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Research Article

On psychobiology in psychoanalysis: salivary cortisol and secretory IgA as psychoanalytic process parameters

Zur Psychobiologie in der Psychoanalyse: Speichel-Cortisol und sekretorisches IgA als psychoanalytische Prozessparameter

Abstract

This study investigates the psychobiological impact of psychoanalysis in its four-hour setting. During a period of five weeks, 20 subsequent hours of psychoanalysis were evaluated, involving two patients and their analysts. Before and after each session, saliva samples were taken and analysed for cortisol (sCortisol) and secretory immunoglobuline A (sIgA). Four time-series (n=80 observations) resulted and were evaluated by "Pooled Time Series Analysis" (PTSA) for significant level changes and setting-mediated rhythms. Over all sessions, sCortisol levels were reduced and sIgA secretion augmented parallel to the analytic work. In one analytic dyad a significant rhythm within the four-hour setting was observed with an increase of sCortisol in sessions 2 and 3 of the week. Psychoanalysis may, therefore, have some psychobiological impact on patients and analysts alike and may modulate immunological and endocrinological processes.

Keywords: psychobiology, psychoanalysis, psychotherapy process research, pooled time series analysis

Zusammenfassung

Die Studie untersucht den psychobiologischen Effekt der Psychoanalyse in ihrem vierstündigen Setting. Über eine Periode von fünf Wochen hinweg wurden 20 aufeinander folgende Stunden von Psychoanalyse evaluiert, wobei zwei Patienten und ihre Analytiker involviert waren. Vor und nach jeder Stunde wurden Speichelproben entnommen und auf Cortisol (sCortisol) sowie auf sekretorisches Immunglobulin A (sIgA) untersucht. Es resultierten vier Zeitreihen (n=80 Beobachtungszeitpunkte), die mit Hilfe der Pooled Time Series Analysis (PTSA) auf signifikante Mittelwertunterschiede und auf Setting-mediierte Rhythmen untersucht wurden. Bezogen auf alle Sitzungen fielen die Cortisol-Spiegel ab und die sIgA-Sekretion stieg parallel zur analytischen Arbeit an. In einer analytischen Dyade konnte ein signifikanter Rhythmus innerhalb des vierstündigen Settings beobachtet werden, der mit einem Anstieg des sCortisols in Sitzungen 2 und 3 der Woche verbunden war. Psychoanalyse könnte somit einigen psychobiologischen Einfluss auf beide, Patienten und Analytiker, ausüben und dabei immunologische und endokrinologische Prozesse modulieren.

Schlüsselwörter: Psychobiology, Psychoanalyse, Psychotherapie-Prozessforschung, Zeitreihenanalyse-Pool

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Introduction

Contemporary psychobiological research in the field of psychotherapy intends to build bridges between psychic events and their psychobiological concomitants. In a context of psychotherapeutic processes, however, studies with biological variables are still rare. Nevertheless, there is a growing interest in clarifying the biological impact of therapeutic actions in natural psychotherapeutic settings.

Experienced clinicians, especially those working in a psychoanalytic psychosomatic field, always "knew" from clinical observation that phases of regression where paralleled by psychosomatic symptoms: Skin lesions, asthma attacks or periods of uncontrollable diabetes mellitus were known as typical signs of regression within the psychotherapeutic process. This formerly quite "mysterious leap" between mind and body, to use Dunbar's [1] famous formulation, is now becoming less mysterious, since investigated by research done in the field of psycho-neuro-immunology [2], [3], [4].

Two parameters, cortisol (sCortisol) and secretory immunoglobuline A (sIgA) in saliva became of continuous interest in clinical psychobiological research, because they were fairly reliable and easy to access, even in clinical field settings. In addition, they show no fixed interrelation and can be used independently in the same saliva sample [5], [6], [7], [8].

