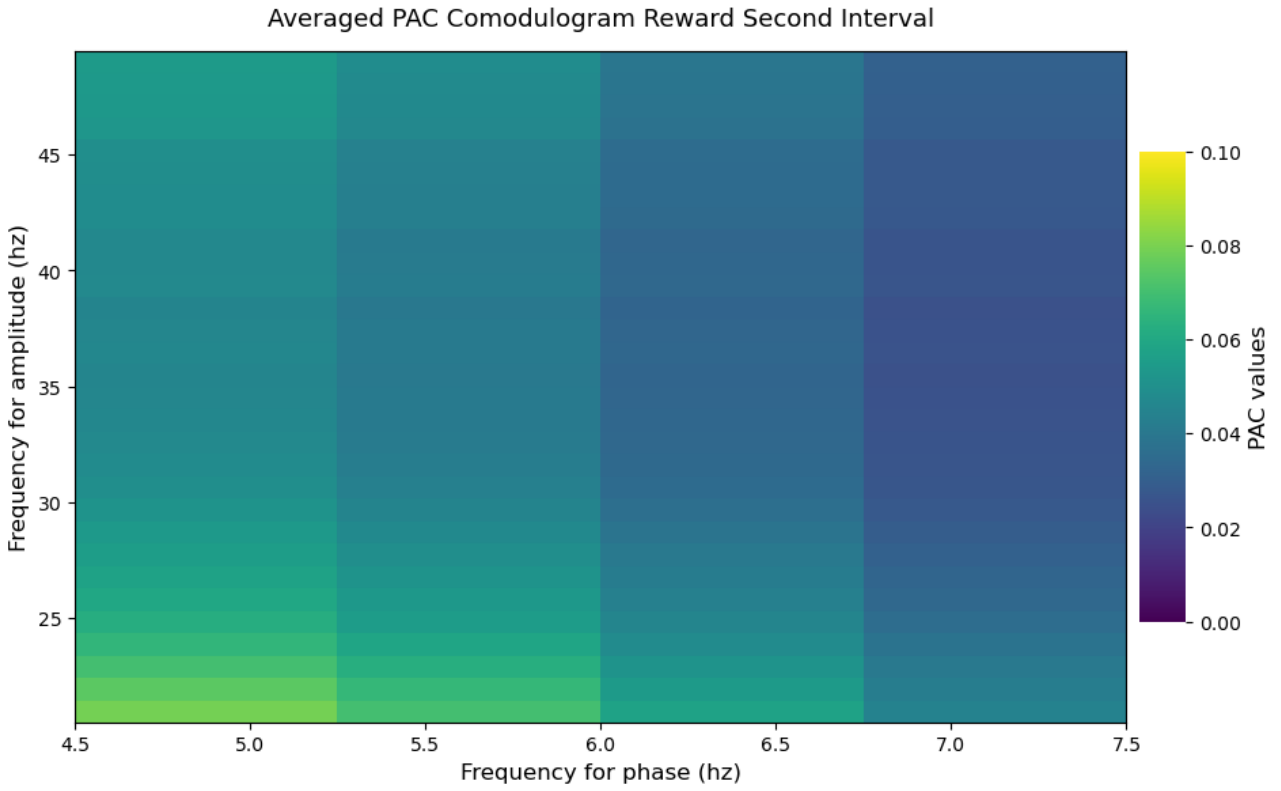


Figure 8: Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for AD Subjects

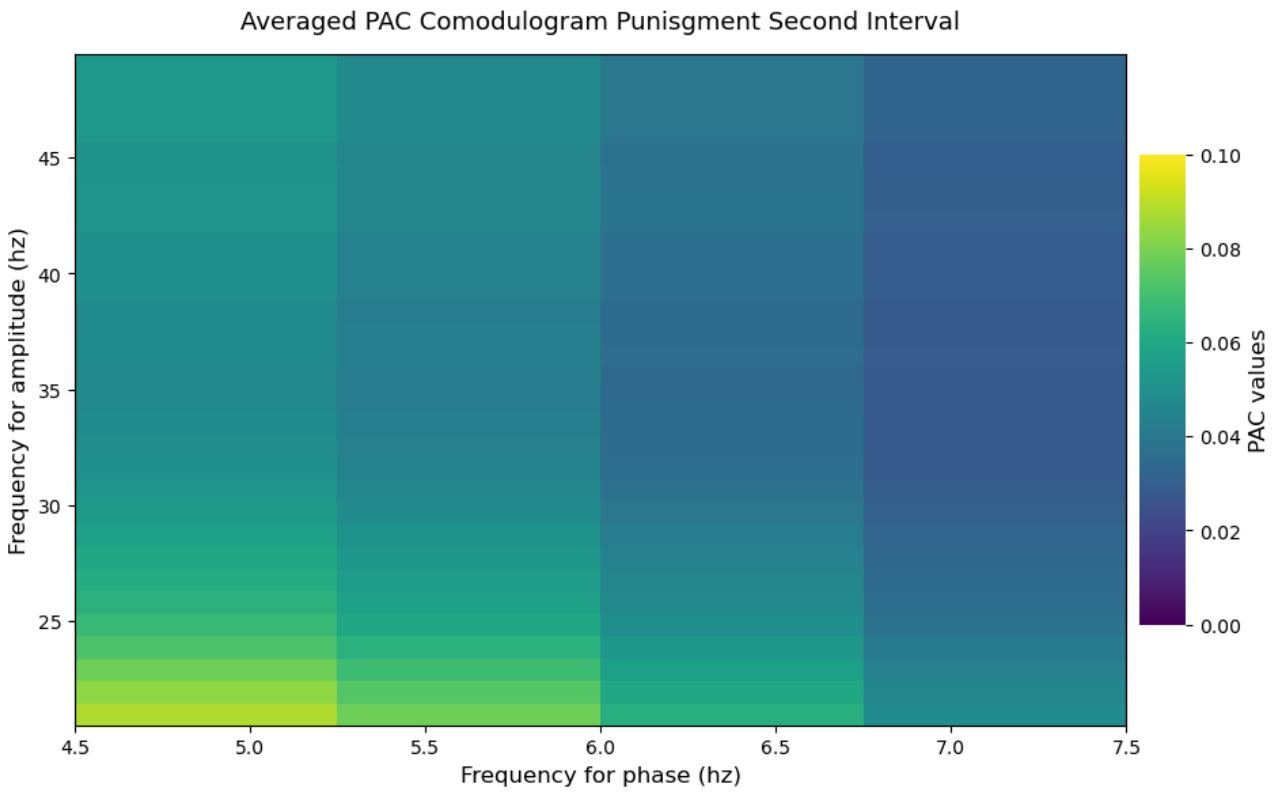


Figure 9: Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for AD Subjects

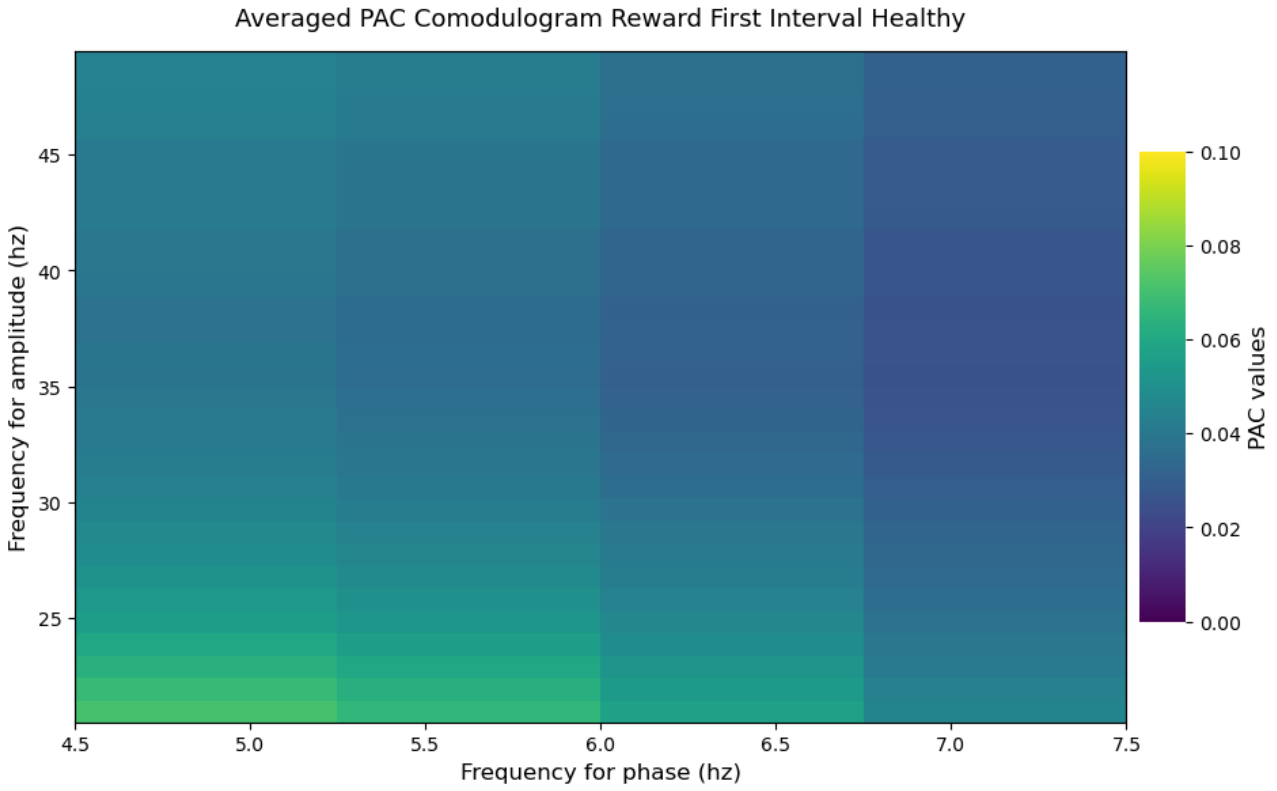


Figure 10: Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for Healthy Subjects

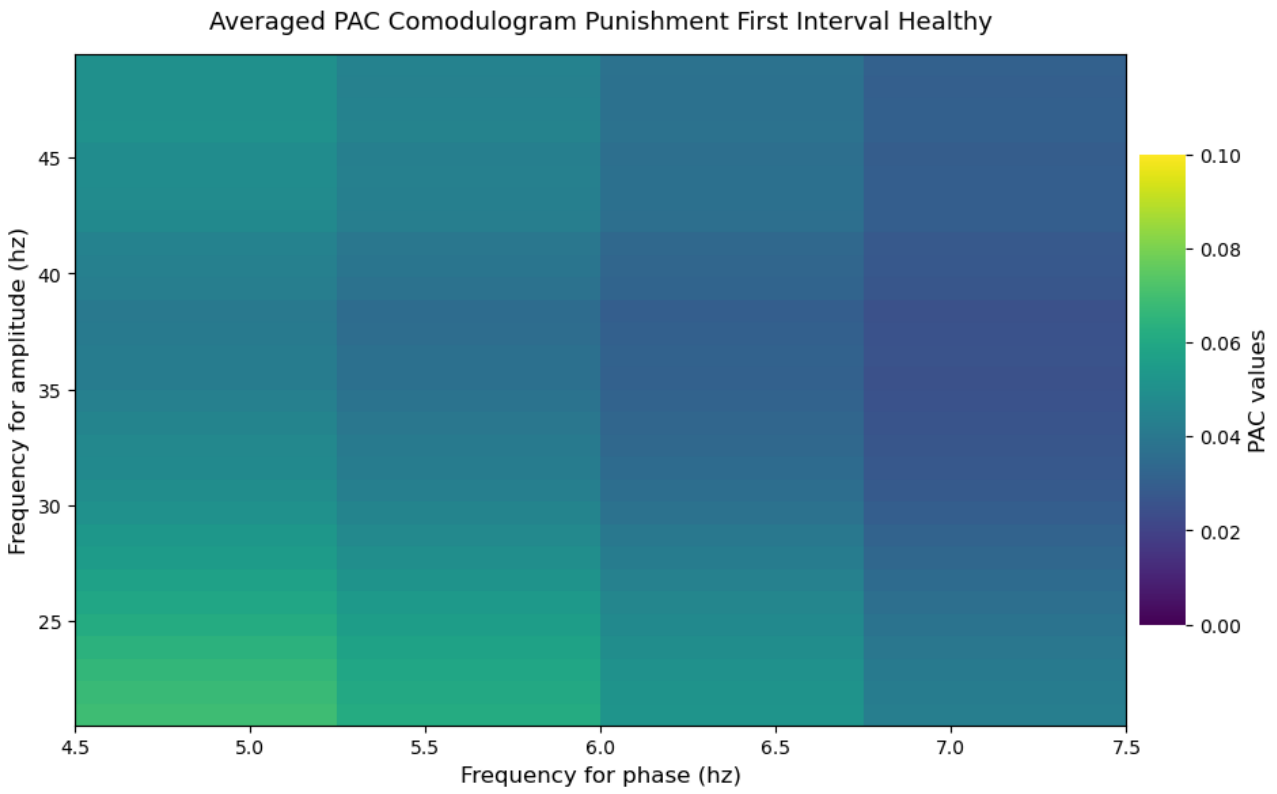


Figure 11: Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for Healthy Subjects

