A comparison between the level of anxiety and aggression patterns in adolescents
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Abstract: The main purpose of this study is a comparison between level of anxiety and aggression patterns in adolescents. Increasing evidence supports the notion that both internalizing (e.g., anxiety) and externalizing (e.g., aggression) behavioral dysregulation are associated with abnormal communication between brain regions. Electroencephalographic (EEG) signals across two electrode sites are said to be coherent with one another when they show consistent phase relations. However, periods of desynchrony with shifting of phase relations are a necessary aspect of information processing. The components of EEG phase reset (‘locking’ when two regions remain in synchrony, and ‘shifting’ when the two regions desynchronize momentarily) show dramatic changes across development. We collected resting EEG data from typically developing 12 to 15-year-olds and calculated phase shift and lock values in the alpha frequency band across 14 pairs of electrodes varying in inter-electrode distance. A composite measure of anxiety levels was positively associated with alpha phase locking at sites over both hemispheres, consistent with changes in connectivity reported during anxious thinking in adults. Associations with anxiety could not be explained by traditional EEG coherence measures and suggest that phase shifting and locking might provide an important non-invasive associate of clinically problematic behavior. A composite measure of participants’ aggression levels was positively associated with phase shifting, particularly in the low alpha frequency range, most strongly over the left hemisphere, consistent with the relatively greater left-prefrontal activity reported in aggressive adults.

Key words: Anxiety, Aggression patterns, Adolescents

1. Introduction
Adolescence is a period characterized by major biological, psychological and social changes that can affect the developing adolescent’s ability to self-regulate and these changes coincide with the onset of many forms of psychopathology. Of particular interest here are increased incidence of anxiety and aggression, markers of emotional and social dysregulation respectively.

Both anxiety and aggression have been associated with specific patterns of communication between neural regions. Aberrant connectivity has been observed in some anxiety disorders and in some of those prone to aggressive behavior (Hofman & Schutter, 2009; van Honk, Harmon-Jones, Morgan, & Schutter, 2010), using fMRI and TMS connectivity techniques.

The direction of these aberrations varies across studies with Liao et al. reporting decreased connectivity in those with social anxiety disorder relative to controls within both motor and visual networks, and increased connectivity in a self-referential network involving medial prefrontal regions. The strength of the coherent activity in some of these networks is associated with symptom severity. Two other research groups report that youth prone to aggressive behavior show reduced intrahemispheric connectivity (specifically between limbic and prefrontal structures important to emotion regulation).

There are, however, electroencephalographic (EEG) coherence and other connectivity measures that may better capture the moment to moment changes in functional connectivity that occur between neural regions. Examples include the work of Hinrichs and Machleidt who used traditional alpha EEG coherence measures and observed globally decreased alpha coherence together with increases in peak alpha frequency during anxious thinking in an adult sample. Knyazev, Savostyanov, and Levin, however, found increased levels of low alpha coherence (adjusted to each participant’s peak frequency, but generally 8–10 Hz) correlated positively with increased levels of state anxiety in an adult sample. Thus, the specific direction of coherence patterns associated with anxiety is unclear at present, and discordant results may be partially attributable to which frequencies within the alpha range are examined.

With respect to aggression, Hinrichs and
Machleidt observed globally increased alpha coherence in participants during aggressive cognition, but their results did not address whether these relations would extend to trait measures of the same construct.

Little other work has addressed the association between EEG measures of connectivity and aggressive behavior. In sum, aberrant connectivity may be associated with anxiety and increased connectivity may be associated with aggressive states. Important for the present work, both Hinrichs and Machleidt and Knyazev et al. report on average coherence values across the whole scalp providing little to no information on the scalp locations of group and state differences despite fMRI and TMS work suggesting that these differences may be regionally specific. In the present study we test whether these reported state differences in coherence extend to stable trait measures and we aim to provide improved topographical detail on the observed effects.

2. EEG connectivity

There are a variety of ways to measure cortical communication or connectivity within EEG recordings, and each may yield different insights into the nature of the communicative differences observed in anxiety and aggression. Traditional EEG coherence measures such as the one used by Hinrichs and Machleidt estimate the strength of the linear cross-correlations between two time series (i.e., recordings from two electrodes) within a frequency band (e.g., alpha). These are linear measures which assume a constant phase value within windows of data, but EEG recordings have been shown to be highly nonlinear. Time-dependent instantaneous phase measures have been used to capture the nonlinear aspect of EEG connectivity, such as the entropy-based method of Tass et al. and the mean phase coherence of Mormann, Lehnertz, David, and Elger. Windowing techniques are used to quantify periods of phase synchronization but are unable to identify specific times when the two time series become dissimilar from one another. EEG signals across two sites are said to be coherent with one another when they show synchronous phase relations, and traditional measures quantify these time periods well.