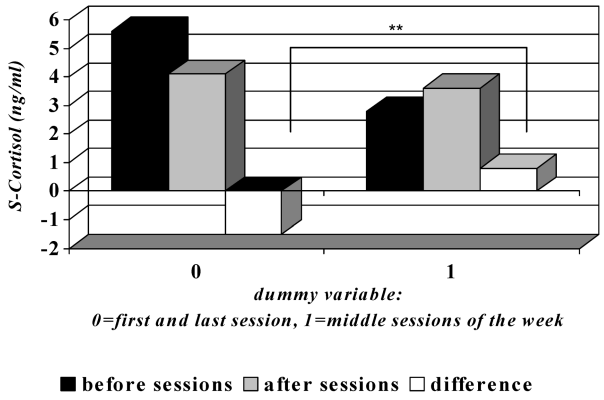
In recent overviews [9], [10], [11], [12], it could be shown that acute stress or emotionally significant moments are connected with sudden saliva cortisol rises. Chronic stress, in contrast, may result in attenuated cortisol responses and accompanied by chronically elevated cortisol levels [13]. Studies evaluating the impact of personality traits for individual differences in cortisol responsivity came to varying, sometimes contradictory conclusions: It seems that the different aspects of depression, namely low self-esteem, reduced self confidence, concomitant anxieties, loneliness and depressed mood were related to an increase of saliva cortisol, whereas positive affect seems to be correlated with lowering of cortisol excretion [14], [15], [16], [17], [18], [19], [20], [21], [22]. Even though, for a given individual, the meaning of "stress" in an individual context cannot easily be equated with "stress" of a given other person, there is a general agreement that a high cortisol level "means" activation and stress, whereas low cortisol levels are associated with relaxation and rest. Long-standing chronic stress seems to be related to slightly elevated cortisol levels and attenuated cortisol responses in acute stress [23]. Many studies showed that the correlation between saliva cortisol and serum cortisol is highly positive (r=.71-.96, [12], [24], [25]), so that the representation of the serum cortisol by the value in saliva is well established. The normal mean of salivary cortisol can be given with 14,32 (+/- 9,1) nmol/l (=5,69 +/- 4,58 ng/ml) at 7 to 9 a.m. (n=662), 4,50 (+/- 3,5) nmol/l (=1,55 +/- 1,32 ng/ml) at 3 to 5 p.m. (n=708) and 1,96 (+/- 1,7) nmol/l (=0,69 +/- 0,53 ng/ml) at 8 to 10 p.m. (n=698), figures in [11] in nmol/l and in [14] in ng/ml respectively. Cortisol is thus a parameter with a high intraindividual variability, following a diurnal circle with its peak in the morning hours and a decline over daytime. However, there are some studies, which show that there is an interindividual variability as well. Smyth et al. [26] found individual differences in the diurnal circle of cortisol over two days in 109 healthy participants with a typical decline in 51%, no significant diurnal pattern in 17% and a diverging pattern on two subsequent days in 31% in this sample. Stone, Schwartz, Smyth, Kirschbaum & Hellhammer [27] resumed the analysis of participants in four studies concerning the diurnal pattern of saliva cortisol and showed that at least 10% of each sample presented no significant diurnal variation. In studies dealing with the half-life of salivary cortisol, values between 55 [28] and 70 [11] minutes are given with a latency of 10 to 20 minutes, so that we can assume that a data-collection carried out directly after the psychoanalytic session at least pictures the main part of the concentration changes due to sessions.

Secretory IgA, the second psychobiological parameter in this study, was reviewed in its reactivity in various meta-analyses [29], [30], [31], [32]. Even though generalizing approaches have to be applied to clarify and interpret the behavior of this parameter, citing as examples interpretations like "relaxation and humor increases IgA-secretion" [33], [34], [35], [36], [37], [38], [39], [40], [41], a personal, very individual "meaning" may influence the variation of this saliva component. sIgA, actively secreted, reflects the ability of a person to defend her- or himself immunologically: sIgA-antibodies are able to protect a person from the invasion of viruses, bacteria, other microbiological agents and, in addition, even from allergens. Low sIgA, therefore, is connected with high susceptibility to infections and to allergies: Classical psychoneuroimmunological studies showed that chronic stress, feelings of loneliness, disgust and depression as well as low power motivation may contribute to lowering of sIgA secretion [17], [42], [43], [44], [45], [46], [47], [48], [49].