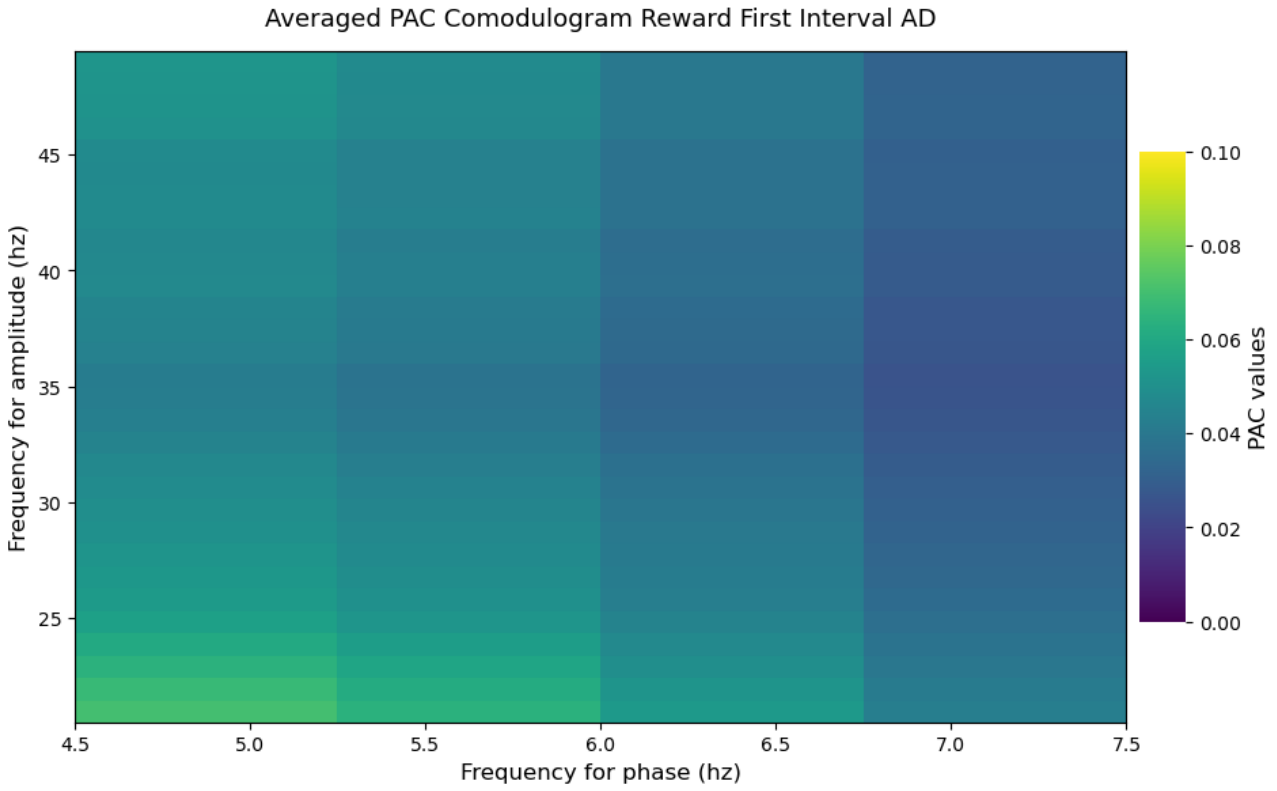


Figure 12: Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for AD Subjects

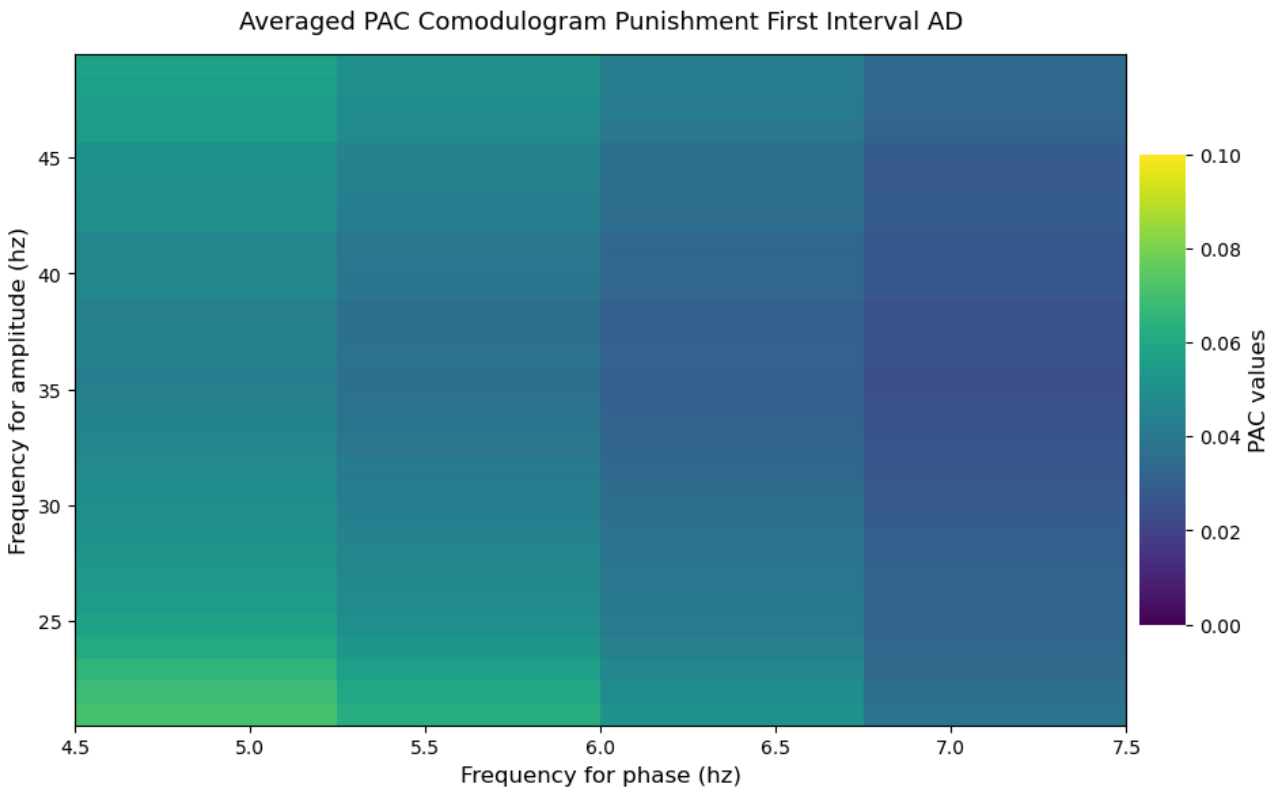


Figure 13: Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for AD Subjects

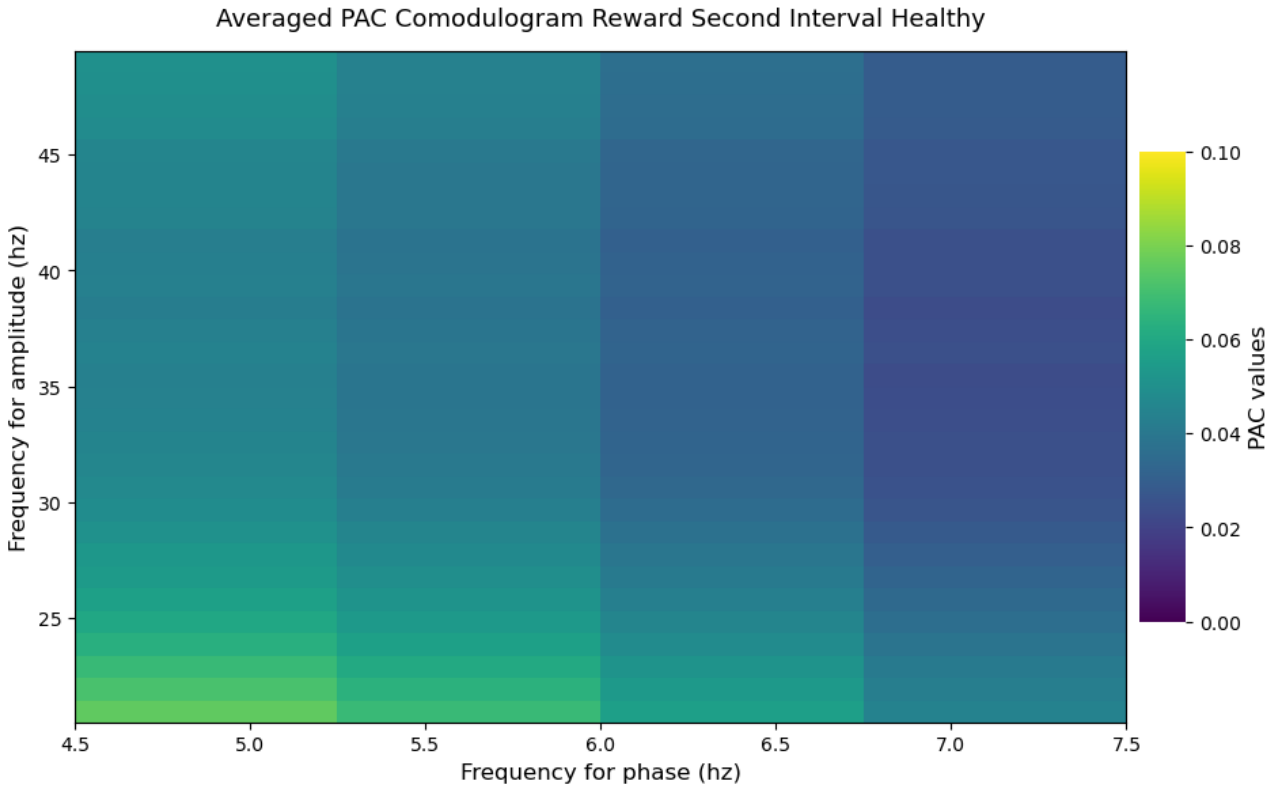


Figure 14: Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for Healthy Subjects

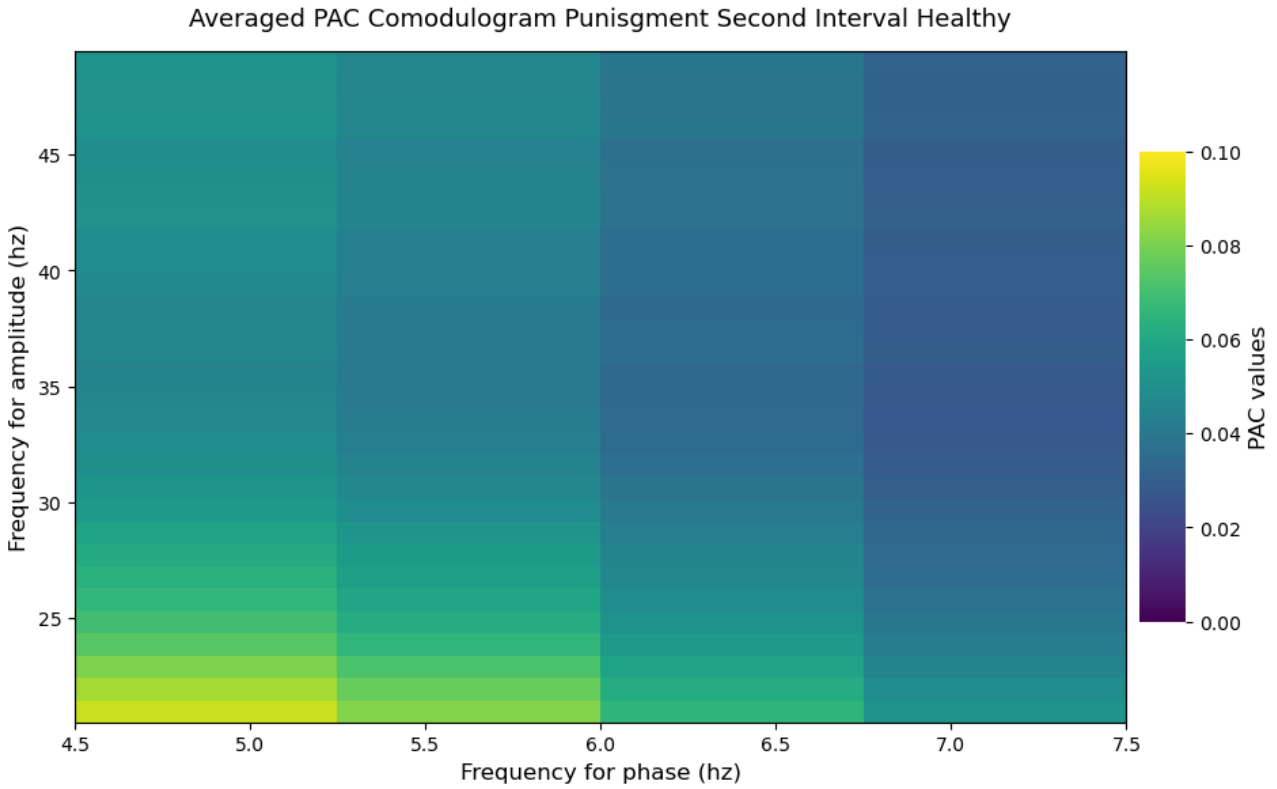


Figure 15: Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for Healthy Subjects