However, periods of desynchrony, characterized by a shifting of phase relations, are a necessary aspect of information processing. Balance between synchronization (phase locking between two regions) and desynchronization (phase shifting) is essential for normal brain function, and windowed measures do not quantify this important dynamic. We suggest that separating out these distinct states of information processing may be important for understanding the cortical communicative differences observed in those with poorly regulated social and emotional functioning (e.g., anxiety and aggression).

Thatcher and colleagues have developed methods to examine phase shift and phase locking events in continuous EEG data, using what is called the phase reset cycle. A phase reset consists of a brief phase shift representing the reorganization of brain resources, and then a prolonged period of phase locking. Phase shift periods typically last from 20 to 80 ms and are followed by a longer period of phase locking which typically lasts 500 to 1000 ms, but actual times depend strongly on the frequency band of interest. Thatcher and colleagues describe phase shifting as a period of uncertainty and instability and phase locking as a period of stability and low uncertainty in neural networks.

During the phase shift period, relevant neural assemblies that are not in a refractory period are identified as available to bind together in a communicative network on the global and/or local level.

When phase locked, these neural assemblies are able to mediate a given cognitive or psychological function. Thus, phase shifting can be conceptualized as a reorganization of resources and a preparatory period for future network integration while phase locking can be conceptualized as the period during which this network integration occurs on either the global or local level. Thatcher et al. suggest that there is an ideal balance of phase shifting and locking necessary for optimal cognitive performance, such that when phase shift duration is too long then there is increased noise in the network and a reduced number of neurons available for subsequent phase locking. Conversely, when phase lock duration is too long then there is less flexibility in the network. We hypothesize that dysregulation in such neural networks may manifest itself as dysregulation in psychological functioning. Phase reset patterns are not static across development.

Thatcher and his colleagues obtained measures of phase reset length across varying distances of the cortex from a large sample of children ages 3 months to 16 years. Interestingly, they report a lengthening of both phase shift and phase locking durations during the adolescent period, consistent with the puberty-linked changes in white matter that have previously been documented in this age range.

One interesting question concerns what implications these changes might have for psychological functioning in adolescence, a particularly vulnerable time for the onset of psychopathology. Our goal was to see whether a more sensitive measure of EEG connectivity (i.e., phase reset), with its ability to parse periods of phase shifting and locking at distinct site pairs, is associated with individual differences in adolescent anxiety and
aggression while controlling for at least one marker of general physical development (e.g., pubertal status).

Using this more sensitive connectivity measure, in addition to dividing alpha into high and low subcomponents, may shed light on the conflicting findings of Hinrichs and Machleidt relative to those of Knyazev et al.

3. Alpha, anxiety and aggression

As mentioned previously, phase reset variables are calculated within particular frequency bands. We chose to examine phase shifting and locking in the alpha frequency band because alpha power is sensitive to anxiety in adolescents, and is increased in calm, meditative states. Moreover, having greater left-prefrontal cortical activity (relative to right prefrontal activity, as measured by alpha asymmetry) is associated with a higher likelihood of engaging in aggressive behavior in adult men. Thus, both connectivity and alpha have been shown to be altered in those showing high levels of anxiety and aggression, leading us to ask whether phase reset variables that presumably index neural network regulation derived from the alpha frequency band would be associated with individual differences in anxiety and aggression and whether traditional coherence measures would also show such associations. If coherence is positively correlated with both levels of anxiety and phase locking but correlated negatively with phase shifting, then we might expect that anxiety would be positively correlated with locking, and negatively correlated with shifting. However, the state of the current literature is insufficient to allow us to make these conclusions. One report suggests that phase shift measures are negatively correlated with traditional coherence and that phase locking measures are positively correlated with coherence (Thatcher et al., 2009), although this report is based on a sample of children aged 5 months to 16 years with no statistical correction for age, and so there is the possibility that this association may be explained by developmental changes in cortical connectivity.

Therefore, we addressed the following research questions, albeit in a somewhat exploratory fashion:

1. Would the previously demonstrated individual differences in EEG connectivity be observed in trait, rather than state measures of anxiety and aggression in adolescents rather than adults?

2. At what frequency of alpha would these effects emerge and where on the scalp would we observe them?

3. Would the observed effects be specific to phase reset variables, or could they be explained by traditional EEG phase coherence, pubertal status, age, or gender?