In acute stress, the behavior of sIgA seems to be varying and more complex. Acute stress may provoke even increases of sIgA secretion [50], [51], [52], [53], [54], [55], [56], [57]. The interpretation of sIgA-data becomes even more difficult, since high saliva flow rate may dilute the sIgA samples [30]. However, this effect tends to be low in unstimulated saliva flow. In some studies however, controlling for the saliva flow rate, the sIgA concentration proved to be independent of saliva flow [6], [10], [58], [59], [60], (cf. [61], [32] as metaanalyses, for a further, more detailed overview see Euler [62], p. 43ff). Despite these difficulties, sIgA may be regarded as the most accessible and, at least fairly, reliable psychoimmunological variable, sensible to immune depression [63].

Concerning the circadian rhythm of sIgA, there is no similar diurnal variation known as it is in salivary cortisol. Kugler et al. [6], [58] found no circadian rhythm, others noted a significant but no uniform within-subject variation over daytime, which seemed to depend on short-term variation [25]. Park & Tokura [64] presented in a study a uniform day-night variation (low IgA in the daytime, high IgA during the night) in the mean of six subjects. It is thus evident, that secretory IgA does not follow a strict circadian rhythm so that this parameter is less affected by changes in the therapeutic timetable. In a pilot study [65], high cortisol differences were found by us predominantly in the middle phase (in hours 2 and 3) of the therapeutic week, using the four-hour schedule of classical psychoanalysis (cf. [66], [67] as a paradigm) (Figure 1). The as-

sociation proved to be significant on a p<0.01 level with a Spearman's Rho of .57 for the nonparametric correlation between sCortisol differences and a dummy-variable (the value of 1 assigned to the two sessions in the middle of the week and 0 to the remaining sessions).



Legend: y-axis: Mean levels of salivary cortisol in ng/ml (before/after sessions and difference) in patient 1 in a pilot study, subdivided (x-axis) in first and last session (=0) of the week versus middle sessions (=1), **p<0.01, Spearman´s Rho.

Figure 1: Saliva cortisol and psychoanalytic setting

Hypotheses

It is a main hypothesis of our study, that we expected elevated cortisol in emotionally upsetting, "hot" and stressful psychotherapeutic encounters. Relaxed and "calm" sessions, the inverse expectation, should be accompanied by a rise of sIgA in saliva, if we transpose reports from the literature about the sIgA-stimulating property of relaxation to our clinical setting.

For the study, we chose to include five-week-sections of analyses with two patients, who suffered similarly from severe depression with somatic symptoms. The clinical picture of these patients will be described in more detail in the following section.

Since these patients were characterized by a disorder of affect regulation corresponding to the clinical picture of alexithymia [68], we also expected low cortisol differences and low sIgA variations as signs of reduced affect. As known from the already cited pilot study, one patient displayed greater cortisol-variations in the middle hours of the therapeutic week with a lowering of pre-session cortisol values, facts, which we interpreted as a possible lowering of her anxieties and defenses during the middle part of the therapeutic week. The expectation was that these findings could be replicated.

Patients and analysts

The first patient was a chronically depressed woman in her late thirties who came to analysis suffering from a loss of vitality and unhappiness. The depressive symptoms were accompanied by multiple somatizations, a clinical picture, which had initially been diagnosed as "Morbus Bechterew". This diagnosis was later abandoned and replaced by a "softer" diagnosis of "Fibromyalgia". Patient 1 was already the subject of the pilot study [65] cited above.

She also suffered from an inability to perceive her emotions and to verbalise them consecutively. Within the analytic sessions, she seemed to be rigid, petrified and motionless. Prolonged phases of tensed silence appeared in which the patient gave the impression of being deeply withdrawn and caught in a "dead", empty and motionless internal life:

"...The topics in the therapy conversations frequently recurred. She talked about the physical pains, the disappointment of various people, (...). She also frequently mentioned her disappointment of the treatment that was experienced by her as unsuccessful, without being able to address the topic more clearly. Again and again if I enquired, she said 'I don't want to think about it' and sank back into silence. (...) There were clear differences between the middle and the remaining hours of the analytic week. We could understand that the patient found weekends terrible and often got aggressive and rigid the last hour in the week. During the vacation interruptions however, she seemed to stay largely without emotions. (...) As a counter-transference, I was especially interested in participating in an investigation on psychobiological parameters in treatments, since I was frequently concerned with the question of the patient's stiffness during the whole time of this treatment." (Quotations from the analyst's case description)