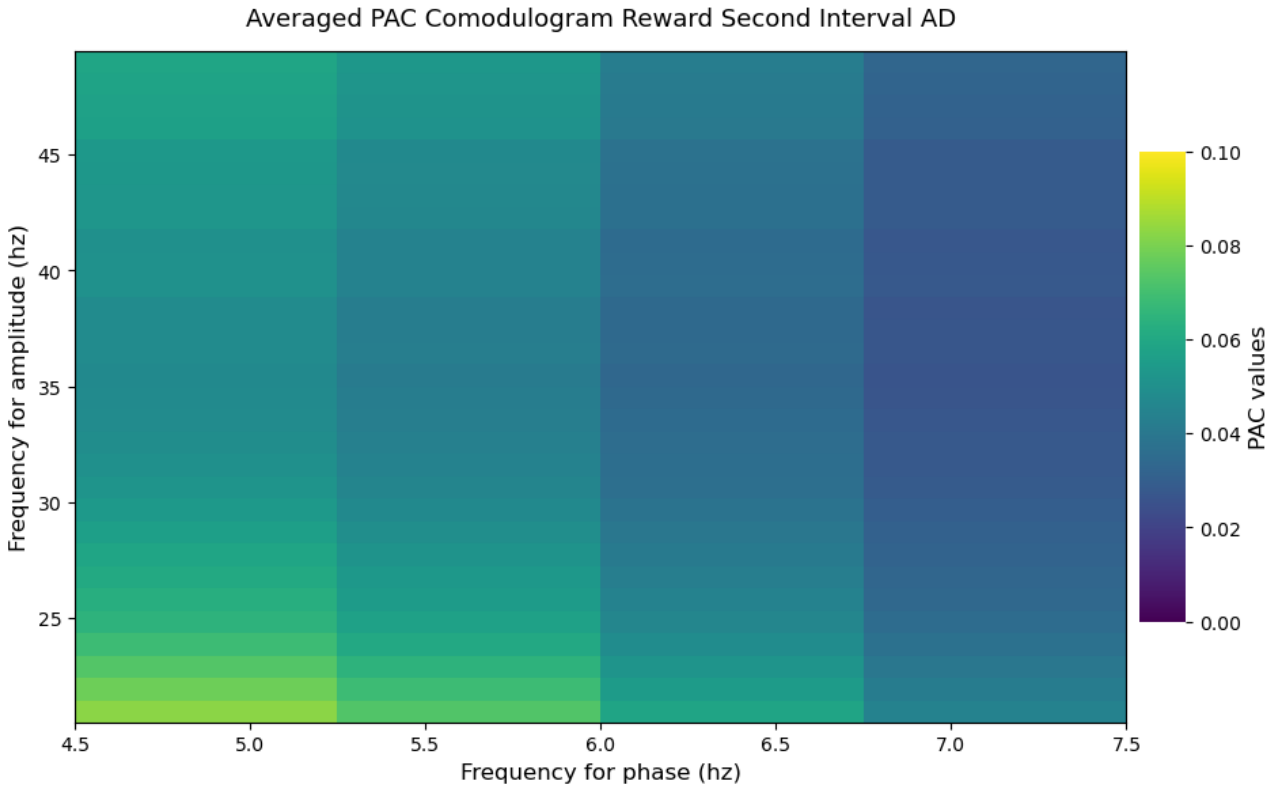


Figure 16: Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for AD Subjects

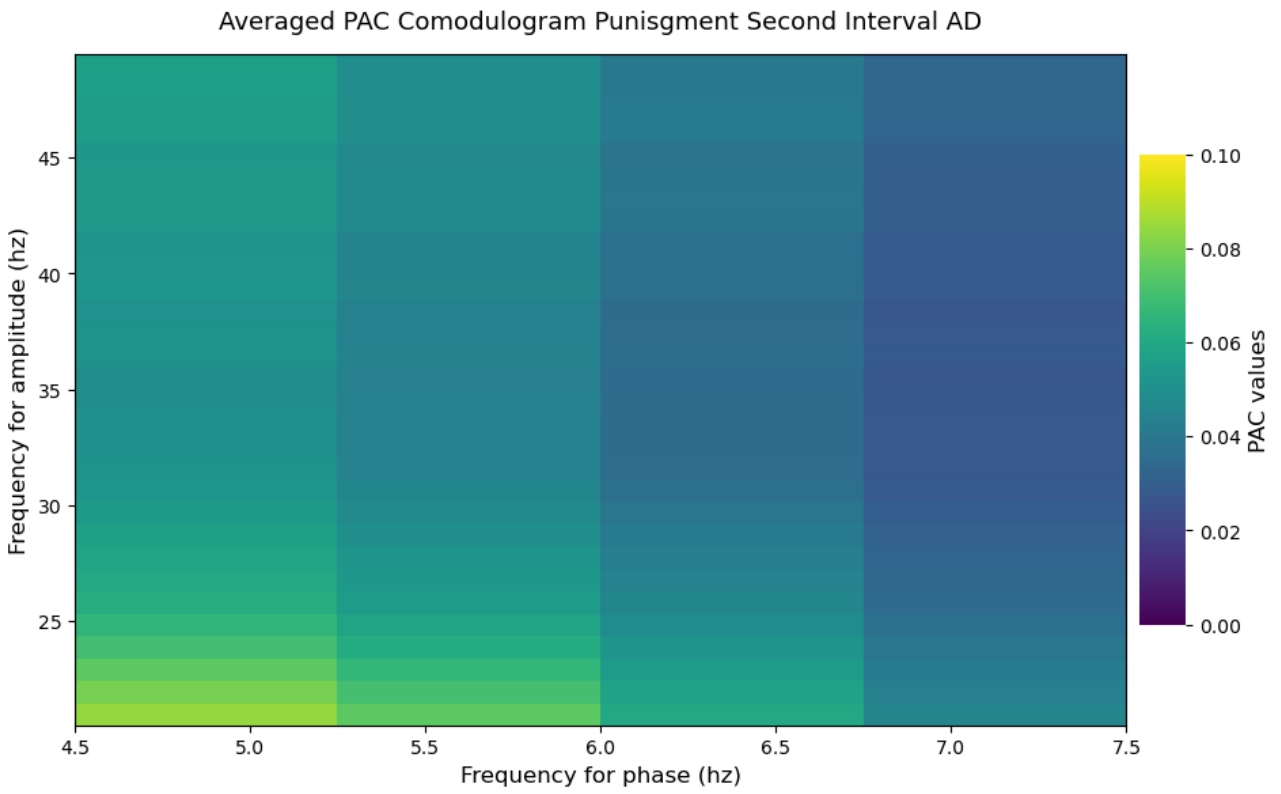


Figure 17: Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for AD Subjects

```
def compute_pac(p_obj, data_channel_1, data_channel_2):
    pha_p = p_obj.filter(500, data_channel_2, ftype='phase')
    amp_p = p_obj.filter(500, data_channel_1, ftype='amplitude')
    pac_result = mean_vector_length(pha_p, amp_p)
    return pac_result

def calculate_PAC_Shuffle(normalized_trials, start_timestep, end_timestep,
    num_permute=50):

    subject_count = normalized_trials.shape[0]
    channel_1 = 3  # 4th channel Fz
    channel_2 = 13  # 14th channel Pz
    trial_count = normalized_trials.shape[2]

    # Initialize PAC object with specified frequency ranges
    p_obj = Pac(idpac=(6, 0, 0), f_pha=(4, 9, 1, 1), f_amp=(20, 51, 1, 1))

    # List to store PAC values (2D arrays for each trial and subject)
    pac_perm = []  # To store permuted PAC values

    # Loop over each subject and trial to compute PAC
    for subject in range(subject_count):
        subject_data = normalized_trials[subject, :, :, :]  # Shape: (17, 20,
    800)

        for trial in range(trial_count):
            # Extract the data for the 4th and 14th channels
            data_channel_1 = subject_data[channel_1, trial, start_timestep:
```

```
    end_timestep]  # Shape: (250,)
27          data_channel_2 = subject_data[channel_2, trial, start_timestep:
    end_timestep]  # Shape: (250,)
28
29          # Check if data contains NaN values in the original data
30          if np.any(np.isnan(data_channel_1)) or np.any(np.isnan(
    data_channel_2)):
31              continue  # Skip this trial if any NaN in the data
32
33          permuted_pac_results = []  # To store PAC values for current trial
    's permutations
34          for _ in range(num_permute):  # Number of permutations
35              shuffled_data_channel_1 = np.random.permutation(data_channel_1
    )
36              shuffled_data_channel_2 = np.random.permutation(data_channel_2
    )
37
38              # Compute PAC for the permuted signals
39              permuted_pac = compute_pac(p_obj, shuffled_data_channel_1,
    shuffled_data_channel_2)
40
41              # Check if permuted PAC is valid (not NaN)
42              if permuted_pac is not None and not np.any(np.isnan(
    permuted_pac)):
43                  permuted_pac_results.append(permuted_pac)
44
45          # Only append results if there were valid (non-NaN) permutations
46          if permuted_pac_results:
47              pac_perm.append(np.stack(permuted_pac_results))
48
49      pac_perm = np.array(pac_perm)
50      pac_perm = pac_perm.squeeze()  # Remove the singleton dimension
51
52      # Average across trials to get a mean PAC for each frequency pair
53      pac_perm_avg = np.mean(pac_perm, axis=0)
54
55      return p_obj, pac_perm_avg
```

## *Significance Testing and p-value Calculation*

- We perform statistical tests to compute the p-values. The PAC values are compared using the standard t-test procedure to verify their significance.
- To assess the statistical significance of the PAC values, we use the `scipy.stats.ttest_1samp` method to calculate the p-value.
- The hypothesis is that the PAC values are significantly different from zero, and the alternative hypothesis is that there is a measurable PAC effect.
- The test should focus on the phase frequency and amplitude frequency points to evaluate how they influence PAC.
- After the computation, we evaluate if the p-value for PAC is less than a defined threshold, such as 0.05. If the p-value is lower than the threshold, we reject the null hypothesis and conclude that there is a significant PAC effect.

```python
def compute_p_values(PAC_main, PAC_perm):
    # PAC_main shape: (30, 4)  -> observed PAC values (frequencies of amp x frequencies of phase)
    # PAC_perm shape: (50, 30, 4) -> permuted PAC values (num_perm, amp_freqs, phase_freqs)

    # Initialize a p-value array with the same shape as PAC_main (30, 4)
    p_values = np.zeros(PAC_main.shape)

    # Loop over each frequency pair (i, j) corresponding to (amp_freq, phase_freq)
    for i in range(PAC_main.shape[0]):  # Loop over amp_freq (30)
        for j in range(PAC_main.shape[1]):  # Loop over phase_freq (4)

            # Perform a one-sample t-test for each (i, j) pair
            t_stat, p_val = stats.ttest_1samp(PAC_perm[:, i, j], PAC_main[i, j], alternative='less')

            p_values[i, j] = p_val

    return p_values

    p_values_reward_first_h = compute_p_values(PAC_main_reward_first_h, PAC_perm_reward_first_h)
    p_values_punishment_first_h = compute_p_values(PAC_main_punishment_first_h, PAC_perm_punishment_first_h)
    p_values_reward_second_h = compute_p_values(PAC_main_reward_second_h, PAC_perm_reward_second_h)
    p_values_punishment_second_h = compute_p_values(
    PAC_main_punishment_second_h, PAC_perm_punishment_second_h)

    p_values_reward_first_a = compute_p_values(PAC_main_reward_first_a, PAC_perm_reward_first_a)
    p_values_punishment_first_a = compute_p_values(PAC_main_punishment_first_a, PAC_perm_punishment_first_a)
    p_values_reward_second_a = compute_p_values(PAC_main_reward_second_a, PAC_perm_reward_second_a)
    p_values_punishment_second_a = compute_p_values(
    PAC_main_punishment_second_a, PAC_perm_punishment_second_a)
```

## ***PAC Computation and Comparison of Values and Statistical Analysis***

- After computing PAC values for each frequency band, the next step is to compute the PAC for each group of individuals, separated by punishment and reward. The PAC values are computed based on the correlation between the phase frequency $f_z$ and the amplitude frequency $P_z$. The final PAC values are then plotted in the comudulogram, shown as colored plots (figure). These plots show the relationship between the amplitude and phase frequency points.

