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Cortisol Synchrony in Psychotherapy for Major Depressive Disorder

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ABSTRACT

Introduction: Accumulating research emphasizes the role of interpersonal coordination in arousal levels, which may manifest as cortisol synchrony, in interpersonal interactions. While the role of cortisol has been investigated in psychotherapy, cortisol synchrony and its characteristics and effect on treatment progress remain a relatively unexplored area. This study aims to explore the existence of distinct patterns of cortisol coordination throughout psychotherapy and test the associations of different coordination patterns with patients' pre-treatment characteristics and treatment progress measures.

Methods: Fifty patient–therapist dyads participated in 16 weeks of psychodynamic treatment for major depressive disorder. Salivary cortisol samples were collected before and after each session at four time points. Self-report questionnaires and treatment session video-coding were used to characterize and differentiate between patterns of cortisol coordination.

Results: Three patterns of cortisol coordination were identified: synchronized, unsynchronized and stable-therapist. These patterns differed in patient characteristics and treatment progress measures in that patients exhibiting a synchronized pattern tended to be more anxious and dominant in their relationships and were more prone to withdrawal ruptures.

Conclusions: Results provide novel evidence regarding variability in patient–therapist cortisol patterns and its putative associations with treatment progress.

1 | Introduction

In psychotherapy, a growing number of findings show that interpersonal coordination occurs during patient–therapist interactions. Interpersonal coordination refers to behavioural, physiological, and emotional or cognitive states, which covary between patients and therapists over time (Wiltshire et al. 2020). The term coordination derives from the field of coordination dynamics (Kelso and Tognoli 2009; Turvey 1990) and encompasses specific patterns of coordination, such as synchronization (Butner et al. 2014). The basis of many interpersonal-based mechanisms of change in psychotherapy has been linked to patient and therapist synchrony in their levels of arousal (Koole and Tschacher 2016). Arousal has been operationalized using different measures, including self-report (Cox and Mackay 1985) and physiological measures (Davis et al. 2018). A standard method of assessing arousal synchrony, mainly outside of psychotherapy, is through the hormone cortisol (Meyer and Sledge 2020). Cortisol release may represent a valid endocrine measure of arousal, as it occurs in response to alerting, arousing or stressing stimuli, providing a regulatory function (Young, Abelson, and Lightman 2004; Rab and Admon 2021). The majority of the studies focusing on the question of whether cortisol

Summary

- Cortisol coordination may occur in a synchronized, unsynchronized or stable-therapist patterns between patients and therapists.
- Patients that formed synchronized cortisol patterns tended to show more anxiety and dominance in relationships.
- Withdrawal ruptures were more frequently observed in therapeutic relationships characterized by synchronized cortisol patterns.

synchrony exists, and of its possible interpersonal aspects, are mainly focused on parent–child (Davis et al. 2018) and romantic partner dyads (Meyer and Sledge 2020). Overall, these studies highlight the aversive interpersonal role of cortisol synchrony, potentially as a marker of the level of arousal in relationships. While cortisol synchrony has been extensively studied in parent–child and romantic partner dyads, its relevance in psychotherapy remains underexplored. There is great potential in exploring patterns of cortisol coordination and its associations with patient–therapist characteristics during psychotherapy, due to its regulatory role in interpersonal interactions (Harrewijn et al. 2020). Thus, we aimed to explore cortisol coordination patterns between patients and therapists in psychotherapy and their associations with treatment baseline and processes measures.

1.1 | Cortisol Synchrony in Parental and Romantic Relationship Studies

In studies examining interpersonal or developmental relationships, dyads have shown varying levels of cortisol synchronization, with different degrees of synchrony observed across subgroups (Papp et al. 2013). Interest in predicting cortisol synchrony has led to studies examining factors like relationship-related anxiety and perceptions of relationship quality as predictors of dyadic mutual cortisol secretions (Williams et al. 2013; Liu et al. 2013). Attachment orientations, commonly studied in interpersonal and developmental research, were found to be associated with cortisol responses. For instance, research indicates that romantic couples with higher attachment avoidance exhibit increased cortisol levels, especially when there is a mismatch in attachment styles between partners of a dyad (Kidd, Hamer, and Steptoe 2011; Harvey et al. 2019). In parent–child relationships, for example, parental attachment anxiety is linked to flatter diurnal cortisol slopes in children, suggesting higher overall cortisol levels (Harvey et al. 2019). However, some studies have found no significant associations between attachment orientations and cortisol responses (Ketay and Beck 2017). These inconsistent findings suggest that the relationship between attachment orientations and cortisol responses may be contextual. While increased cortisol synchrony often correlates with aversive interactions, the extent of cortisol synchronization between patients and therapists during psychotherapy sessions, along with the predictors of this coordination pattern, remain understudied.

Beyond exploring predictors of synchrony, research on cortisol synchronization has delved into its potential interpersonal outcomes. For instance, Kalomiris and Kiel (2018) found that children in highly synchronized mother–child dyads exhibited fewer anxiety symptoms over time, while Yirmiya et al. (2023) discovered adverse effects of increased cortisol levels in war-exposed mother–child dyads. Furthermore, studies have examined how cortisol synchrony relates to dyadic interaction quality, with findings suggesting associations with both positive and negative outcomes. For instance, increase in relationship quality (Pauly et al. 2021), or decrease in marital satisfaction (Saxbe and Repetti 2010). However, current research has mainly focused on individual interactions or established relationships, leaving gaps in our understanding of cortisol synchrony formation. Exploring cortisol synchrony in short-term psychotherapy settings can fill this gap, providing insights from relationship initiation to conclusion.