Her male psychoanalyst was in his late forties, trained according to international standards, working in a private practice. In 1999, the time of the investigation, the analysis had been going on for a period of about nine years. The sessions took place regularly, at 10 a.m. on Mondays, Tuesdays and Wednesdays. The last session of the week was held generally on Thursdays but sometimes on Fridays, respectively.

The second patient was a male in his mid-fifties with an equally chronic symptomatology in form of a recurrent depressive disorder with somatic symptoms. He was in his first year of analysis, but had previously gone through various psychodynamic therapies, among which were group therapy over a period of five years, in-patient psychotherapy in psychosomatic hospital settings over periods of several months in two different years and a previous psychoanalysis in his late twenties, over a period of three years. Besides the physical symptoms, he suffered from an inability to invest in close relationships and, as a consequence, he felt lonely and had chosen to pursue a withdrawn, socially inhibited life. Within the sessions the patient felt uncomfortable, tensed and got frightened. The four-times-a-week schedule of psychotherapy gave him the impression to get "far too close" to his analyst:

„The background of his depressive phases seemed to be his deeply rooted fears starting closer relations to other people. As a result of it Mr M. was very lonesome and led a very secluded life. At the time of the examination Mr M. was unemployed and lived alone." (Quotations from the analyst's case description)

His male psychoanalyst, also trained according to international standards, was in his early forties. The sessions took place in a private practice from 8 to 9 a.m., on a regular schedule, Mondays, Tuesdays, Wednesdays and Fridays.
All participants were non-smokers and free of a regular medication (for clinical details about the participants under study cf. [62], p. 14ff, 21f).

Methods

Design

The study described in the following was carried out within a single-case oriented time-series analysis design [69], [70]. With the aim to combine single subject research approaches with ways of generalisation, a pooled time series analysis approach was chosen. Due to possible psychobiological changes in psychoanalysis, we decided to place the investigation in the morning hours because cortisol concentration has its peak in most individuals at about 8 a.m. and decreases afterwards sharply during the day. In the mornings, a high variability of his parameter could be expected as well.

Data collection and psychobiological essays

Over a period of five weeks with 20 resulting sessions, corresponding to four psychoanalytical hours per week, the following variables were used to examine psychological and psychobiological changes. Our design based on the previously mentioned pilot study. Saliva samples were drawn before and after each session using the Sarstedt Salivette® sampling device: Saliva is collected with a cotton swab over a period of approximately three minutes, which is placed into a small flask of polystyrol afterwards. After having been centrifuged, all saliva samples were stored at -20 °C in a refrigerator. After thawing, a commercial enzyme immunoassay (DRG, Marburg) was performed to measure salivary cortisol concentrations [11], [71], [72], [73]. All samples were analysed within one lot to avoid interassay variations. The intraassay variance of the coefficients was less than 8 percent. Secretory IgA concentrations were measured by laser-nephelometry using a BN100 (Dade Behring, FRG) adapted for sIgA measurements as described by Hennig [10].

Moods

Parallel to the determination of psychobiological parameters the Self Assessment Mannequin (SAM) - a non-verbal pictorial mood questionnaire - was used, which covers three dimensions of emotional reactivity with 5 gradations each (valence: pleasant=1 versus unpleasant=5, arousal: aroused=1 versus calm=5 and power: submissive=1 versus dominant=5, German adaptation by Hamm & Vaitl [74] from the original English version by Lang [75]).

Setting

To measure weekly variations ("rhythm") of the parameters, a dummy variable was constructed with a value of 0 on sessions 1 and 4 of the week, while 1 was assigned to sessions 2 and 3 of the psychoanalytic process.