4. Methods

4.1. Participants

Eighty-four typically developing 12–14 year-olds (43 female) were invited to participate in a larger study investigating the neurocognitive correlates of adolescent self-regulation. Participants were right-handed, and without psychiatric or neurological conditions.

Both participants and their parents/guardians provided written consent and all procedures received clearance from the university Research Ethics Board in accord with the Declaration of Helsinki. Participants were given $25 each for their participation.

4.2. EEG recording

Participants rested for four minutes while fixating on a cross at the middle of a black computer screen in a dimly lit room. Seven of the 128 channels on the system (EGL, Eugene, OR) were allocated to non-EEG psychophysiological recordings, and from the remaining 121 channels, 12 lateral EEG sites conforming to the standard 10–20 system were used in the analyses presented here (see Fig. 1). Sampling rate was 500 Hz and impedances were maintained below 30 kO throughout recording. Data were re-referenced offline to the average of all 121 sites, filtered offline (1–30 Hz) and corrected for eye movements using the Gratton and Coles procedure (Gratton, Coles, & Donchin, 1983). A semi-automated artifact rejection procedure (±50 IV/data point and ±100 IV/max–min criteria) was used to reject poor windows of data which were verified as such in subsequent manual examinations of the data. The number of useable seconds of data did not relate to any of the psychological, maturational or physiological measures that are the focus of this study (all r’s < 0.11, all p’s > 0.3).

5. Results

5.1. Pubertal status, age, anxiety, and aggression

Given the rapid biological and psychological changes during adolescence, we first wished to determine whether variance in anxiety and aggression could be predicted by age, pubertal status, sex, and/or their interaction, and to then examine neurophysiological effects in light of these. Females reported significantly higher levels of anxiety than males (t(83) = 2.85, p =.006). Anxiety levels were not correlated with age, pubertal status, or the interaction of pubertal status and sex (see Table 1 for values). Males and females did not differ in levels of reported aggression (t(83) = 1.51, p =.13). Aggression scores were significantly correlated with pubertal status and the interaction of pubertal status and sex.

Aggression and anxiety scores were highly
correlated with one another (see Table 1) and remained highly correlated once pubertal status, sex and their interaction were partialled out, \( r(80) = .47, p < .001 \).

<table>
<thead>
<tr>
<th></th>
<th>Shift duration (ms) – M(SD)</th>
<th>t value</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>LH average</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F7–T5</td>
<td>27.32(2.12)</td>
<td>2.756</td>
<td>.007</td>
</tr>
<tr>
<td>F3–P3</td>
<td>25.31(1.60)</td>
<td>1.782</td>
<td>.079</td>
</tr>
<tr>
<td>F3–C3</td>
<td>25.24(2.08)</td>
<td>1.740</td>
<td>.086</td>
</tr>
<tr>
<td>O1–C3</td>
<td>25.42(1.83)</td>
<td>3.276</td>
<td>.002</td>
</tr>
<tr>
<td>O1–F3</td>
<td>30.46(3.47)</td>
<td>3.337</td>
<td>.001</td>
</tr>
<tr>
<td>F3–O1</td>
<td>25.13(1.52)</td>
<td>1.595</td>
<td>.115</td>
</tr>
<tr>
<td>F3–F7</td>
<td>29.63(2.91)</td>
<td>1.037</td>
<td>.303</td>
</tr>
<tr>
<td>RH average</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F4–F8</td>
<td>32.25(2.87)</td>
<td>2.911</td>
<td>.005</td>
</tr>
<tr>
<td>F4–C4</td>
<td>28.72(2.78)</td>
<td>3.316</td>
<td>.001</td>
</tr>
<tr>
<td>F4–P4</td>
<td>24.96(1.81)</td>
<td>2.646</td>
<td>.010</td>
</tr>
<tr>
<td>O2–C4</td>
<td>24.99(1.95)</td>
<td>5.719</td>
<td>.000</td>
</tr>
<tr>
<td>O2–P4</td>
<td>29.52(3.16)</td>
<td>5.567</td>
<td>.001</td>
</tr>
<tr>
<td>F4–O2</td>
<td>25.24(1.62)</td>
<td>1.289</td>
<td>.201</td>
</tr>
<tr>
<td>F8–T6</td>
<td>26.90(2.16)</td>
<td>3.402</td>
<td>.001</td>
</tr>
</tbody>
</table>