- The results from PAC computation across different frequency points are then examined. The PAC values are analyzed for the effects of punishment and reward. The comparison between these values can help reveal the effects of different experimental conditions.

- Using the MVL method, we compute the PAC values and plot them for analysis. The significant differences between the groups in the comodulogram are checked for statistical

significance using t-tests. The results will determine whether there is a significant change in PAC values due to the presence of different conditions, i.e., punishment versus reward.

- The analysis aims to clarify how PAC values vary when different experimental conditions (punishment and reward) are applied. We assess the change in PAC values across different frequency bands and amplitude points. The results will be examined for statistical significance using standard methods such as t-tests and plotting the comodulogram.
- After performing the t-test for PAC values, the results are compared across different groups (punishment versus reward) to determine whether significant differences are observed.

```
PAC_main_reward_first_h[p_values_reward_first_h > 0.05] = 0
PAC_main_punishment_first_h[p_values_punishment_first_h > 0.05] = 0
PAC_main_reward_second_h[p_values_reward_second_h > 0.05] = 0
PAC_main_punishment_second_h[p_values_punishment_second_h > 0.05] = 0

PAC_main_reward_first_a[p_values_reward_first_a > 0.05] = 0
PAC_main_punishment_first_a[p_values_punishment_first_a > 0.05] = 0
PAC_main_reward_second_a[p_values_reward_second_a > 0.05] = 0
PAC_main_punishment_second_a[p_values_punishment_second_a > 0.05] = 0
```

```
# Plot the comodulogram of the averaged PAC
plt.figure(figsize=(10, 6))
p_obj_reward_first_h.comodulogram(PAC_main_reward_first_h, title="Averaged PAC Comodulogram Reward First Interval Healthy", cmap='viridis', vmax=0.1, vmin=0)
plt.tight_layout()
plt.show()

# Plot the comodulogram of the averaged PAC
plt.figure(figsize=(10, 6))
p_obj_punishment_first_h.comodulogram(PAC_main_punishment_first_h, title="Averaged PAC Comodulogram Punishment First Interval Healthy", cmap='viridis', vmax=0.1, vmin=0)
plt.tight_layout()
plt.show()

# Plot the comodulogram of the averaged PAC
plt.figure(figsize=(10, 6))
p_obj_reward_first_a.comodulogram(PAC_main_reward_first_a, title="Averaged PAC Comodulogram Reward First Interval AD", cmap='viridis', vmax=0.1, vmin=0)
plt.tight_layout()
plt.show()

# Plot the comodulogram of the averaged PAC
plt.figure(figsize=(10, 6))
p_obj_punishment_first_a.comodulogram(PAC_main_punishment_first_a, title="Averaged PAC Comodulogram Punishment First Interval AD", cmap='viridis', vmax=0.1, vmin=0)
plt.tight_layout()
plt.show()

# Plot the comodulogram of the averaged PAC
plt.figure(figsize=(10, 6))
```

```
    p_obj_reward_second_h.comodulogram(PAC_main_reward_second_h, title="
Averaged PAC Comodulogram Reward Second Interval Healthy", cmap='viridis',
vmax=0.1, vmin=0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_punishment_second_h.comodulogram(PAC_main_punishment_second_h, title
="Averaged PAC Comodulogram Punisgment Second Interval Healthy", cmap='
viridis', vmax=0.1, vmin=0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_reward_second_h.comodulogram(PAC_main_reward_second_a, title="
Averaged PAC Comodulogram Reward Second Interval AD", cmap='viridis', vmax
=0.1, vmin=0)
    plt.tight_layout()
    plt.show()

    # Plot the comodulogram of the averaged PAC
    plt.figure(figsize=(10, 6))
    p_obj_punishment_second_h.comodulogram(PAC_main_punishment_second_a, title
="Averaged PAC Comodulogram Punisgment Second Interval AD", cmap='viridis',
     vmax=0.1, vmin=0)
    plt.tight_layout()
    plt.show()
```

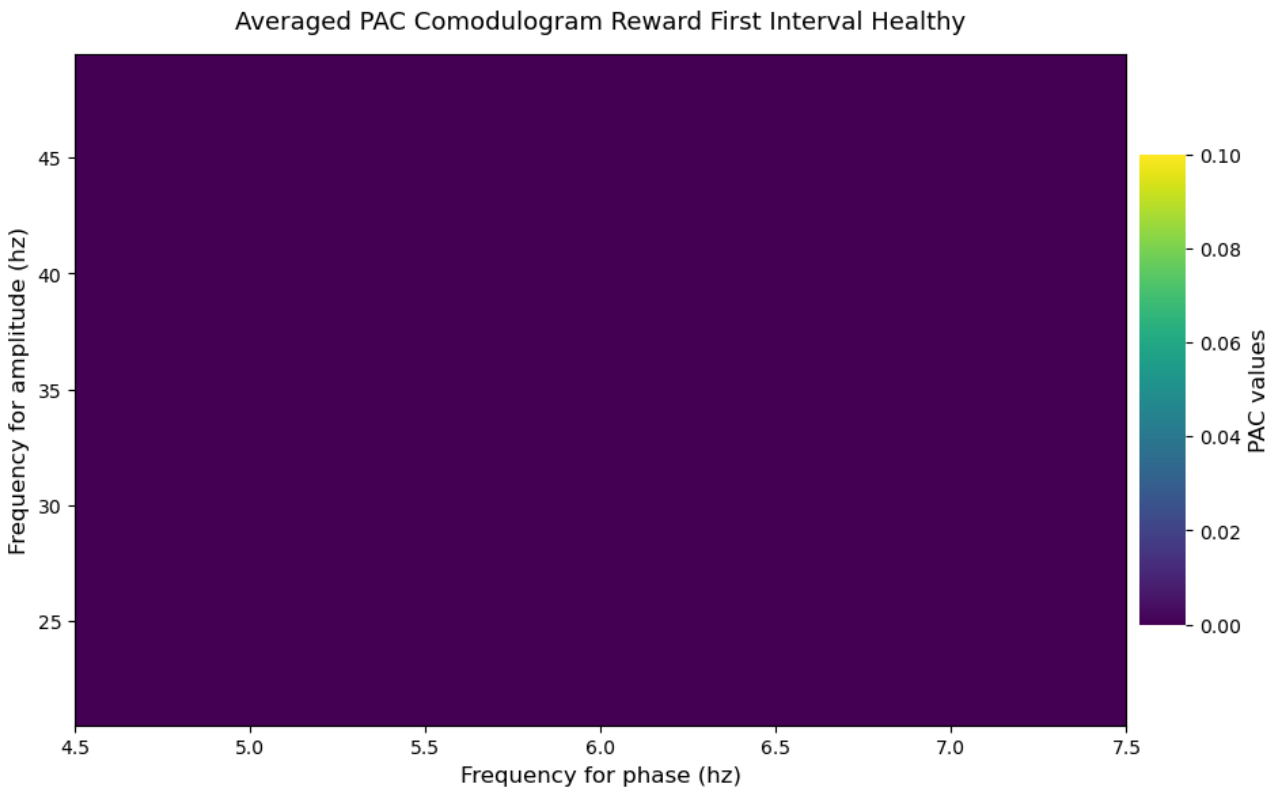


Figure 18: Significant Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for Healthy Subjects

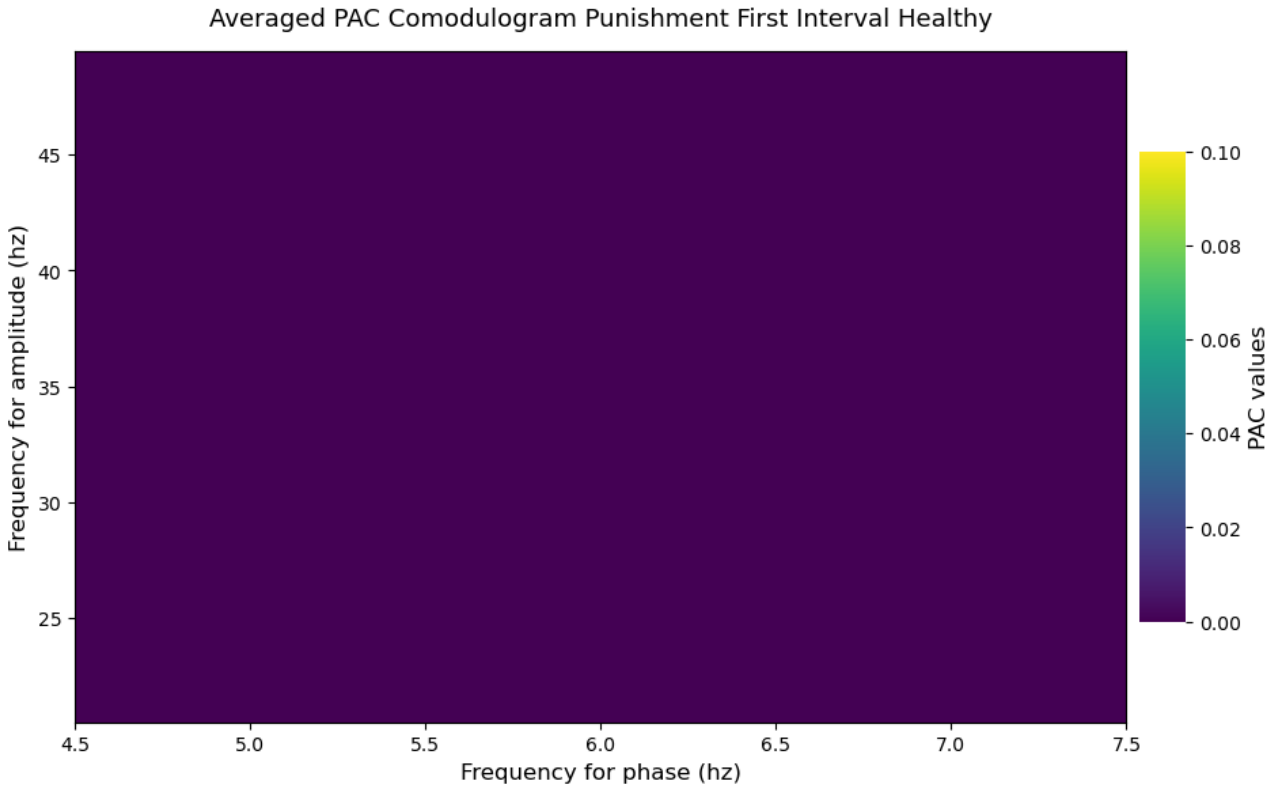


Figure 19: Significant Main Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for Healthy Subjects