1.2 | Arousal Coordination Dynamics: In Psychotherapy and Beyond

While research on cortisol synchrony in psychotherapy remains relatively limited, studies have focused on other coordination and synchrony dynamics of arousal levels between patients and therapists (Karvonen et al. 2016; Atzil-Slonim et al. 2023). For example, a meta-analysis investigating the occurrence of synchrony versus pseudo-synchrony found that, on the sample level, synchrony of arousal levels occurs significantly more than pseudo-synchrony (Atzil-Slonim et al. 2023). Findings suggest a potential link between patient–therapist arousal synchrony and interpersonal outcomes. A systematic review found associations between alliance ratings and arousal coordination, measured by vocal pitch, between patients and therapists (Wiltshire et al. 2020). Furthermore, research indicates the potential for coordination of arousal levels between patients and therapists under specific circumstances (Imel et al. 2014; Bryan et al. 2018; Wieder and Wiltshire 2020). Bryan et al. (2018) demonstrated that dyadic emotional bonding, assessed by self-report questionnaires, correlated with patient–clinician synchrony in arousal and emotional states, assessed by audio recordings. Wieder and Wiltshire et al. (2020) found that therapist vocally encoded emotional arousal levels predicted shifts in patient vocally coded emotional arousal levels, indicating a one-sided regulation of patient emotional arousal. These findings underscore the importance of further exploration into arousal coordination dynamics, particularly regarding cortisol, which has been identified as a leading indicator of interpersonal arousal in patient–therapist dynamics across modalities (Timmons, Margolin, and Saxbe 2015). Although studies support the occurrence and effect of coordination in arousal levels, little is known about possible distinct patient–therapist coordination patterns that may form.

Outside of psychotherapy studies, different patterns of interpersonal coordination have been identified. Butler and Randall (2013) and Butler (2017) discussed emotion co-regulation patterns in dyads and described interpersonal dynamics that relate to different levels of co-regulation. These co-regulating interpersonal dynamics may contribute to understanding cortisol

patterns in psychotherapy, akin to how coordination in cortisol levels regulates arousal in dyads like parents and children (Fleck et al. 2023).

Drawing from the theoretical framework by Butler and Randall (2013) and Butler (2017), we posit that diverse forms of co-regulation may give rise to distinct patterns of cortisol coordination within patient–therapist dyads. This study's conceptual model revolves around the exploration of various forms of arousal co-regulation in cortisol secretion during therapy sessions, possibly manifested as distinct forms of cortisol coordination, between patients and therapists (Figure 1).

2 | Objective

Although systematic approaches to quantify synchrony exist (Tschacher and Ramseyer 2009; Butler 2011), they primarily rely on extensively studied measures. In contrast, the present study aims to investigate a relatively unexplored phenomenon: the level of synchrony between patients and therapists in their cortisol changes during psychotherapy sessions, and other potential patterns of cortisol coordination that may manifest during psychotherapy. Unlike many studies involving multiple consecutive observations per individual or dyad, this study focuses on cortisol samples collected from patients and therapists before and after sessions, once a month. Given the lack of knowledge on this phenomenon and the type of data collected, we chose a bottom-up approach in an exploratory manner. Bottom-up approaches have been proposed as especially suitable for phenomena considered unexplored in this setting (Hill 1990; Swaraj 2019). In line with our chosen exploratory approach, we employed visual inspection due to the unexplored properties of the collected data. Kazdin and Tuma (1982) and Kazdin (2021) defined visual inspection as the process of forming judgements about the reliability or consistency of effects by visually examining graphed data. Visual inspection serves as a filter or screening device, allowing clear and potent effects over time to be identified. The insensitivity of visual inspection in detecting weak effects has been regarded as an advantage, encouraging investigators to focus on identifying robust effects (Kazdin and Tuma 1982; Kazdin 2021). We utilized visual inspection to identify distinct patient–therapist cortisol coordination patterns in psychotherapy, marking the first exploration in this research domain. The overarching goal of the present study was to

a. explore the occurrence of cortisol synchrony and other patterns of cortisol coordination in psychotherapy, and their associations with patient treatment baseline and processes measures. We aim to identify distinct patterns of cortisol coordination in psychotherapy. We hypothesize the emergence of three patterns based on synchrony dynamics literature: synchronized (similar patient–therapist changes in cortisol levels), unsynchronized (different patient–therapist changes in cortisol levels) and stable-therapist (characterized by consistent and stable therapist cortisol levels