|                | Lock duration (ms) – M(SD)  |         |     |
| LH average     |                             |         |     |
| F7–T5          | 524.82(158.31)              | 2.313   | .023|
| F3–P3          | 514.91(101.50)              | .845    | .401|
| F3–C3          | 540.85(121.83)              | 1.803   | .075|
| O1–C3          | 543.52(165.16)              | 1.007   | .317|
| O1–F3          | 501.73(165.28)              | 2.152   | .034|
| F3–O1          | 606.76(147.17)              | 3.235   | .002|
| F3–F7          | 562.17(146.19)              | 2.747   | .007|
| RH average     |                             |         |     |
| F4–F8          | 505.29(120.25)              | .757    | .451|
| F4–C4          | 516.83(102.04)              | .261    | .795|
| F4–P4          | 519.83(124.12)              | .221    | .825|
| O2–C4          | 546.83(140.97)              | .854    | .396|
| O2–P4          | 556.25(153.74)              | 1.345   | .182|
| F4–O2          | 580.78(168.68)              | 1.765   | .081|
| F8–T6          | 525.15(109.15)              | 1.662   | .100|
5.2. Pubertal status, sex and phase reset variables

Males and females differed in the average length of phase shifting calculated in the full alpha range in the right hemisphere where females had significantly longer shift durations. There was a trend towards this same pattern in the left hemisphere. When pairs of sites were analyzed, females had significantly longer shift durations than males in the full alpha range at eight pairs of sites and a trend towards longer shift durations at an additional three pairs of sites (p’s 6.08). None of these site pairs could be considered a long range connection (P18 cm). Males had significantly longer average left hemisphere lock durations than females. Further analysis identified three pairs of sites with significantly longer lock durations and there was a trend for males to have longer lock durations at an additional two pairs of sites (p’s 6.08). Only one of these pairs of sites showing significant sex differences (F3–O1) is considered a long range connection. Pubertal status was different across the genders, as would be expected, with females more advanced (t(82) = 3.25, p =.003), and thus the gender differences in phase reset durations could have been due to differences in pubertal maturation. Post hoc analyses indicated that the duration of phase shifting in the full alpha range correlated positively with pubertal status for both left and right hemisphere sites (r(82) =.29, p =.008; r(82) =.27, p =.015, respectively), and that these relationships were stronger for males than females. Phase locking calculated in the high alpha range was negatively correlated with pubertal status in females only (r(41) =.37, p =.015; r(41) =.32, p =.034, for the left and right hemispheres respectively).

Notably, these same relationships were not evident when age was used as an indicator of maturation. Age was not correlated with phase shifting or locking in the full alpha range, or in its sub-bands (all r’s 6.06, all p’sP.50; see Table 1 for values), and is therefore not used in subsequent analyses. Thus, sex, pubertal status, and their interaction could have affected our results and were used as covariates in a later stage of our analysis.

5.3. Potential confounds and alternate explanations

In order to rule out a series of alternate explanations, we re-ran these analyses including a number of control variables. As described above, females reported significantly higher levels of anxiety than males. Anxiety and aggression were highly correlated in the present sample, and so we wanted to partial out any shared variance between the two measures in subsequent analyses. Moreover, cortical communication has been shown to change as a function of pubertal status, and in theory changes as a function of cortical activation (as reflected in EEG power). Phase shifting and locking durations were also correlated. We additionally aimed to see whether our results were specific to phase reset measures or extended to coherence measures as well. We ran four sets of regression analyses which involved entering the control variables into the regression analysis along with both of the phase reset variables to predict each psychological measure, and then examining the independent contribution of each phase reset variable to the prediction of each of the psychological measures by examining the t-test associated with each variable’s beta weight. We limited these analyses to the alpha frequency sub-band for which the associations were the strongest and did not focus on specific site pairs but rather whole hemisphere effects. We present regression tables only for the most complex set of analyses which include all control variables.

5.4. Puberty, sex, and their interaction

In order to control for the role of puberty, sex and their interaction on the associations between phase shifting and locking with aggression and anxiety, these three control variables were entered into a regression analysis along with our reset variables to predict anxiety and aggression. We did not control for age; as reported earlier, age was not related to our measures of communication or to our psychological measures. Pubertal scoring ranged considerably as expected in this age cohort (M = 13.09, SD = 3.06; Range = 6–19). Adding pubertal status, sex and their interaction into the regression analysis did not alter the relationships between phase shifting and aggression or between phase locking and anxiety; nor did it produce new relations between the predictors and outcomes.

Right and left hemisphere phase locking were still significantly predictive of anxiety levels (t(74) = 2.98, p =.004; t(74) = 3.03, p =.003, for the right and left hemispheres respectively). Left hemisphere shifting in the low alpha range was still positively associated with aggression when these control variables were included (t(74) = 2.05, p =.044).