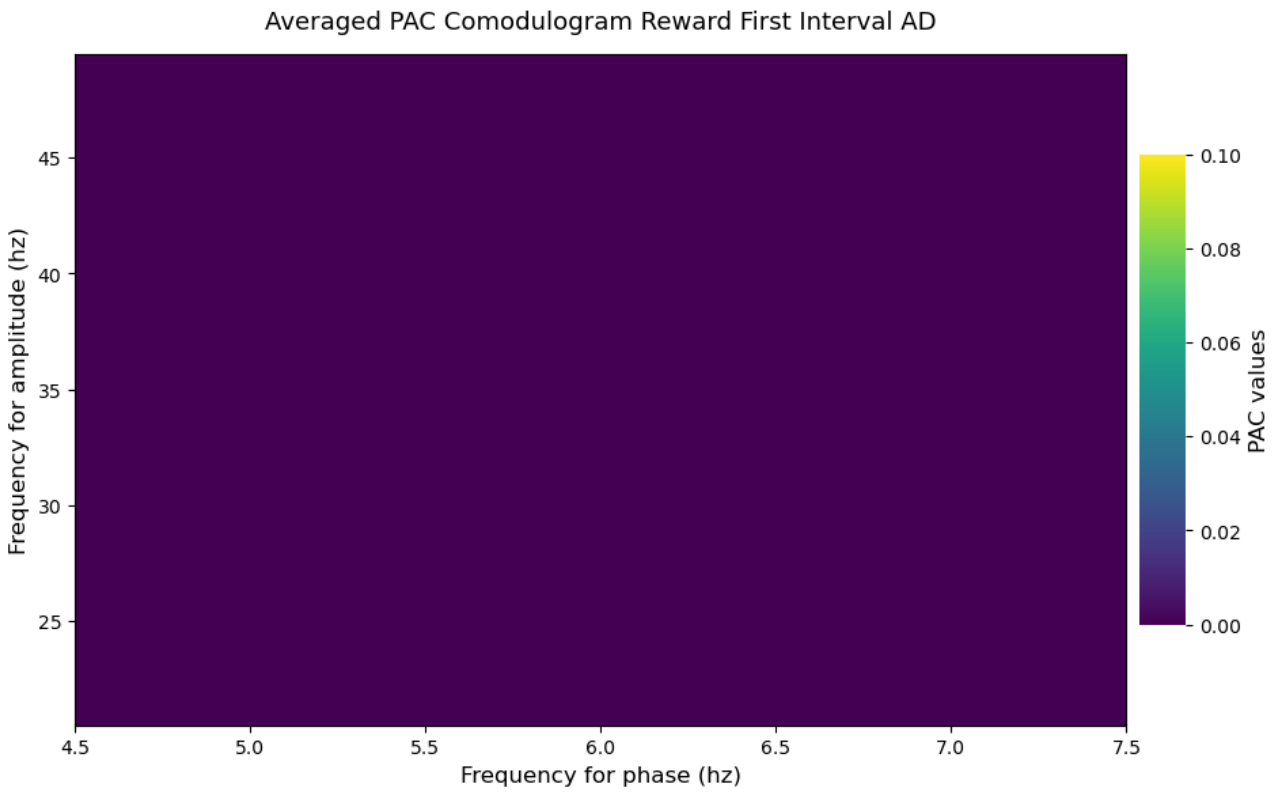


Figure 20: Significant Main Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for AD Subjects

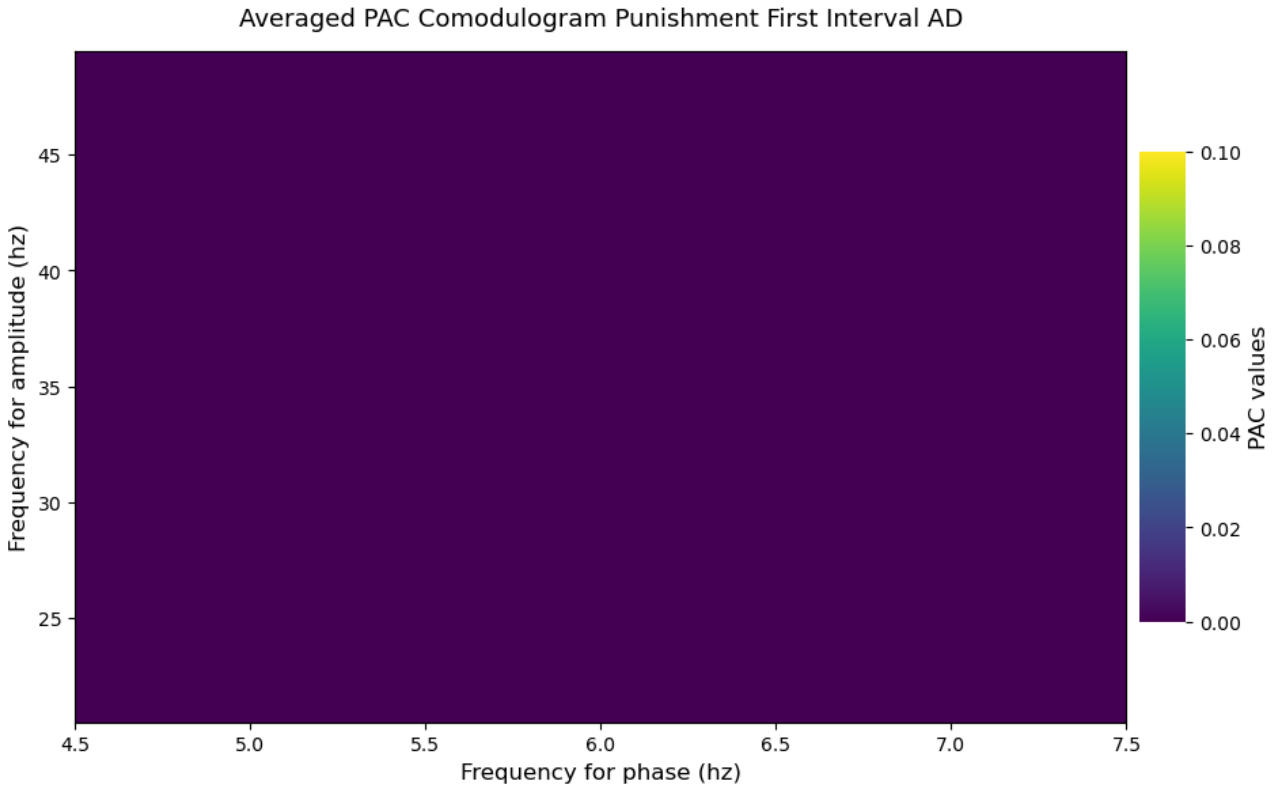


Figure 21: Significant Main Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [0, 500] After Feedback for AD Subjects

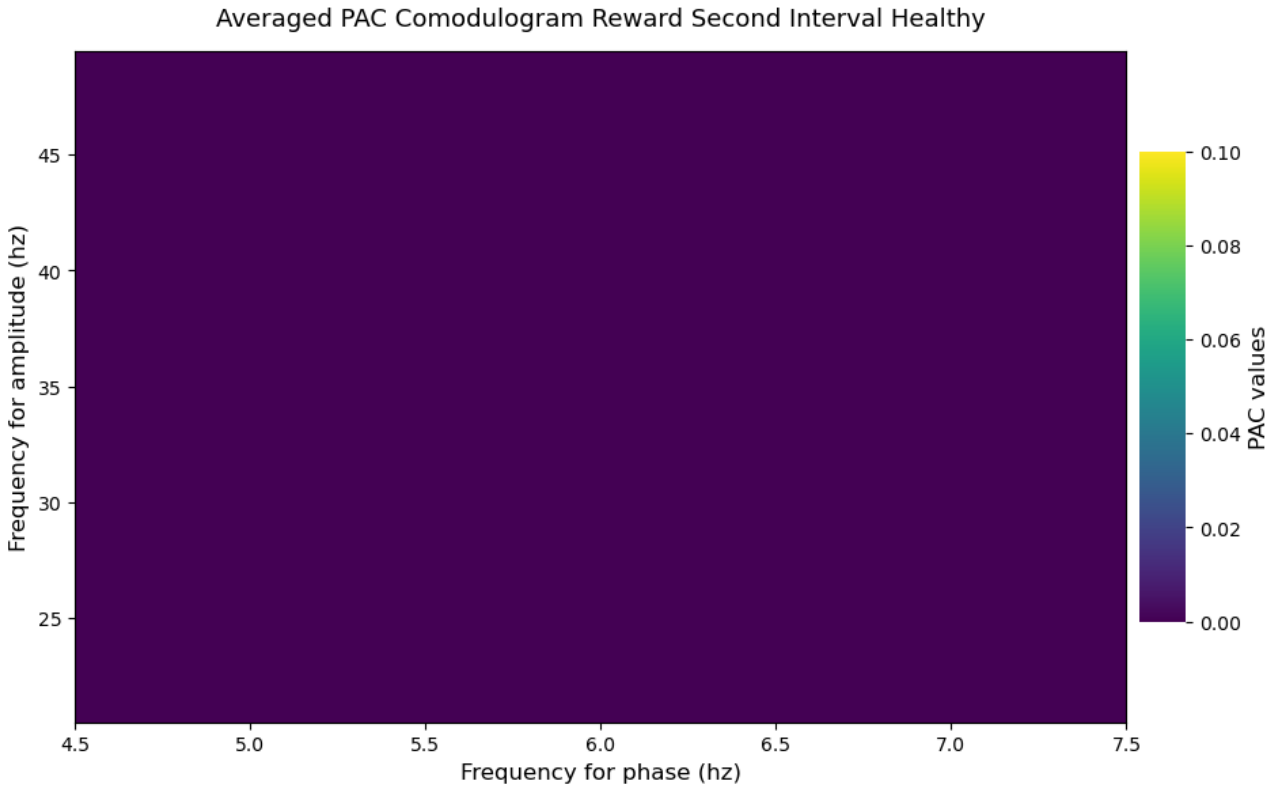


Figure 22: Significant Main Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for Healthy Subjects

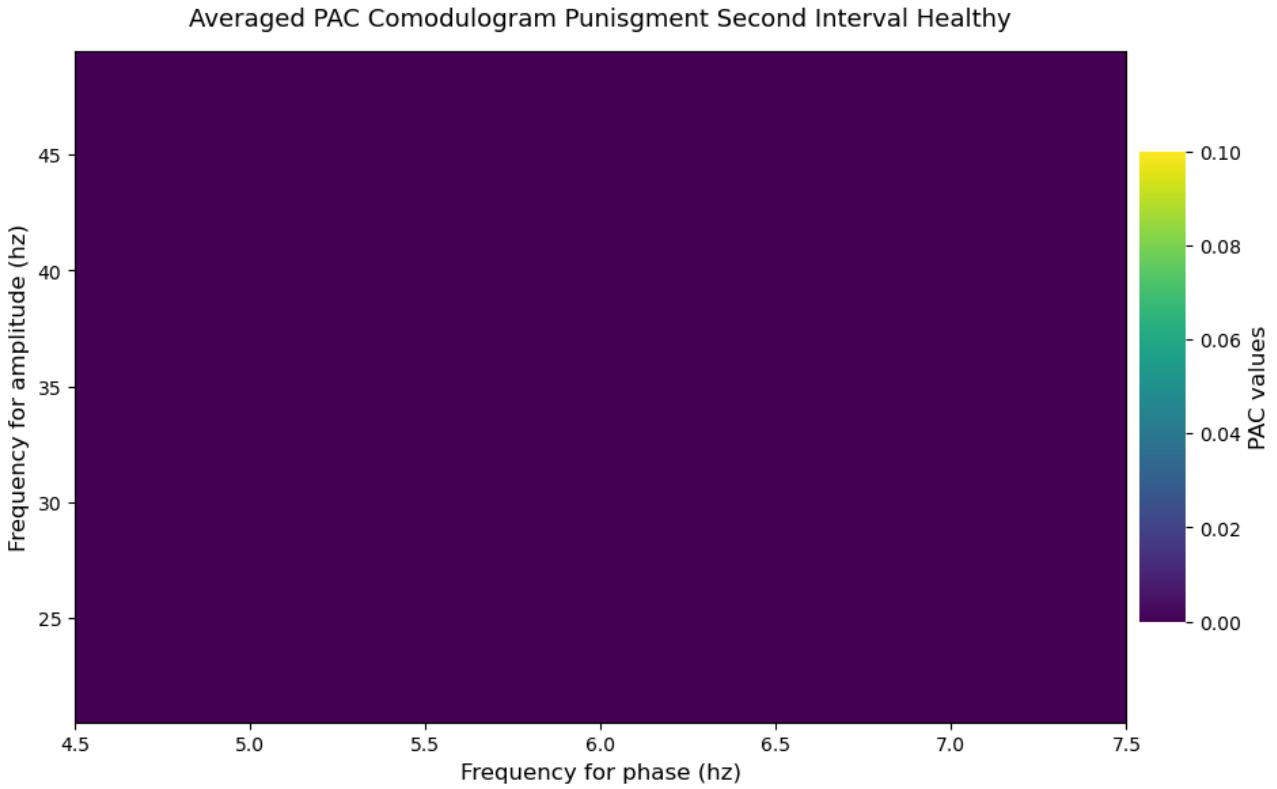


Figure 23: Significant Main Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for Healthy Subjects