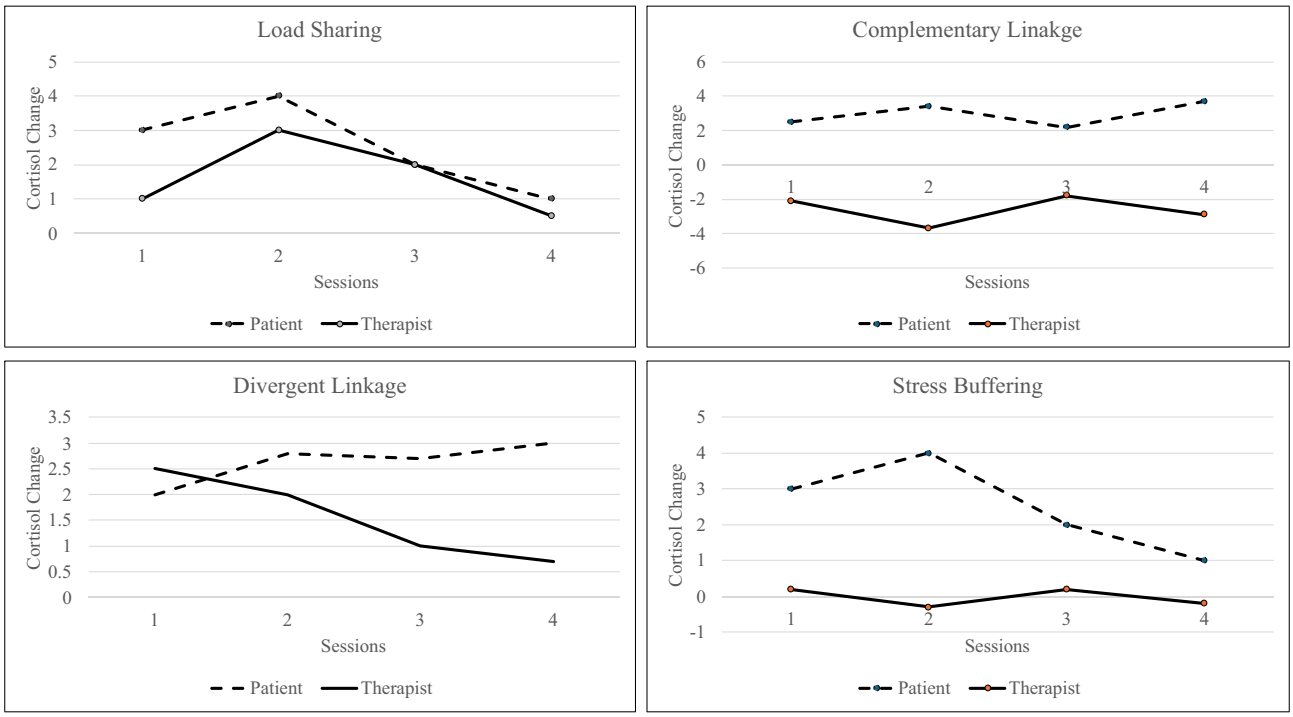

FIGURE 1 | Conceptual model – types of interpersonal dynamics as manifested in cortisol change responses. *Note:* Butler and Randall (2013) and Butler (2017) described the following interpersonal dynamics (among others): (a) Load sharing, where both members of a dyad respond to the increasing arousal levels of one of the members. In the context of cortisol coordination, this pattern could manifest as synchronized directions of cortisol level changes in dyads (Butler and Randall 2013). (b) Complementary linkage, where opposite emotional responses occur in a dyad, which may result in a synchronized, but anti-phased pattern. (c) Divergent linkage, where different emotional reactions occur for both members of the dyad, resulting in an unsynchronized pattern (Butler 2017). (d) Stress buffering, where one person's presence buffers another's stress response, without necessarily increasing their arousal levels (Butler and Randall 2013). In cortisol coordination terms, these dynamics may manifest as a pattern of a one-sided shift in cortisol levels, which also may result as an unsynchronized pattern.

throughout treatment, resulting in minimal variation irrespective of patient fluctuations). In studies on synchrony across various modalities, both in-phase and anti-phase patterns are commonly classified as synchronized (e.g., Ramseyer and Tschacher 2011). This classification is based on the occurrence of a mutual reaction in time, which accounts for synchronization. Thus, anti-phase and in-phase patterns will be included in the synchronized pattern;

b. identify and differentiate pre-treatment patient characteristics by using interpersonal self-report measures to characterize patients belonging to each synchrony pattern subgroup. Based on the literature on parent–child and romantic dyads, we hypothesize that patients will differ in synchrony patterns in terms of their attachment orientations and interpersonal dynamics;

c. characterize synchrony patterns by the tendency of the patient to react to conflicts occurring in treatment, as manifested by interpersonal ruptures and the resolutions to these ruptures provided by the therapist. Ruptures may manifest as uncooperative reactions of patients during therapy, either by withdrawing from the conversation or by confronting the conflict. Resolutions manifest as therapists attending to the patient's ruptures (Eubanks, Muran, and Safran 2018). Importantly, while ruptures may stem from the patient's unwillingness or defensives during therapy, ruptures may also stem from therapists misunderstanding or insensitivity towards their patients (Safran, Muran, and Eubanks-Carter 2011). We hypothesize that patterns will differ in their tendency to either withdraw, confront or resolve interactions during treatment. Specifically, based on the literature on interpersonal co-regulation indicating that dyadic synchronicity supports co-regulation (Butler and Randall 2013; Butler 2017), we hypothesize that in synchronized dyads, therapists will be more attentive to ruptures, allowing them to provide more resolutions.

To test these aims, this study will use data collected from two RCTs (Zilcha-Mano et al. 2018, 2021) providing psychotherapy for patients diagnosed with major depressive disorder (MDD). The goals and hypotheses of the present study find support in research on cortisol interdependence within dyads (Levi et al. 2024). These findings underscore the moderating role of patient–therapist relationship quality and highlight the influence of cortisol interdependence on patient symptom change. Notably, these findings were derived from examining the same patient–therapist dyads as in the present study. Psychotherapy for MDD was selected based on extensive literature highlighting the role of cortisol (Fischer et al. 2017; Laufer et al. 2018) and synchrony in MDD treatment (Paulick et al. 2018; Altmann et al. 2021).

3 | Methods

3.1 | Participants

The RCT recruited 100 patients with MDD through advertisements offering free treatment for depression. The protocol for collecting saliva samples was implemented after the trial had already started, so 50 patients were not sampled. The data from the remaining 50 patients were used in this study. Inclusion criteria were (a) meeting MDD diagnostic criteria according to structured clinical interviews for the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association 2013) scores above 14 on the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton 1967) at two evaluations occurring 1 week apart, and current MDD as measured by the Mini-International Neuropsychiatric Interview (Sheehan et al. 1998); (b) any medication taken by patients had to have been dosage stable for at least three months before entering the study, and patients had to be willing to maintain a stable dosage throughout treatment; (c) age between 18 and 60 years old; (d) Hebrew language fluency; and (e) provision of written informed consent.

Exclusion criteria were (a) current risk of suicide or self-harm (HRSD suicide item >2); (b) current substance abuse disorder; (c) current or past diagnosis of schizophrenia or psychosis, bipolar disorder or severe eating disorder requiring medical monitoring; (d) history of organic mental or bodily disease; and (e) participating in psychotherapy in the last 3 months.

Patients were enrolled in manualized psychotherapy for MDD, as part of randomized control trials (Zilcha-Mano et al. 2018, 2021). Patients received sixteen 50-min sessions of supportive-expressive treatment (Luborsky 1984, 1995), a time-limited psychodynamic therapy adapted for depression, either in an expressive-focused condition (including the use of expressive techniques, such as interpretation, confrontation, clarification), or in a supportive-focused condition (including the use of supportive techniques, such as affirmation and empathic validation).

All 50 patients included in the study completed the 16-session manualized psychotherapy provided as a part of the RCT. The study was approved by the relevant Institutional Review Board, and informed consent was obtained from all participants involved in the study. For each patient, therapy sessions occurred at a fixed time and day of the week. The mean patient age was 31.50 (SD = 7.88), and 31 patients were women. The mean years of education was 14.48 (SD = 1.37), and 22 participants reported a higher-than-average income status. At intake, four patients were using anti-depressant medication alongside their treatment. Also, at intake, four participants were diagnosed with comorbid post-traumatic stress disorder. Participants were asked to refrain from eating, drinking (other than water), smoking and having intimate contact with others (e.g., hugging) for at least 30 min before the saliva sample procedure.

3.2 | Therapists and Treatments

Seven therapists, all with formal training in psychodynamic treatment and at least 5 years of experience, participated in the current study. Therapists received individual and group supervision, both while training and during the active phase of the RCTs. Six of the therapists were women. Overall, therapists had an average age of 39.60 (SD = 5.87) and an average of 11.10 years of clinical experience (SD = 5.95). Therapists provided sixteen 50-min sessions of short-term psychodynamic psychotherapy treatment.

3.3 | Procedure and Measures

3.3.1 | Salivary Cortisol

Eight hundred saliva samples, gathered from both patients and therapists, underwent analysis. Collected at sessions 4, 8, 12 and 16, two samples were obtained per participant: 30 min before session, and immediately at post-session. Participants used Sarstedt Salivette containers, holding cotton swabs in their mouths for 2 min. Participants also reported potential factors affecting cortisol levels (e.g., medication, alcohol and menstrual cycle). Samples were stored at −20°C and sent to the daacro GmbH &Co. KG lab, University of Trier, for analysis. Intra- and inter-assay coefficients of variance (CV) were calculated. Intra-assay CVs of less than 10% and inter-assay CVs of less than 15% are generally acceptable (Hanneman et al. 2011). Cortisol change throughout treatment was calculated as delta scores (post-session minus pre-session) for each session. Notably, these cortisol samples were also used in another study (Levi et al. 2024), showing an association between patient and therapist cortisol levels. This supports the validity of using salivary cortisol to investigate our hypotheses regarding interpersonal factors in psychotherapy.

3.3.2 | Experiences in Close Relationships

Patient attachment orientations in relationships were assessed at intake using the Experiences in Close Relationships (ECR; Fraley et al. 2011), a 9-item self-report questionnaire. ECR examines attachment on two scales: Anxiety (Cronbach's $\alpha = 0.89$) and avoidance (Cronbach's $\alpha = 0.92$), on a Likert scale ranging from 1 (*Strongly disagree*) to 7 (*Strongly agree*). Scores were calculated separately for avoidance (ranging between 6 and 42) and anxiety (ranging between 3 and 21). Higher scores relate to greater levels of insecure attachment orientations within each scale.

3.3.3 | Inventory of Interpersonal Problems

Patients' interpersonal difficulties were assessed at intake using the short version of the Inventory of Interpersonal Problems questionnaire (IIP; Barkham, Hardy, and Startup 1996), a 32-item inventory regarding interpersonal behaviours. The IIP examines behaviours on eight different scales, rated on behaviour frequencies on a Likert scale from 0 (*Infrequent*) to 4 (*More persistent*). Scores are calculated separately for each scale, resulting in two factors, identifiable as Dominance (DOM) and Love (LOV; Alden, Wiggins, and Pincus 1990). For this analysis, DOM (Cronbach's $\alpha = 0.77$) and LOV (Cronbach's $\alpha = 0.80$) scores were used as baseline measures to characterize synchrony patterns. Lower DOM scores relate to more aggressive behaviours in relationships (i.e., being overly controlling) while higher scores relate to submissive behaviours (i.e., being overly compliant). Lower LOV scores relate to being more distant in relationships (i.e., being overly cold), and higher scores relate to being warmer in relationships (i.e., being overly dependent).

3.3.4 | Rupture Resolution Rating System

The Rupture-Resolution Rating System (3RS; Eubanks, Muran, and Safran 2015) was used as the treatment progress measure. The 3RS assesses the working alliance between patients and therapists during five sessions of treatment (sessions 2, 4, 6, 10 and 12). Coders watched the dyad's treatment sessions, divided into 5-min segments, and noted events of interpersonal non-collaboration or agitation. These moments were marked as ruptures, classified as either withdrawal or confrontation. Ruptures were also coded for frequency, of which scores were summed and averaged to gain mean rupture scores separately for withdrawal and confrontation ruptures. Coders also coded and scored moments when therapists addressed patient ruptures, which resulted in mean resolution scores. 3RS resolution ratings indicate resolution attempts by the therapist during the therapeutic session. Resolutions were coded for frequency, of which scores were again summed and averaged to gain mean resolution scores. Interrater reliability for withdrawal ruptures in the current study was intraclass correlation ICC $(1,2) = 0.92$; interrater reliability for confrontative ruptures in the current study was ICC $(1,2) = 0.89$; and interrater reliability for resolutions in the current study was ICC $(1,2) = 0.88$. Due to the ongoing RCT and constraints related to the timing of human coding, 3RS data were unavailable for one dyad. Consequently, treatment progress analyses were conducted on a sample of 49 dyads out of the original 50.

3.4 | Statistical Analysis Overview

3.4.1 | Preliminary Analysis

To investigate cortisol change within treatment for patients and therapists, nested within dyads, we utilized a proc mixed model (Littell et al. 2006) to analyse the trajectory of cortisol changes over time, distinguishing between patients and therapists at the sample level. We evaluated various trend models, including no trend in time, a linear trend and a linear trend based on the log of time (Curran and Bauer 2011). The model comparison involved examining fixed intercept models, models with a linear trend related to session numbers, and models incorporating a linear effect associated with the log of the session.

The best-fitting model was chosen based on the Bayesian information criterion (BIC). For patients, the linear time trend model was the most suitable. Our findings suggest that, at the aggregate level, patients show a reduction in the cortisol change they experience from pre- to post-session over the course of treatment ($b = -0.13$, $SE = 0.06$, $p = 0.03$). Conversely, in the case of therapists, the model depicting a linear trend based on the log of time was the most appropriate. Our analysis indicated a trend of increasing cortisol changes from pre- to post-session over the course of treatment among therapists; however, the effect of the log of time was not statistically significant ($b = 0.54$, $SE = 0.31$, $p = 0.08$).

3.4.2 | Cortisol Pattern Identification

For each patient and therapist, the pre- and post-session cortisol samples were used to calculate cortisol change,

resulting in patient cortisol change and therapist cortisol change observations. Since cortisol was sampled four times across treatment, each dyad consists of eight cortisol change observations. For each dyad, cortisol change observations were visualized on a figure to construct visible trend lines between cortisol change observations. Our focus was on assessing the concurrent patient and therapist cortisol change trends during treatment, aligning with the investigation of trends or slopes, as outlined by Kazdin and Tuma (1982). A total of 50 graphs were constructed, representing cortisol change trend lines in patient–therapist dyads.

The categorization involved three raters, advanced PhD students in clinical psychology, with expertise in studying synchrony across modalities, including patient–therapist synchrony based on interdisciplinary measures and fluctuations in the working alliance. Raters independently identified and categorized dyads based on cortisol trend patterns. These raters were briefed about the existing literature before applying the visual inspection approach, a customary practice in exploratory analyses with limited existing literature (Fife and Rodgers 2022). Consistent with exploratory and visual inspection approaches (Kazdin and Tuma 1982; Kazdin 2021), raters had the flexibility to categorize without predetermined or specific categories. The degree of agreement between the raters was calculated.

3.4.3 | Kruskal–Wallis Test

The Kruskal–Wallis test (McKight and Najab 2010) was chosen to test for differences between synchrony patterns. This statistical test was chosen for several reasons. First, due to the nominal nature of our target variable, we relied on a nonparametric test, which allowed for a reliable test of differences between synchrony patterns. Second, our sample did not yield normal distributions in treatment progress and outcome measures; the Kruskal–Wallis test allows testing for differences between subgroups in variables that are not normally distributed. The level of statistical significance was 0.05.

4 | Results

4.1 | Patterns of Cortisol Coordination

Raters categorized 46 dyads similarly, resulting in an interrater reliability score of ICC (2,3) = 0.92. Three types of cortisol patterns were identified: synchronized cortisol (SC), unsynchronized cortisol (USC) and stable-therapist cortisol (STC). The SC pattern ($n = 18$) is characterized by similar cortisol delta score patterns in at least three out of the four time-points, throughout treatment. Within this pattern, there were two patterns indicating a synchronized dyad; one in which patient and therapist cortisol changes co-occurred in the same direction and, relatively, in the same amounts, and a second in which patient and therapist cortisol changes co-occurred in a complementary manner in opposite directions, also relatively in the same amounts.

The USC pattern ($n = 16$) is characterized by a lack of similar cortisol patterns between patients and therapists throughout treatment. In this pattern, patient and therapist cortisol changes co-occur in different directions and in different amounts.

The STC pattern ($n = 16$) is characterized by a stable cortisol change in the same direction and amount in the therapist throughout treatment, resulting in a 'flat' line, irrespective of patient responses. Examples of each pattern are presented in Figures 2, 3 and 4.

4.2 | Baseline Measures

A Kruskal–Wallis H test showed no statistically significant difference in ECR Avoidance or IIP LOV scores between different cortisol coordination patterns. However, statistically significant differences were found for ECR Anxiety and IIP DOM scores between coordination patterns. Post hoc Mann–Whitney tests were conducted to evaluate pairwise differences among the three patterns, controlling for Type 1 error across tests by using the Bonferroni approach. The results of these tests indicated significant differences between the SC pattern and the STC. Descriptive and test statistics of ECR and IIP scores per coordination pattern are presented in Tables 1 and 2.

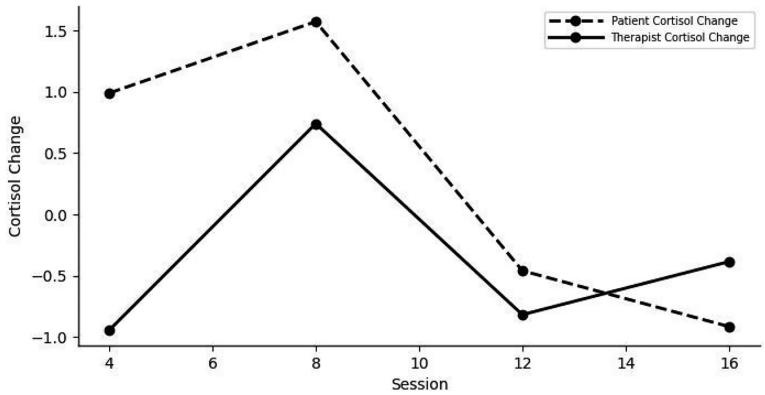

FIGURE 2 | Synchronized cortisol pattern. *Note:* Example of a development of a synchronized cortisol pattern throughout treatment. The *y*-axis represents cortisol change values for patients and therapists. The *x*-axis represents the four time-points (sessions 4, 8, 12 and 16) when cortisol was sampled.

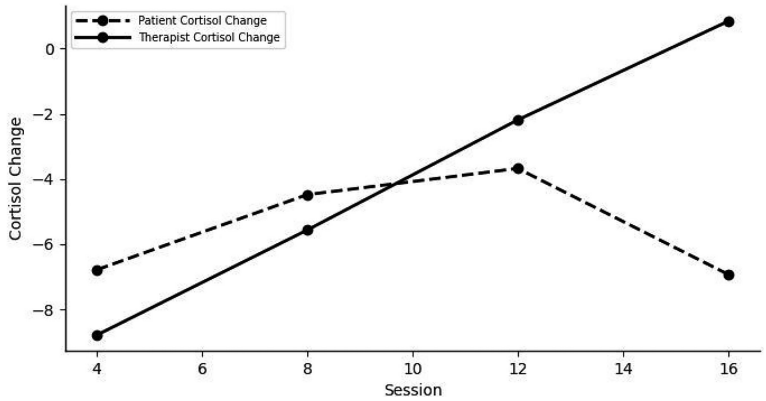

FIGURE 3 | Unsynchronized cortisol pattern. *Note:* Example of a development of an unsynchronized cortisol pattern throughout treatment. The *y*-axis represents cortisol change values for patients and therapists. The *x*-axis represents the four time-points (sessions 4, 8, 12 and 16) when cortisol was sampled.

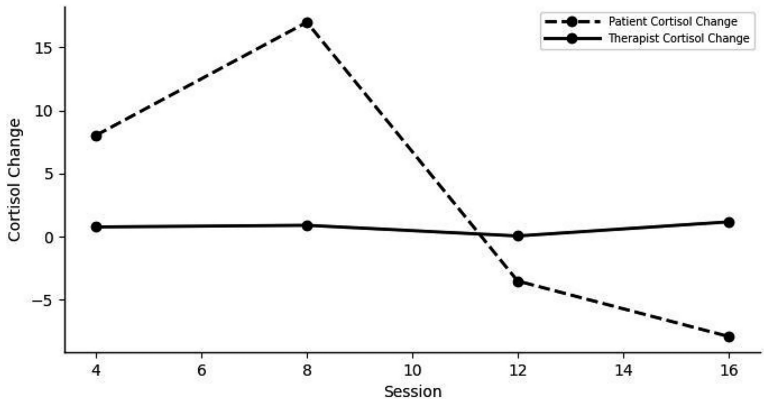

FIGURE 4 | Stable-therapist cortisol pattern. *Note:* Example of a development of stable-therapist cortisol pattern throughout treatment. The *y*-axis represents cortisol change values for patients and therapists. The *x*-axis represents the four time-points (sessions 4, 8, 12 and 16) when cortisol was sampled.

4.3 | Treatment Progress Measures

Analyses on 3RS data were conducted on 49 out of 50 patient–therapist dyads: 3RS data coding is still in process (as of the time of current analysis) as a result of an ongoing RCT. A Kruskal–Wallis H test showed no statistically significant difference in confrontation rupture or in resolution scores per session between different cortisol coordination patterns. However, statistically significant differences were found for withdrawal rupture scores between coordination patterns. Post hoc Mann–Whitney tests were conducted to evaluate pairwise differences among the three patterns, controlling for Type 1 error across tests by using the Bonferroni approach. The results of these tests indicated significant differences between the SC pattern and the STC pattern. Descriptive and test statistics of withdrawal rupture scores per session, per coordination pattern, are presented in Tables 3 and 4.

4.4 | Sensitivity Analyses

Accumulated findings highlight factors influencing cortisol fluctuations, including age and gender (Van Cauter, Leproult, and Kupfer 1996; Almeida, Piazza, and Stawski 2009), BMI scores (Schorr et al. 2015) and co-morbid disorders (e.g., borderline personality disorder; Walter et al. 2008; post-traumatic stress disorder, Meewisse et al. 2007). We utilized ordinal logistic regression (Decarlo 2003) with separate analyses for each of the following dependent factors: ECR anxiety, IIP dominance and 3RS withdrawal ruptures. Furthermore, cortisol pattern category was introduced as an additional factor. Each test controlled for patient age, BMI, gender, gender match with their therapists, co-morbid BPD, co-morbid PTSD and patient medication use during therapy. In addition, we also controlled therapist identity to discern any possible therapist effects. Furthermore, due to the diurnal pattern of cortisol (Upton et al. 2023), we controlled for session timing. Based on existing literature and our sample size, we divided session timing into three periods: morning (8:00–12:00, $n = 17$), noon (12:00–17:00, $n = 19$) and afternoon (17:00–21:00, $n = 14$). The mean session time was 13:30 (PM), with standard deviation of 3.7. Session time varied randomly, with all therapists meeting patients at different times of the day (no therapist was limited to a certain period of time-of-day in this study). Notably, all differences found between cortisol coordination patterns remained statistically significant.

TABLE 1 | ECR avoidance, ECR anxiety, IIP DOM and IIP LOV score mean, mean rank, test statistic and *p*-value, by cortisol pattern.

Measure	Pattern	*n*	M (SD)	Mean rank	Test statistic (χ^2)	*p*-value
ECR avoidance	SC	18	4.06 (1.16)	28.11	0.981	0.612
	USC	16	4.11 (1.16)	24.75		
	STC	16	4.03 (0.96)	23.31		
ECR anxiety	SC	18	3.98 (1.07)	32.14	6.394	0.041*
	USC	16	3.10 (1.14)	23.69		
	STC	16	3.30 (1.08)	19.84		
IIP DOM	SC	18	−8.84 (7.57)	32.53	7.514	0.023*
	USC	16	−10.98 (9.54)	24.09		
	STC	16	−13.49 (6.42)	19		
IIP LOV	SC	18	3.28 (9.75)	25.50	0.201	0.904
	USC	16	3.15 (11.40)	26.66		
	STC	16	3.84 (9.18)	24.34		

Abbreviations: ECR = experiences in close relationships questionnaire (Fraley et al. 2011); IIP = inventory of interpersonal problems (Barkham, Hardy, and Startup 1996); IIP DOM = dominance subscale; IIP LOV = love subscale; SC = synchronized cortisol pattern; STC = stable-therapist cortisol pattern; USC = unsynchronized cortisol pattern.
*$p < 0.05$.