6. Discussion

Some researchers have reported significant associations between globally measured alpha coherence and levels of anxiety and aggression in adult populations, although no work has been done to date on EEG alpha connectivity and stable levels of psychological wellbeing during adolescence, a particularly vulnerable time for the onset of social and emotional dysregulation. We did not want to limit ourselves to traditional EEG coherence techniques measured globally across the scalp, and so our study was aimed at uncovering whether relatively more
advanced connectivity metrics with their ability to index the regulatory properties of neural assemblies would be associated with individual differences in anxiety and aggression in young adolescents, at what frequency of alpha these effects would emerge, and in what hemisphere and at what scalp locations they were evident. We chose to employ phase reset calculations for this purpose, and our results suggest that this metric of cortical dynamics is associated with anxiety and aggression levels in typically developing adolescents.

Firstly, we found that phase reset variables vary across sex and pubertal status. Males showed longer locking durations than females, especially over the left hemisphere at interelectrode distances smaller than 18 cm. Females showed longer shift durations than males within this same range of interelectrode distances, and these gender differences were more pervasive than the locking differences, involving more site pairs and therefore presumably more neural assemblies. Moreover, longer shifting durations were associated with greater pubertal status in the left and right hemisphere, with the left hemisphere showing the sex differences described above. These results are consistent with the work of Thatcher et al. who report a lengthening of the phase shift duration during this developmental period. The general pattern seems to be that longer shift durations are indicative of greater maturity, although there may be a threshold to this effect as Thatcher et al. report that excessively long shifts lead to poor network organization. Since pubertal status is associated with brain maturation and females begin puberty at an earlier age than males, it is not surprising that we found females to have longer shift durations. An unexpected finding is that males had longer locking durations than females but locking variables were not associated with pubertal status. However, our study was not designed to chart the development of phase reset variables and our attempts to replicate the developmental trends of Thatcher et al. may have been under-powered. It seems apparent that a larger sample of participants covering a greater age range should be applied to this hypothesis of maturation being associated with longer shift and shorter lock durations.

We found that pubertal status rather than age related to our physiological measures. Pubertal status and hormonal markers thereof often predict more variance than age, or additional variance above age in adolescent mental health and adolescent risk-taking. In at least one study, puberty-linked white matter changes were not attributable to age.

Turning to our main hypotheses, those adolescents with higher levels of anxiety showed longer phase locking in the full alpha range at pairs of sites across both hemispheres. Dividing alpha into its relatively higher and lower frequency subcomponents showed that these associations are due to the combination of low and high alpha together and not a smaller frequency range within the broader band. These results converge with findings of abnormalities in alpha generation in anxious 14–15 year olds (Eismont et al., 2008). Six out of the nine site pairs that demonstrated significant zero-order correlations with anxiety involved at least one frontal site and this is consistent with the observation that frontal networks show specific abnormalities in those with anxiety disorders (Liao et al., 2016). Our results extend these findings by suggesting that abnormalities may be specific to phase locking between sites, analogous to ruminative thought patterns reported in anxiety. Anxious individuals report becoming fixated on particular anxiety-provoking thoughts, consistent with our results suggesting that this may be associated with the prolonged locking of neural assemblies mediating these thought processes, leading to a consequent reduction in the flexibility of the system. The prolonged locking durations were observed at both the local (short range) and global (medium to long range) connectivity lengths across both hemispheres. Although previous MRI work has found aberrant connectivity patterns in some subcortical networks in anxious adults (e.g., involving the insula and the basal ganglia; Liao et al., 2016; Marchand, 2016), EEG is not able to directly measure such connectivity, and so we are unable to speculate on how our work integrates with this previous body of literature.

**Conclusion:**

These results are also not attributable to volume conduction; as mentioned above, a well-chosen threshold value greatly reduces the effect of volume conduction on phase reset analysis. Additionally, the selection of electrode combinations used in this study provides a natural check for the effect of volume conduction (Thatcher et al., 2017). The effect of volume conduction decreases monotonically as a function of the square of the distance, so when it is the source of connectivity between distant electrodes, then there must also be connectivity between any intermediate electrodes between them. We see that there is a significant correlation between O1–C3 but not at the intermediate O1–P3 pair and we see connectivity between F7–T5 but not from F7–C3, thus we do not expect volume conduction is a contributing factor in this analysis.

Overall, alpha phase reset variables appear to be a good marker for cortical activation, and communication between sites and are able to dissociate adolescent experiences of anxiety and aggression. Anxious adolescents show prolonged periods of phase locking but few differences in phase
shifting while the reverse seems to be true of adolescents high on aggression. These results suggest that phase shifting and locking may be associated to an even greater extent in a population where these characteristics are more severe and are clinically problematic.

References:


