

# Depression, Anxiety, and Parental Warmth as Correlates of Stress-Hormonal Regulation in Transgender Youth

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## Background

- The adapted **minority stress model** proposes that transgender populations exhibit poorer mental and physical health outcomes due to an increased likelihood of experiencing stigmatization, discrimination, and victimization (1).
- Given this perspective, transgender youth are hypothesized to be more likely to exhibit physiological differences in the activity of the **Hypothalamic-Pituitary Adrenal (HPA) axis**, a biological system responsible for mediating whole-body responses to stress via hormonal regulation (2). When individuals are confronted with psychosocial stressors, this typically results in the immediate activation of the HPA axis, leading to elevated levels of biomarkers for inflammation, such as C-Reactive Protein (CRP), as well as deviations in the release of cortisol (3). However, few studies have examined the hormonal stress profiles of transgender youth specifically, with disparities in HPA axis activity as a potential mediator for mental health outcomes. **The purpose of the current study is to analyze potential differences in the diurnal cortisol patterns and C-Reactive Protein (CRP) profiles of transgender youth, according to the variables of depressive symptoms, anxiety, and parental warmth.**
- CRP** is a plasma protein produced by the liver that is sensitive, at least in the short term, to the effects of psychosocial stressors and has been widely used as a biomarker for systemic inflammation (3). Numerous studies have suggested that elevations in CRP concentrations can be linked to the suppression of immune functioning and is a significant diagnostic risk factor for cardiovascular disease (3). In healthy individuals, salivary CRP concentrations have been shown to range from 35-217 pg/mL, for saliva collected via the passive drool method (4).
- Cortisol** is the major glucocorticoid hormone synthesized and secreted by the adrenal cortex, whose release is primarily stimulated by physical or psychological stress (5). Normal cortisol release in the body follows a diurnal rhythm, in which peak levels occur shortly after awakening and gradually declines throughout the day (6). Mean salivary cortisol concentrations in normal, healthy adolescents (ages 12-18) have been reported to range from 0.021–0.883 µg/dL in the morning, which is significantly higher when compared to evening values of ≤0.259 µg/dL (7). Pathophysiological indications of this rhythm in the context of chronic exposure to stress can be indicated by a blunted change in cortisol from morning to evening, and lower HPA axis reactivity to acute stress challenge (the latter not measured in the current study) (8).

### The objectives for this study include:

- To evaluate average daily change in cortisol levels ( $\Delta y$ ), average evening cortisol levels, and average morning CRP levels in transgender youth, measured from daily salivary samples,
- To determine whether there is any distinction in the cortisol diurnal rhythm and CRP levels between transgender youth with greater parental warmth and those with lower parental warmth, and finally,
- To analyze potential correlations between measured cortisol values and transgender youth depression and anxiety scores, as well as compared with average CRP levels.

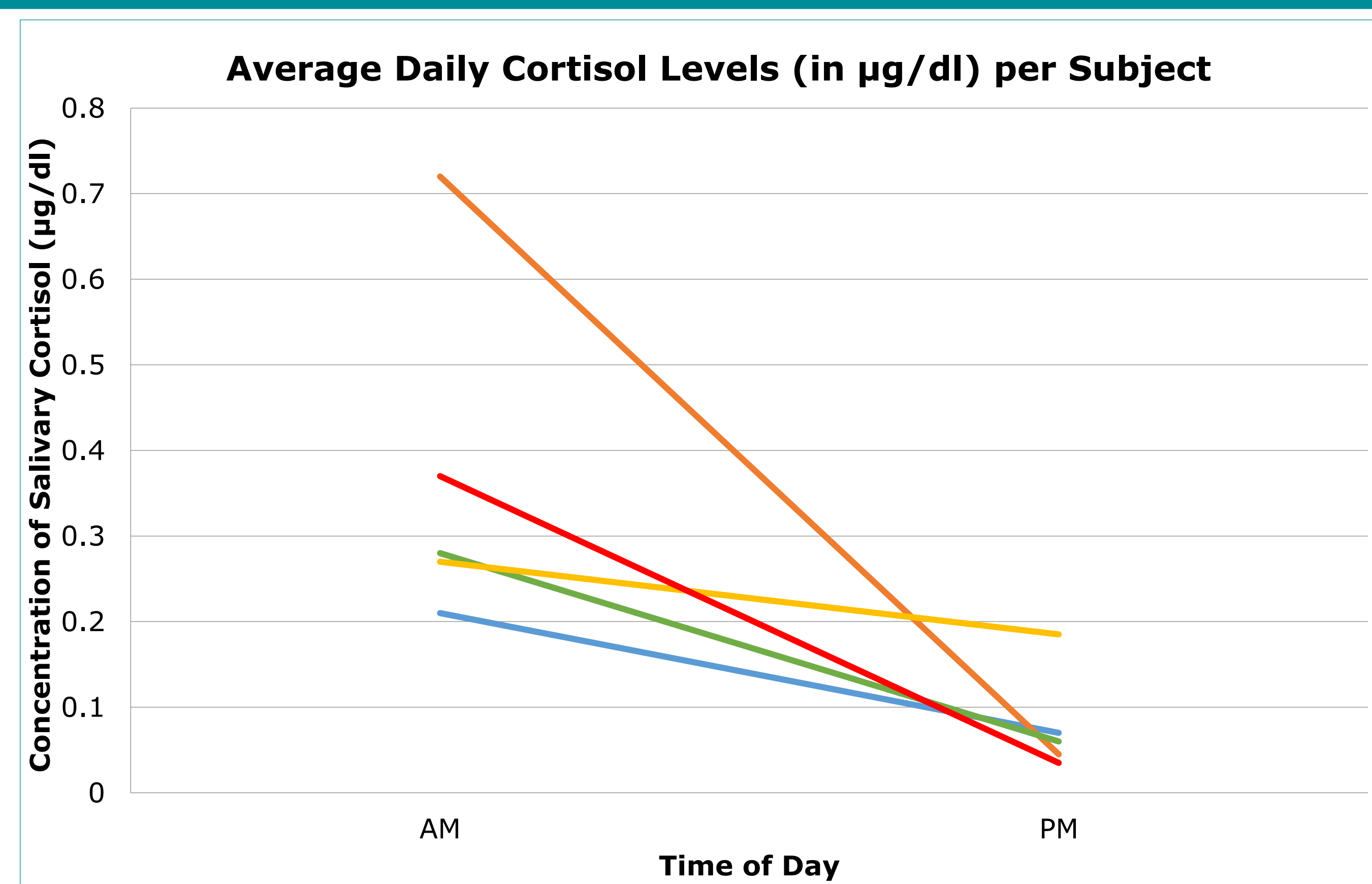
## Methods

**Sample:** The sample consisted of 5 families recruited from the Southwestern United States, each comprising of a transgender youth and at least one caregiver. The participants were recruited as part of a pilot study focused on providing meditation and compassion training for transgender youth and their families, conducted over a 6-week period. The mean age of the sample ( $n=5$ ) was 15.5 years ( $SD = 0.58$ ), and consisted of 100% White/Caucasian and 80% transmasculine teens.

**Measures:** At baseline, each participant provided 4 salivary samples over the course of two consecutive days using the oral salivette and storage tube method. The first daily sample was collected upon awakening (i.e. morning sample) and the second sample at bedtime (i.e. evening sample). The samples were then immunoassayed for their cortisol and CRP content.  $\Delta y$  was defined as the concentration difference between the evening and morning cortisol levels. The  $\Delta y$ , evening cortisol levels, and morning CRP levels were then calculated as an average for each individual across both days. **Parental warmth** (9), **depressive symptoms** (10), and **anxiety symptoms** (11) were measured using standardized measures from the baseline survey administered prior to the intervention.

**Analysis:** A Pearson correlation was then calculated for each variable with respect to average daily change in cortisol levels ( $\Delta y$ ), average evening cortisol levels, and morning CRP levels. A correlation was also calculated for the parental and teen warmth scores in order to cross-verify the reliability of the teen and parent self-reporting.

## Results



- The average morning cortisol concentration for the sample across both days was 0.37 µg/dl ( $SD=0.23$ , range= 0.07-0.89), while the average evening cortisol levels was 0.08 µg/dL ( $SD=0.08$ , range= 0.03-0.19). The  $\Delta y$  for the sample was -0.29 µg/dL ( $SD=0.23$ , range= -0.09 to -0.68).
- The sample exhibited a mean morning CRP level of 1,259.14 pg/mL ( $SD=831.55$ , range=504.66-2,626.81), which is notably elevated compared to that of normal, healthy individuals (reference range=35-217 pg/mL).

Table 1. Correlations.

	Parental Warmth (Teen Score)	Parental Warmth (Parent Score)	Depressive Score	Anxiety Score
Average Cortisol $\Delta y$ (µg/dl)	-0.63	-0.40	0.67	0.38
Average Evening Cortisol (µg/dl)	-0.67	-0.75	0.36	0.44
Average Morning CRP (pg/ml)	-0.59	-0.52	0.28	0.37

- Depressive symptoms and  $\Delta y$  were strongly correlated ( $r=0.67$ ), indicating that transgender youth with greater depressive symptoms exhibited a blunted change in cortisol from morning to evening. The correlation between  $\Delta y$  and anxiety appeared to be less strong ( $r=0.38$ ). Higher levels of parental warmth were associated with a greater  $\Delta y$  ( $r=-.40$  to  $-.63$ ), suggesting that parental warmth is a promotive factor.
- Higher morning CRP concentrations were also strongly associated with lower parental warmth ( $r=-0.59$  for self-reported and  $-0.52$  for parent-reported), as well as moderately correlated with greater anxiety ( $r=0.37$ ) and depressive ( $r=.28$ ) symptoms.

## Conclusions and Implications

- The results of this study provide preliminary evidence for parental warmth, depression, and anxiety as correlates of deviations in stress-hormonal dysregulation in transgender youth. Parental warmth appears to be a promotive factor in regulating pathophysiological changes in the diurnal cortisol rhythm and CRP release. Transgender youth with greater perceived parental warmth were also less likely to exhibit depressive or anxiety symptoms.
- These patterns suggest that transgender youth with a greater sense of parental warmth are less likely to experience HPA axis dysregulation, and are therefore physiologically capable of returning to normal, relaxed states by the end of the day. On the other hand, transgender youth with less parental warmth tended to display a flattened diurnal cortisol slope due to elevated cortisol evening levels—a pathological indication of exposure to chronic stress.
- The small sample size and lack of racial/ethnic diversity limit the generalizability of the results, thus a future study with larger samples is needed. However, the novelty of the current study in analyzing stress-hormonal regulation among transgender youth, along with the unique method of validating parental warmth self-reporting, offers great value to the study. The findings offer insight into the promotive role of parental support in health outcomes of transgender youth.
- Despite the seemingly increased visibility of transgender individuals in contemporary society, there continues to be limited research on the physical and mental health outcomes of this minority population. Understanding the underlying biological mechanisms that link HPA activity to disparities in mental health outcomes in transgender youth is an important, understudied field of research inquiry.

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