TABLE 2 | ECR anxiety and IIP DOM score mean, mean rank, test statistic and *p*-value, by cortisol pattern.

Measure	Pairwise comparison	Test statistic (*U*)	Sig. (*p*)	Adj. Sig.
ECR anxiety	SC-USC	8.451	0.091	0.274
	USC-STC	3.844	0.456	1
	SC-STC	12.295	0.014*	0.042*
IIP DOM	SC-USC	8.434	0.092	0.277
	USC-STC	5.094	0.323	0.969
	SC-STC	13.528	0.007**	0.021*

Abbreviations: ECR = experiences in close relationships questionnaire (Fraley et al. 2011); IIP = inventory of interpersonal problems (Barkham, Hardy, and Startup 1996); IIP DOM = dominance subscale; IIP LOV = love subscale; SC = synchronized cortisol pattern; STC = stable-therapist Cortisol pattern; USC = unsynchronized cortisol pattern.
*$p < 0.05$, and **$p < 0.01$.

4.5 | Exploratory Analysis

As an exploratory analysis, we investigated differences between coordination patterns in treatment outcome. We included this analysis in the online supplement.

5 | Discussion

The present study aimed to explore cortisol coordination patterns and characterize their associations with patient characteristics and the progress of treatment. Three cortisol patterns were identified: synchronized, unsynchronized and stable-therapist cortisol patterns. These patterns were found to have distinct patient characteristics. In addition, these patterns differed in their treatment progress, manifested as differences in the occurrence of withdrawal ruptures.

5.1 | Coordination Pattern Identification

Consistent with the first hypotheses and existing literature on synchrony in interpersonal relationships, three coordination patterns emerged: synchronized, unsynchronized and stable-therapist. The synchronized pattern reflects concurrent cortisol responses between patients and therapists during sessions, similar to Butler and Randall's (2013) load-sharing dynamic. Here, both patient and therapist react similarly to each other's cortisol changes, possibly in response to changing arousal levels. Conversely, the unsynchronized pattern entails nonconcurrent cortisol responses, suggesting Butler's (2017) divergent linkage dynamic. In this scenario, changes in one individual's arousal levels do not evoke corresponding reactions in the other. Lastly, the stable-therapist pattern reveals consistent therapist cortisol changes regardless of patient cortisol levels. The implications of the stable-therapist pattern are multifaceted. This pattern

TABLE 3 | Withdrawal rupture, confrontation rupture and resolution scores per session mean, mean rank, test statistic, and *p*-value, by cortisol pattern.

Measure	Pattern	*n*	M (SD)	Mean rank	Test statistic (χ^2)	*p*-value
Withdrawal ruptures	SC	17	0.89 (1.04)	158.54	6.336	0.042*
	USC	16	0.68 (0.97)	139.57		
	STC	16	0.63 (0.85)	129.60		
Confrontation ruptures	SC	17	0.51 (0.56)	148.93	5.352	0.069
	USC	16	0.58 (0.67)	153.26		
	STC	16	0.39 (0.48)	127.41		
Resolutions	SC	17	0.23 (0.27)	141.47	0.122	0.941
	USC	16	0.32 (0.46)	145.46		
	STC	16	0.26 (0.35)	142.40		

Abbreviations: SC = synchronized cortisol pattern; STC = stable-therapist cortisol pattern; USC = unsynchronized cortisol pattern.
*$p < 0.05$.

TABLE 4 | Withdrawal rupture posthoc pairwise comparisons with Bonferroni correction, test statistic, *p*-value and adjusted *p*-value.

Pairwise comparison	Test statistic (*U*)	Sig. (*p*)	Adj. Sig.
SC-USC	18.970	0.114	0.342
USC-STC	9.970	0.413	1.000
SC-STC	28.940	0.013*	0.040*

Abbreviations: SC = synchronized cortisol pattern; STC = stable-therapist cortisol pattern; USC = unsynchronized cortisol pattern.
*$p < 0.05$.

may indicate a therapist's physiological regulation in response to patient arousal (Fisher 2011; Kramer et al. 2020), aligning with the concept of stress buffering (Butler and Randall 2013). Alternatively, the stable-therapist pattern might reflect therapist indifference, which could undermine the therapeutic alliance (Hayes et al. 2018; Cavalera et al. 2021). Understanding the origins and effects of the stable-therapist pattern can be beneficial in clinical training, by instructing therapists to take note of their own arousal levels. Overall, these cortisol coordination patterns align with existing literature on interpersonal synchrony and coordination.

5.2 | Treatment Baseline and Progress Measures

Consistent with the second hypothesis, differences in attachment orientations were observed among the three cortisol patterns. Regarding attachment avoidance, no significant differences emerged among cortisol patterns. However, for attachment anxiety, significant differences were found between the synchronized and stable-therapist patterns. Specifically, patients exhibiting the synchronized pattern displayed higher levels of attachment anxiety, in line with previous literature associating attachment anxiety with pronounced cortisol responses (Williams et al. 2013; Hsiao et al. 2014; Houbrechts et al. 2023). In psychotherapy contexts, such responses might potentially elicit mutual cortisol reactions in therapists, who could exhibit heightened engagement when treating patients with elevated anxiety levels (Daly and Mallinckrodt 2009; Westra et al. 2012). Similarly, studies suggest that children with greater attachment anxiety respond favourably to collaborative interactions, potentially contributing to synchronized cortisol patterns (Bodner et al. 2019). Thus, higher attachment anxiety levels may foster interpersonal experiences characterized by concurrent arousal and increased responsiveness to collaborative behaviours, possibly resulting in synchronized cortisol patterns. Furthermore, patient interpersonal tendencies also supported the second hypothesis, showing differences in interpersonal dominance among cortisol patterns. While no prior studies have explored the relationship between IIP scores and cortisol in interpersonal interactions, existing literature suggests a potential negative association between cortisol levels and dominance (van der Westhuizen and Solms 2015; Mehta and Prasad 2015). Our findings suggest that patients exhibiting the synchronized pattern perceive themselves as less dominant and more anxious in relationships, aligning with previous research on social status, anxiety and dominance.

Partially consistent with the third hypothesis, differences were found between synchrony patterns only for the tendency to withdraw from conversations, but not for confronting conflicts or providing resolutions. Patients in the synchronized pattern tended to display more withdrawal ruptures than those in the stable-therapist pattern. Interestingly, prior research suggests that higher synchrony levels may be associated with confrontational ruptures (Deres-Cohen et al. 2021). Further investigation

is needed to explore the link between ruptures, resolutions and mutual cortisol changes.

Regarding treatment outcome, no differences were found between coordination patterns, possibly indicating that cortisol patterns have no effect on treatment outcome. However, the absence of distinctions might also be attributed to study limitations, warranting further research before definitive conclusions can be made. See Data S1 for further discussion.

While our study suggests a potential link between patient and therapist cortisol levels, it is important to consider alternative explanations. For instance, patient behaviours or disclosures may elicit stress responses in therapists, influencing their cortisol levels. Conversely, therapists' reactions could impact patient cortisol levels. Given the complexity of psychotherapeutic dynamics and the limitations of our design, caution is warranted in interpreting our findings. Notably, we advise exercising caution in interpreting the current work until it is replicated in future research. However, this study provides preliminary insights into cortisol coordination in therapy settings, underscoring the importance of further research to explore these complexities and enhance our understanding of interpersonal dynamics in psychotherapy. Overall, further investigation and replication are needed to substantiate our results. Therefore, it is important to consider the preliminary nature of this study when drawing conclusions about client approaches.

5.3 | Clinical Implications

Understanding cortisol coordination patterns within patient–therapist dyads offers valuable insights that may enhance psychotherapy practice. Our findings suggest that individual differences in attachment orientations and interpersonal tendencies may influence cortisol synchrony during therapy sessions. This implies that therapists should be attentive to relational dynamics and patient distress signals, as they possibly could impact cortisol synchrony and therapeutic progress. Patients in synchronized cortisol patterns may experience more withdrawal ruptures, suggesting the potential need for therapists to actively address relational disruptions and enhance therapeutic alliance (Lindqvist et al. 2023). Additionally, therapists may possibly benefit from considering their own arousal as potential indicators of patient experience. Overall, incorporating this understanding of cortisol synchrony into clinical training may foster better practice in the future.

5.4 | Limitations

This study had several important limitations. First, the relatively small sample size restricts the generalizability of the results, potentially overlooking additional subtle patterns. Thus, dyads exhibiting in-phase or anti-phase patterns in their cortisol changes were both included under the synchronized pattern. Furthermore, cortisol was sampled over four sessions to broadly analyse trends throughout the treatment. Increasing sampling resolution could offer finer insights and could aid in revealing more nuanced and complex patterns of cortisol change in future studies. For example, an interesting future direction would be to distinguish between the leading roles of the patient and therapist when assessing their cortisol coordination.

Second, we relied on human coding when categorizing synchrony patterns, which are sensitive to various subjective biases. Future studies on cortisol synchrony in psychotherapy could use statistical methods to differentiate between synchrony patterns (for more, see Kleinbub, Talia, and Palmieri 2020). Third, due to an absence of in-session video recording analyses it remains unknown in what context mutual changes in cortisol levels occur; hence, our ability to pinpoint moments in therapy sessions that are associated with cortisol changes is limited. Future studies should investigate the mechanism between cortisol coordination and other methods of in-session arousal assessments, to gain a more integrative picture of this dynamic.

Fourth, the present study is indicative of between-group differences, so causal relations cannot be inferred. Fifth, it is important to note that the majority of the sample was female, although results remained similar when controlling for patient gender and dyad-gender-match. Future investigations should aim for a more representative participant pool that encompasses a broader spectrum of gender diversity.

Notably, this study may be limited in its ability to definitively determine cortisol synchrony between patients and therapists due to the complexity of psychotherapeutic interactions. Factors such as the exploratory nature of our categorization approach, lack of information on the measurement moment, and potential medication effects on cortisol levels could bias our findings. Furthermore, although findings remain similar when controlling for time of the day, we cannot preclude the possibility that the diurnal changes of cortisol did not affect our results. Therefore, future psychotherapy studies should systematically explore the association between the dynamic level of cortisol diurnal patterns and patterns of synchrony. Additionally, the inherent challenge of distinguishing between true synchrony and individual responses to shared stressors within therapy sessions warrants cautious interpretation of our results.

Finally, the present study was conducted as part of a larger trial on the efficacy of specific forms of psychodynamic psychotherapy. Therefore, our findings may not be generalizable to other social contexts.

6 | Conclusions

This study examines cortisol coordination patterns in psychotherapy sessions and their associations with patient characteristics and therapist conflicts. Although preliminary, findings align with research on interpersonal synchrony, underscoring the significance of attachment orientations and interpersonal tendencies in shaping cortisol coordination. Through identifying different cortisol patterns, we elucidated distinct patient traits and observed differences in treatment progress. Further exploration of the mechanisms underlying cortisol dynamics in therapy sessions could deepen the understanding of the interplay between physiological processes and therapeutic progress, potentially enhancing the effectiveness of psychotherapeutic interventions.

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Ethics Statement

The study was conducted using data retrieved from two RCTs, according to the guidelines of the Declaration of Helsinki. The relevant ethical committee approved the execution of the studies.

Consent

Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

When this research was carried out, the informed consent form for the participants stated that we would keep the data strictly confidential. Therefore, if uploading data, we must seek consent from our participants and the consent of the ethics committee. Therefore, the data are not currently available.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.