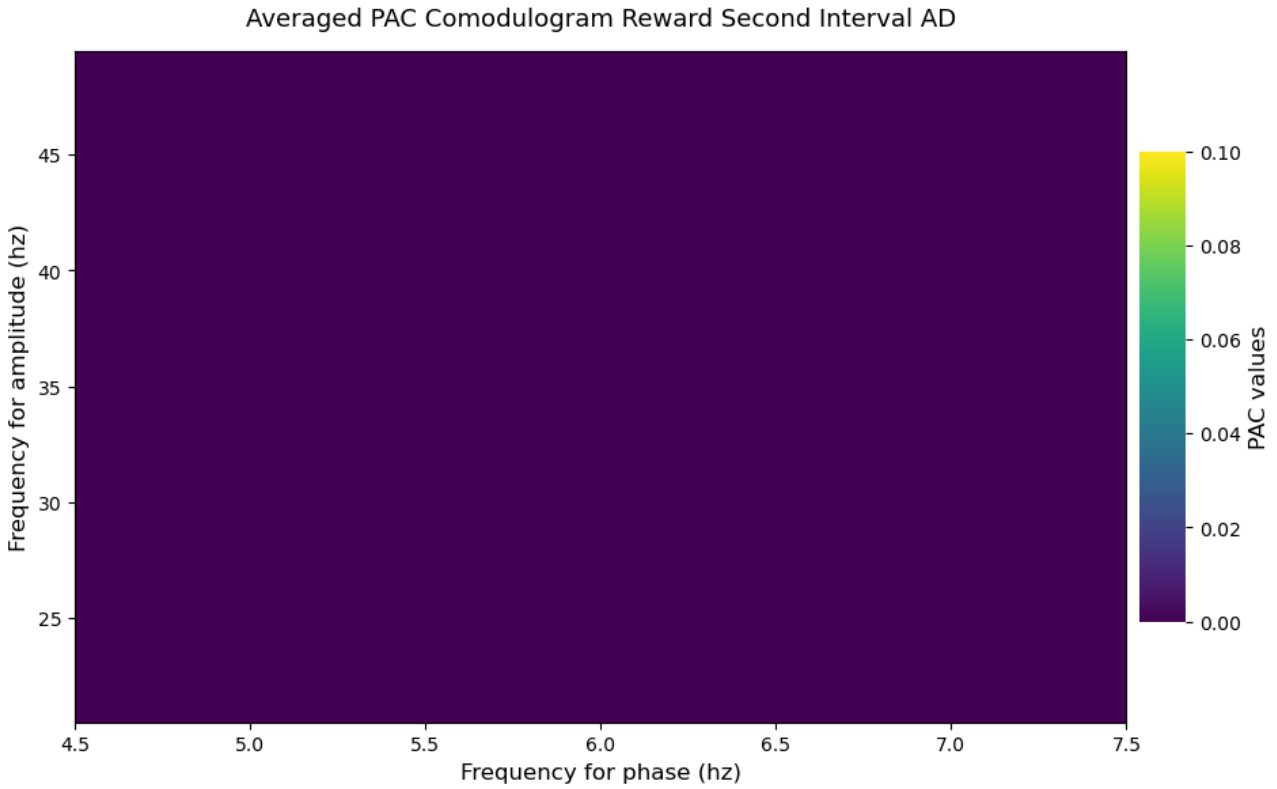


Figure 24: Significant Main Main PAC for Reward Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for AD Subjects

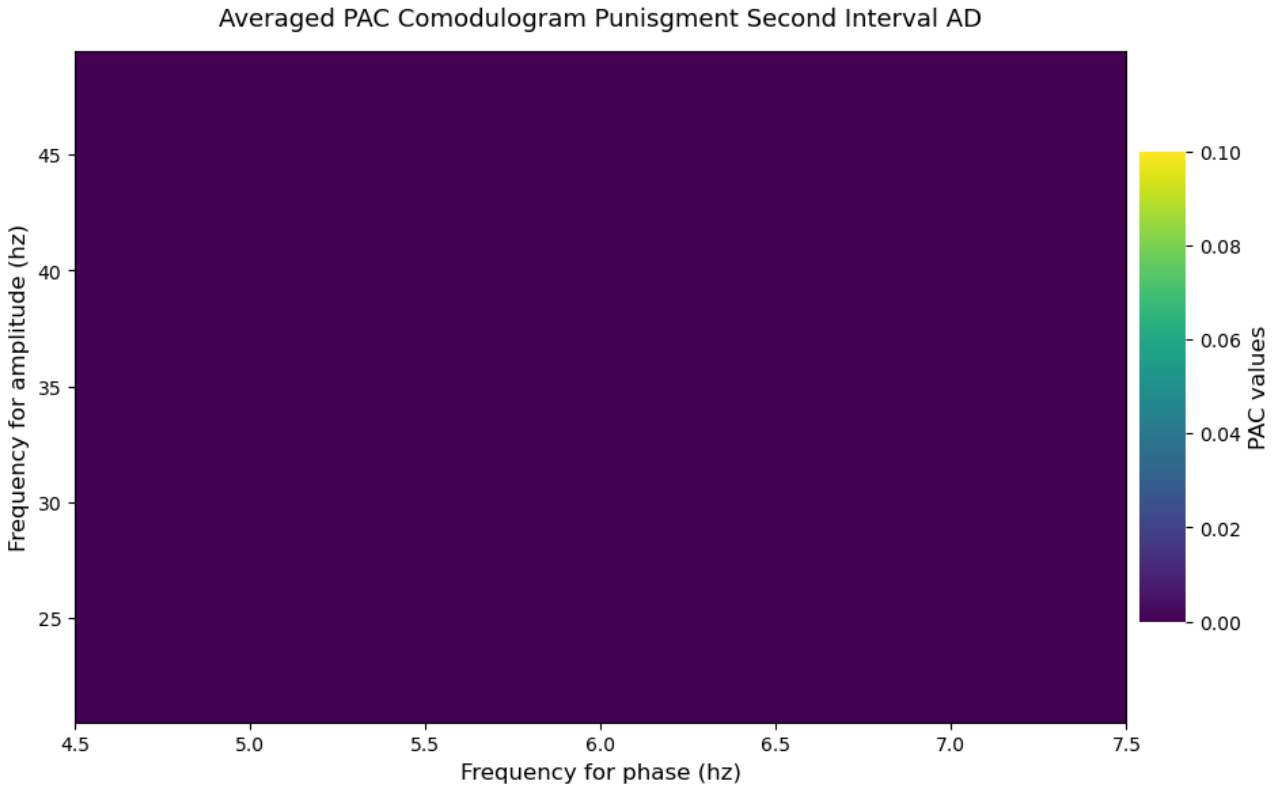


Figure 25: Significant Main Main PAC for Punishment Data Between Amplitude Pz of and Phase of Fz for [500, 1000] After Feedback for AD Subjects

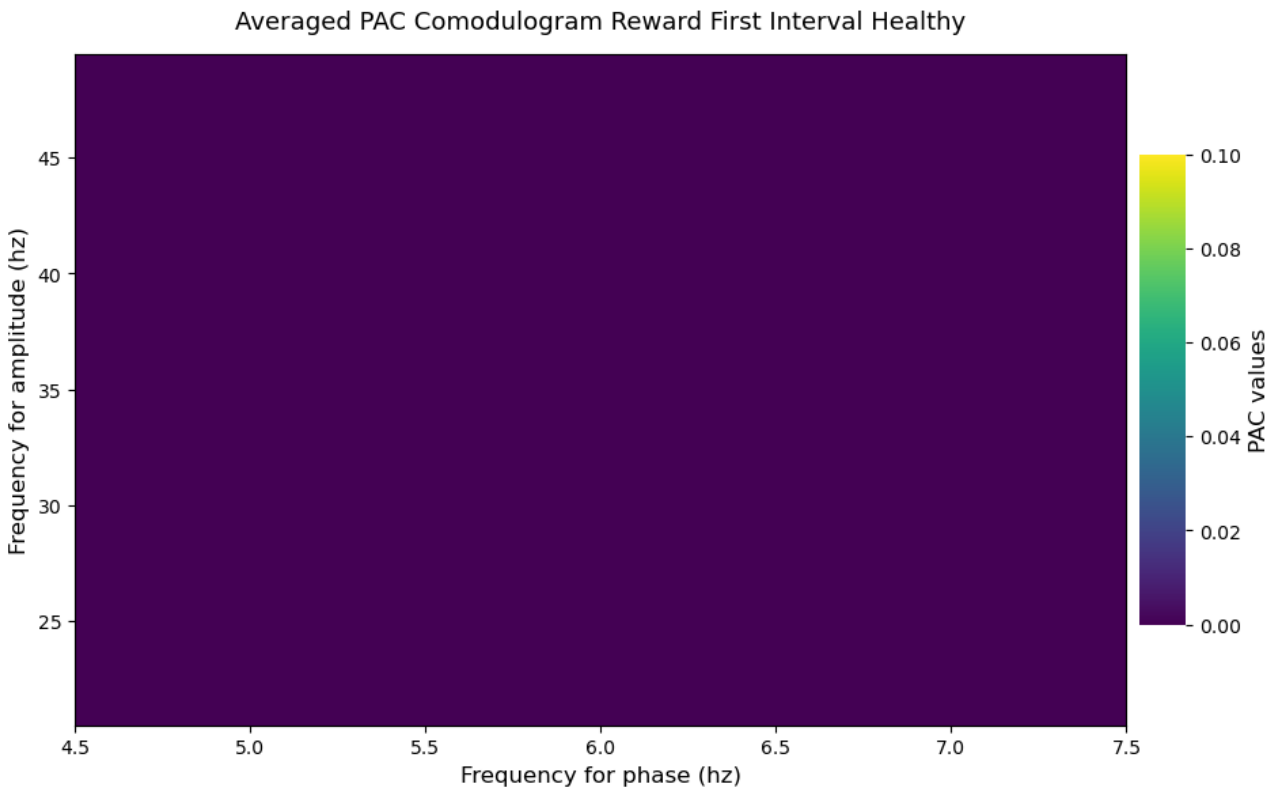


Figure 26: Significant Main Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for Healthy Subjects

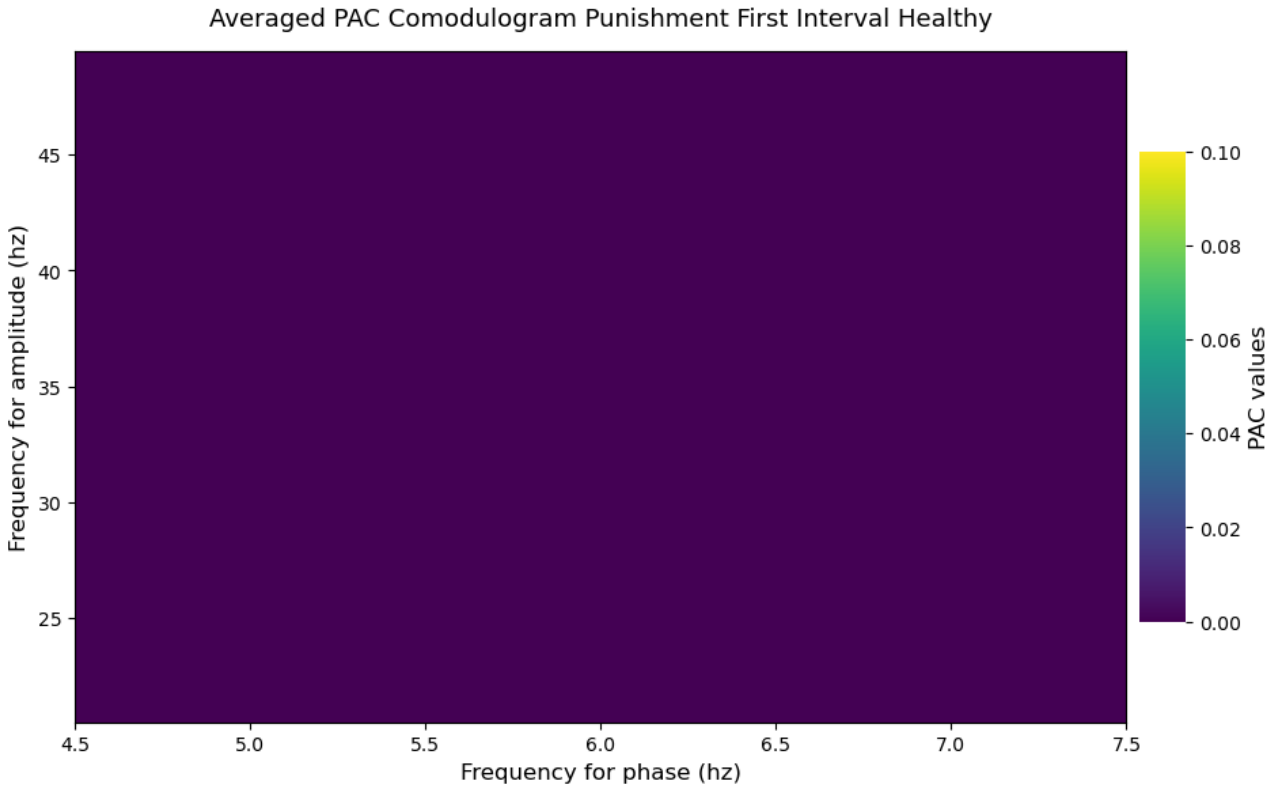


Figure 27: Significant Main Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for Healthy Subjects