Model

In the final evaluation, we employed salivary cortisol (sCortisol) and secretory IgA (sIgA) as dependent variables and moods and the dummy variable reflecting the setting as independent variables. Since we studied four participants (two patients and two analysts) simultaneously, a multiple regression time-series model in form of a pooled time-series analysis (PTSA, [76]) was estimated. Four aggregated time series of 40 (*20 x 2*) data points in each series resulted and were analysed by EViews 4.0-software (QMS, 1997).
In general, time-series models are trying to clarify complex interacting variables in their mutual interdependencies over time. In the case of pooled time series analysis, a model studies simultaneously the interaction of a given dependent with a set of independent variables. The analysis is thus performed at the same time diachronically within subjects and across the subjects, synchronically [77], [78], [79] (see for a methodological critique [80]). To account for serial dependencies, AR-regressors were introduced to the models for each dependent variable, estimated separately for each participant (individual estimation of AR-parameters for lag 1 and lag 2), and added to the final multiple regression model. Automatic identification criteria were applied to check for the goodness of fit of the model, with a Durbin-Watson statistics of 2.0 and proof of "white noise" with insignificant correlogram-Q-statistics and histogram-normality-tests in the residuals. The prerequisite of a time-series analysis as a statistical tool is that all observations be equidistant. Since a seven-day analysis is not feasible for clinical purposes, we decided on a four-day week of psychoanalytic work as data basis, just parallel to the usual applications of time-series analyses in the five-day week of stock exchanges.

Results

Descriptive statistics

To give a general overview, the statistical values for both key parameters (summarizing all participants and sessions) are displayed in Table 1. Taking all these observations together, positive differences are shown for sIgA, negative differences are found for sCortisol. The maximum and minimum values showed considerably variation.

Table 1: Differences of sIgA and sCortisol for all participants and over all sessions

	IGA3	CORT3
Mean	4.75	-1.04
Median		-1.10
Maximum		5.84
Minimum	-2.64	-8.19
Std. Dev.	5.60	2.71
Schewness	1.08	0.10
Kurtosis	3.48	3.39
Jarque-Bera	16.36	0.64
Probability	0.0003	0.7266
Observations	80	80
Data sets	4	4

Legend: IGA3 = differences of sIgA in mg/dl, CORT3 = differences of sCortisol in ng/ml

In Figures 2-9 the differences (before/after the session) of both parameters for every individual participant over the course of all sessions (1-20) were depicted. The first number indicates the week; the second number indicates the session of a corresponding week (1\1-4\4). The figures underscore the considerable variation in time and between subjects, which could be discovered in the data set. Furthermore the overall increase of sIgA and the overall decrease of sCortisol become obvious. With regard to the first analytic dyad a slight rhythmicity concerning the sCortisol differences over the course of all sessions can be assumed just by following the original data.