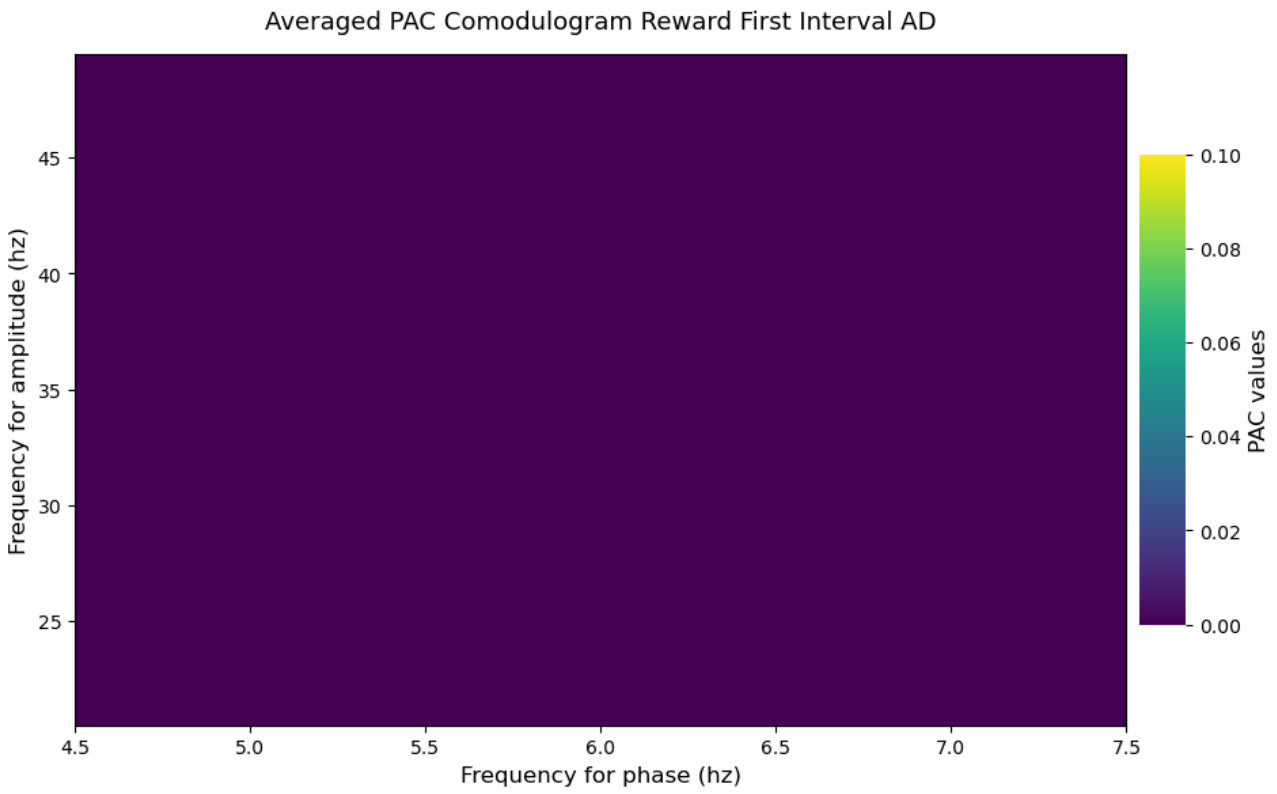


Figure 28: Significant Main Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for AD Subjects

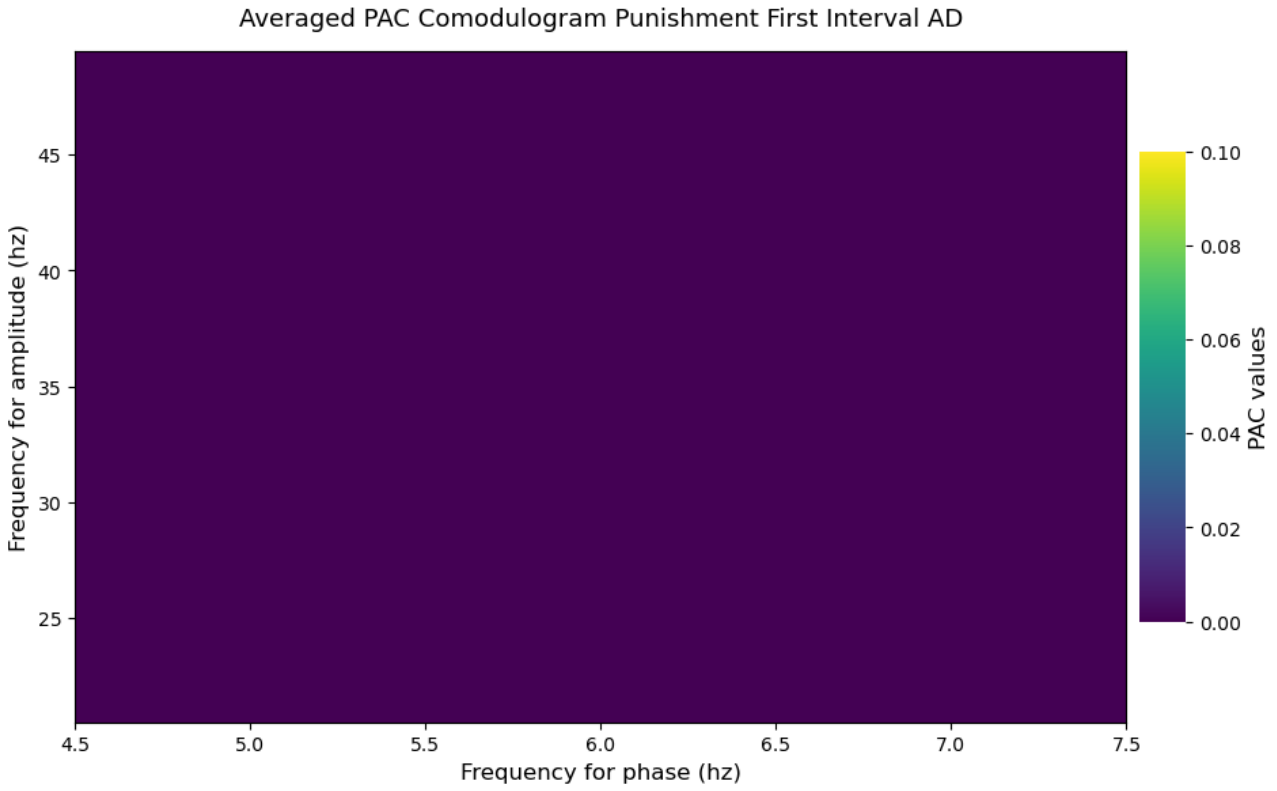


Figure 29: Significant Main Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [0, 500] After Feedback for AD Subjects

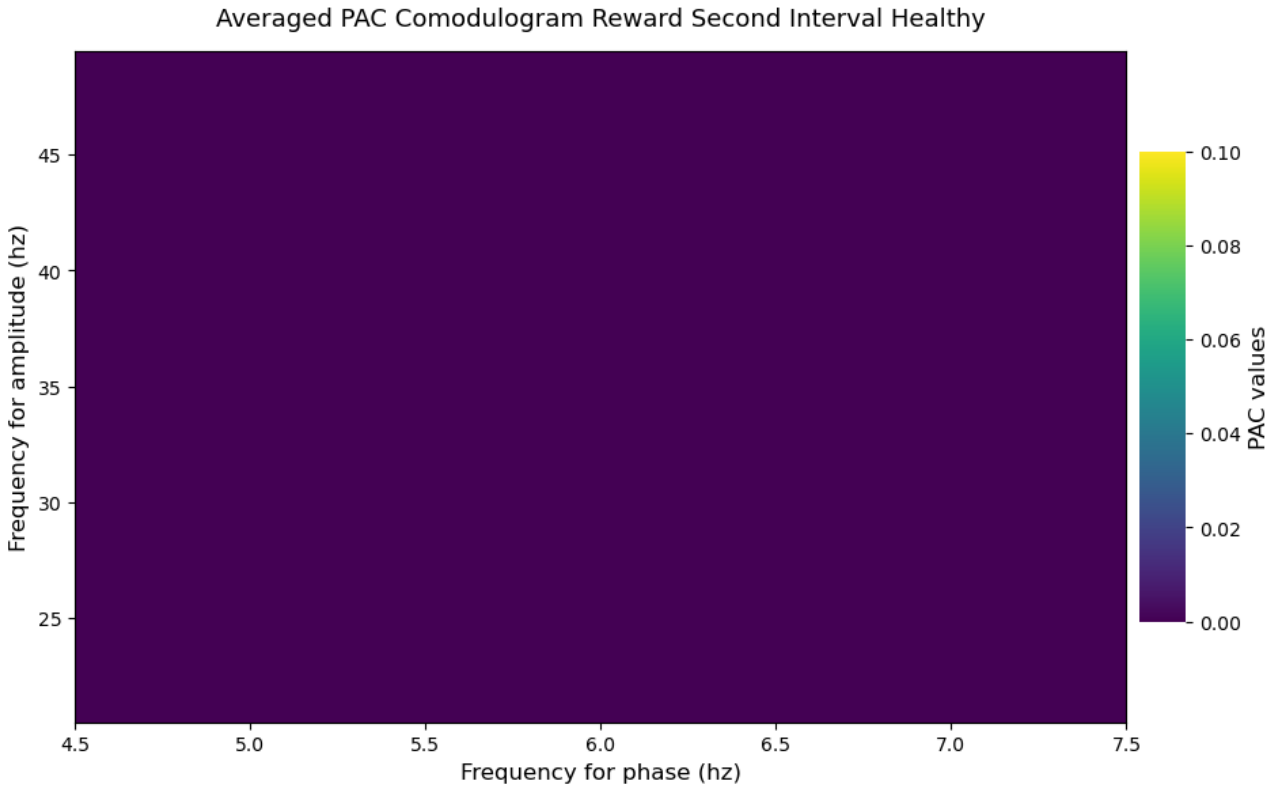


Figure 30: Significant Main Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for Healthy Subjects

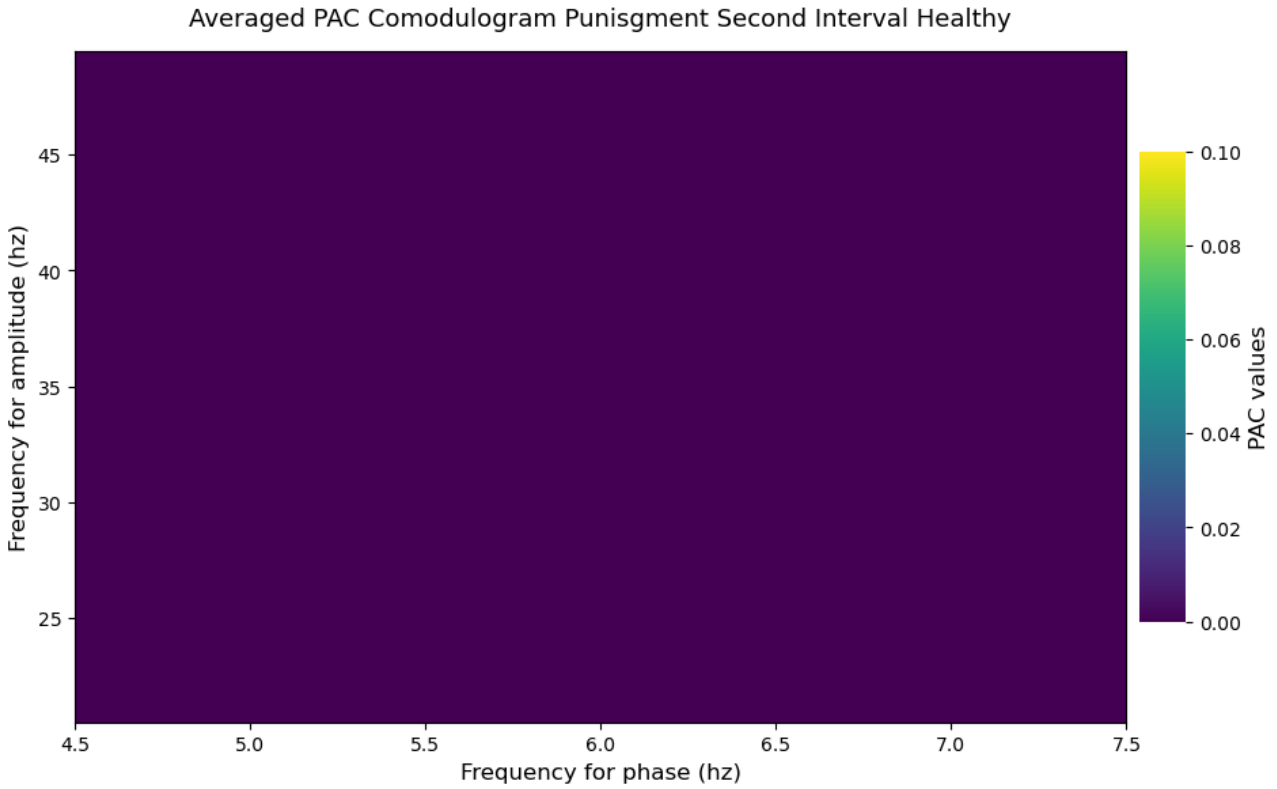


Figure 31: Significant Main Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for Healthy Subjects

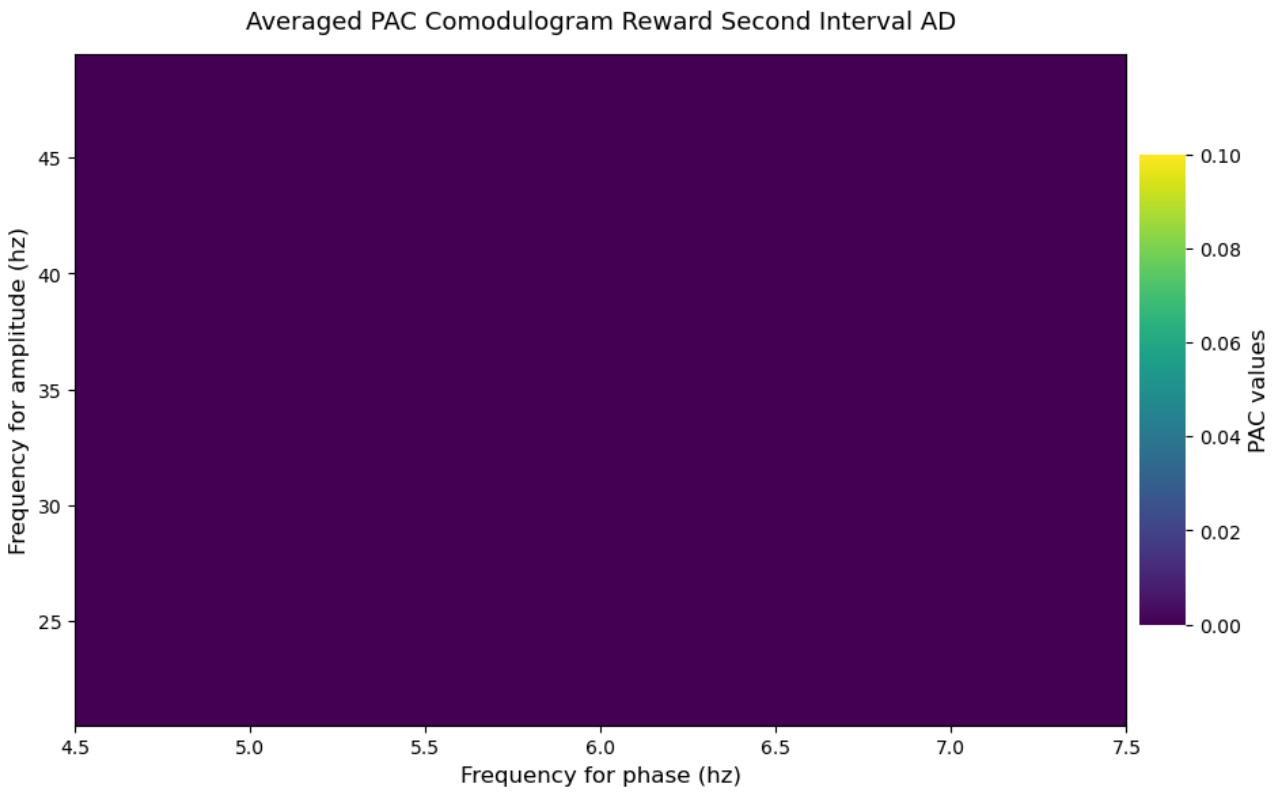


Figure 32: Significant Main Main PAC for Reward Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for AD Subjects

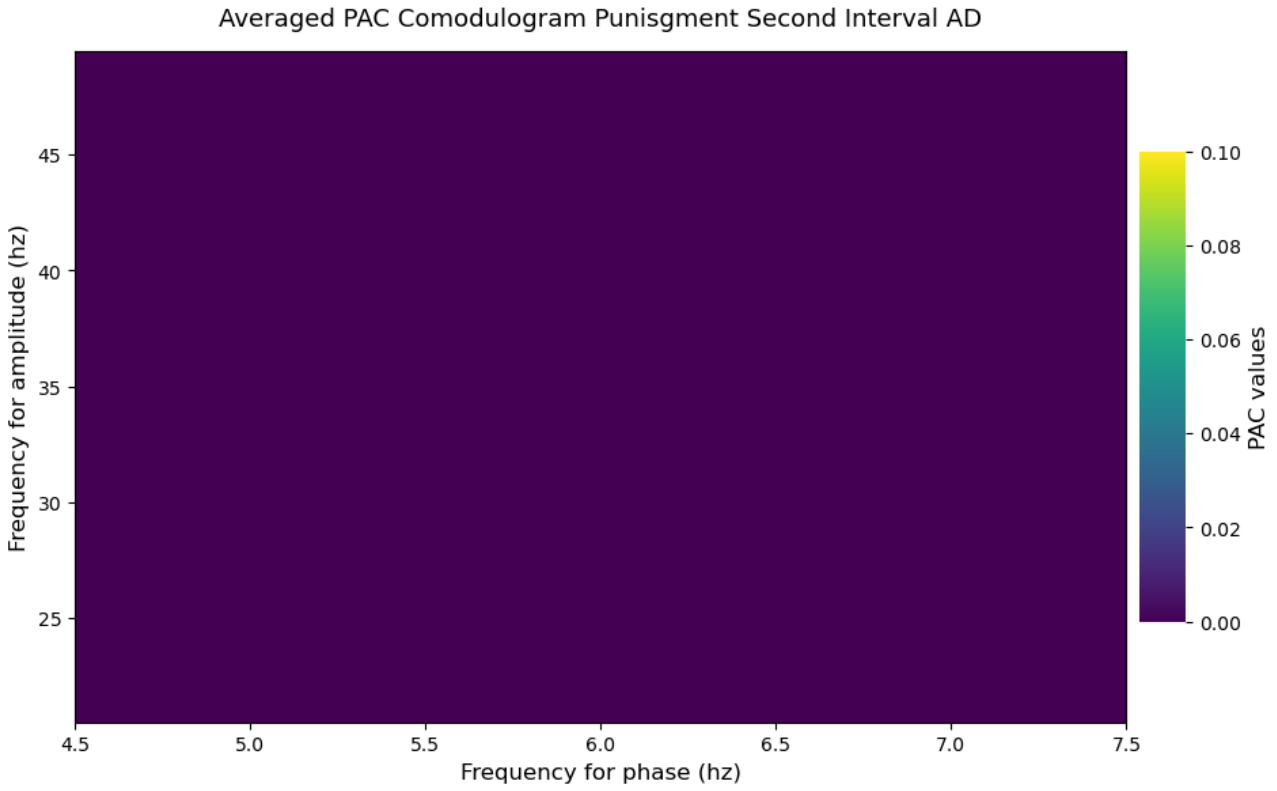


Figure 33: Significant Main Main PAC for Punishment Data Between Amplitude Fz of and Phase of Pz for [500, 1000] After Feedback for AD Subjects

Soloution

**1. Based on the mathematical framework of the MVL method, explain why this method is more susceptible to bias in long-range signals?**
**Answer:** The MVL method (Maximum Variance Linear) relies on statistical estimations of the data, and when dealing with long-range dependence (LRD) signals, the method might become sensitive to such correlations over long timescales. The long-range dependence in the signal means that the values of the signal are correlated over long periods, leading to potential biases in the variance calculations, which MVL relies on. This can cause MVL to overestimate or underestimate the underlying relationships within the signal, particularly when the signal exhibits a significant degree of autocorrelation over time.

**2. How does removing the effect of long-range dependence in the results of PAC with the MVL method influence the test?**
**Answer:** Removing the long-range dependence from the signal prior to applying the PAC (Partial Autocorrelation) method with the MVL method improves the precision of the results. Long-range dependence often introduces spurious correlations, which can distort the true relationships between variables. By removing these effects, PAC can more accurately identify the direct dependencies between time series, leading to a more reliable and unbiased interpretation of the data.

**3. Does the comodulogram show any differences in the interaction between reward and punishment in each group?**
**Answer:** Yes, the comodulogram does show differences in the interaction between reward and punishment for the respective groups. In the comodulogram analysis, the PAC (Partial Autocorrelation) values are used to assess the coupling between the amplitude and phase of signals. These interactions can vary depending on the condition of reward or punishment. Changes in PAC values and their distributions across different frequency bands indicate how the signals in each group respond differently to reward and punishment. Thus, such a difference is likely to be observed in the patterns of the comodulogram.

**4. Is there a difference between the two groups in the response to reward and punishment?**
**Answer:** Yes, there is a difference between the two groups in their response to reward and punishment, as indicated by the differences in the comodulogram patterns. The variation in PAC values, particularly across different frequency ranges, suggests that the two groups process reward and punishment signals differently. The nature of these differences can be attributed to the neural or cognitive mechanisms underlying each group's responses, which may vary due to factors such as health status or experimental conditions.

**5. Is there any difference in the frequency bands of PAC computed for FZ and PZ in the different conditions (reward, punishment, and intervals)?**
**Answer:** Yes, there is a difference in the frequency bands of PAC (Partial Autocorrelation) computed for FZ and PZ in the different conditions. In the provided comodulogram data, PAC values vary across different frequency ranges for both the amplitude and phase signals. This indicates that the interaction between the signals at different frequencies behaves differently in FZ and PZ, especially in response to conditions like reward, punishment, and interval changes.

These differences in PAC values can reveal how the coupling of these signals shifts in response to specific conditions, reflecting variations in neural activity and information processing at different locations (FZ and PZ) during reward and punishment contexts.

**6. In general, provide a neuroscience hypothesis based on the results of functional connectivity between the Fz and Pz regions in the brain during reinforcement learning. In fact, by referencing scientific sources and articles, first investigate the general relationships between Pz and Fz, specifically what the brain's performance, especially in learning, can be described as, and then, based on that, provide a hypothesis for the results of PAC and the differences between groups or events. Make sure that your hypothesis is entirely correct, but the logical coherence of it is required.**

**Functional Roles of Fz (Frontal) and Pz (Parietal) Regions**

**Fz (Midline Frontal Cortex):**

- Associated with executive functions, reward processing, and decision-making in reinforcement learning (RL).
- Theta oscillations (4–8 Hz) in frontal regions are linked to error detection, feedback processing, and adaptive behavior [**?**].

**Pz (Midline Parietal Cortex):**

- Involved in attentional resource allocation, sensory integration, and memory retrieval.
- Gamma oscillations (30–80 Hz) in parietal regions correlate with attentional focus and task-relevant information processing [**?**].

**Fronto-Parietal Connectivity in Learning**

Functional connectivity between Fz and Pz, particularly theta-gamma phase-amplitude coupling (PAC), is critical for integrating reward signals (frontal) with sensory and attentional processes (parietal). Studies suggest:

- Theta oscillations in frontal regions modulate gamma activity in parietal areas during learning [**?**].
- Effective fronto-parietal communication enhances RL by updating action-outcome associations [**?**].

**Hypothesis**

"Individuals with stronger theta-gamma PAC between Fz and Pz electrodes during reinforcement learning will demonstrate faster behavioral adaptation to feedback, reflecting enhanced integration of reward signals (frontal) and attentional updating (parietal). Group differences in learning rates may arise from variability in this fronto-parietal oscillatory coupling."

**Mechanistic Explanation**

**Feedback Processing:** Fz theta oscillations encode reward prediction errors, which are relayed to Pz to guide attentional shifts toward task-relevant stimuli.

**Phase-Amplitude Coupling (PAC):** Theta phase in Fz may temporally organize gamma amplitude in Pz, enabling efficient transfer of reward-related information to sensory systems.

**Group Differences:** Learners with weaker PAC might rely on suboptimal strategies (e.g., model-free RL), while stronger PAC could indicate model-based learning.

**References**

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**Conclusion**
This hypothesis aligns with established roles of fronto-parietal networks in RL and provides a testable framework for analyzing neurophysiological data. While speculative, it integrates known mechanisms of oscillatory coupling and learning efficiency.