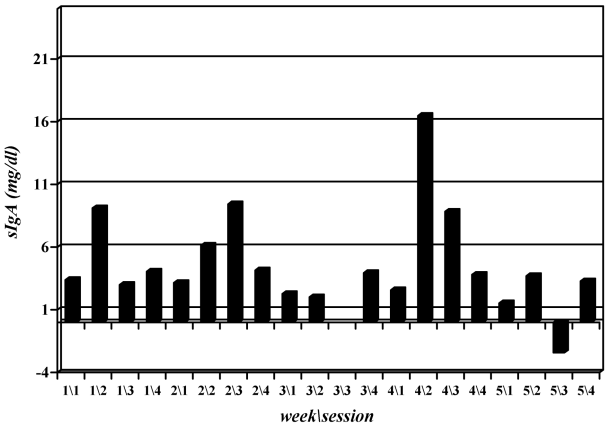


Figure 2: sIgA differences therapist 1

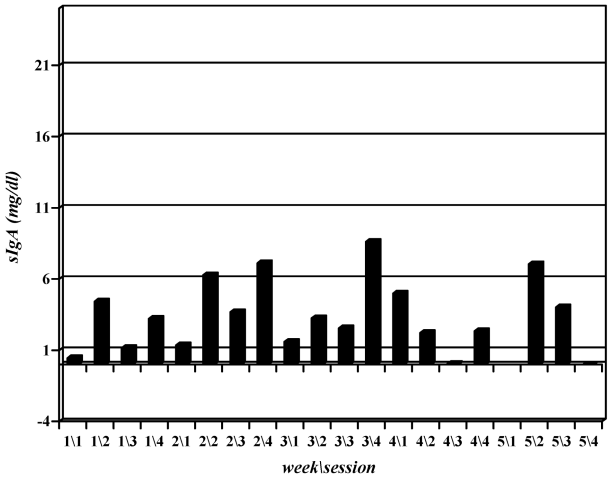


Figure 3: sIgA differences patient 1

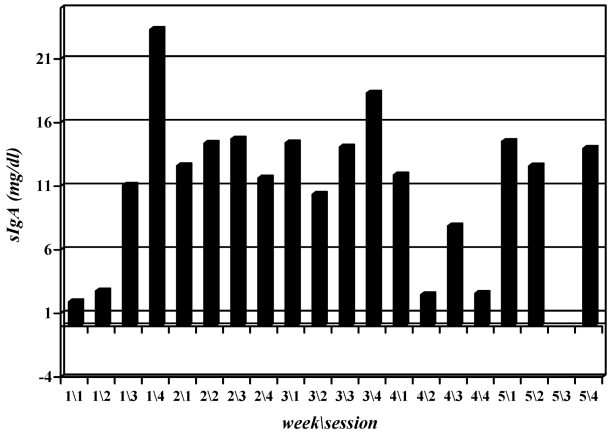


Figure 4: sIgA differences therapist 2

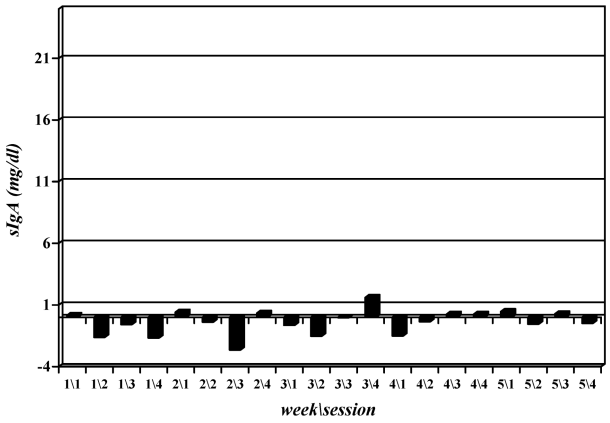


Figure 5: sIgA differences patient 2

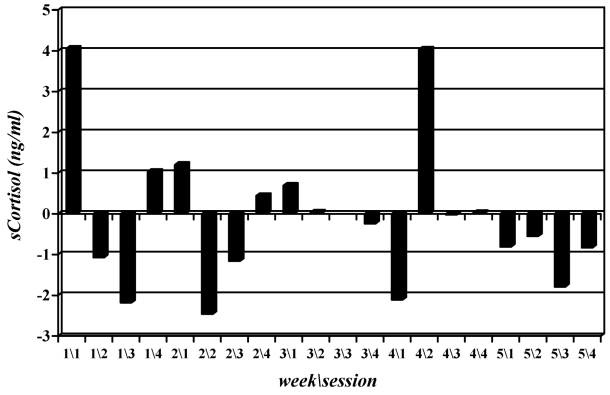


Figure 6: sCortisol differences therapist 1

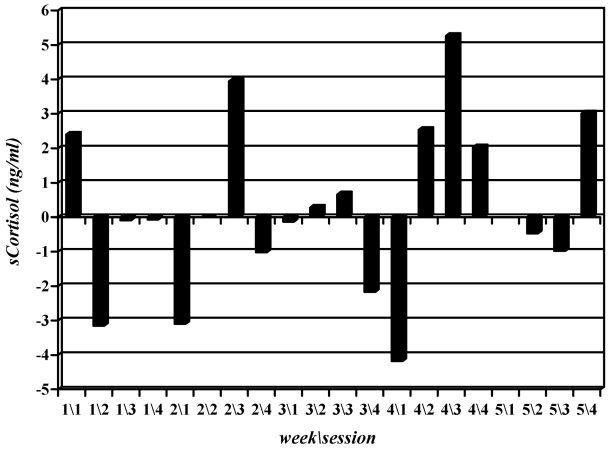


Figure 7: sCortisol differences patient 1

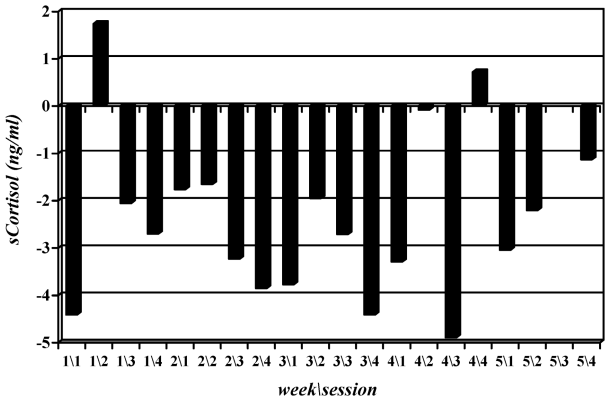


Figure 8: sCortisol differences therapist 2

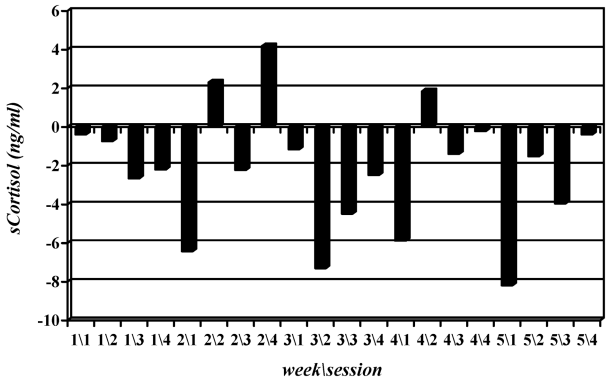
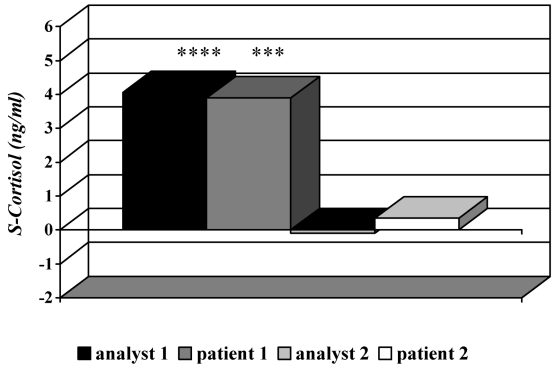
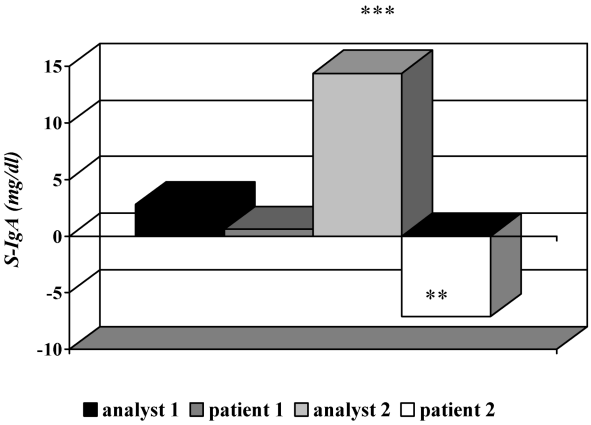


Figure 9: sCortisol differences patient 2



Legend: y-axis: sCortisol concentrations in ng/ml, x-axis: individualized multiple regression coefficients, predicting sCortisol differences in sessions 2 and 3. ***p<0.001, t-test, cf. Table 2, area "setting".

Figure 10: Individual differences in cortisol response to psychoanalytic sessions



Legend: y-axis: sIgA concentrations in mg/dl, x-axis: individualized multiple regression coefficients, predicting sIgA differences in sessions 2 and 3. ***p<0.001, t-test, cf. Table 2, area "setting".

Figure 11: Individual differences in sIgA response to psychoanalytic sessions

Pooled time series analysis

The results of the pooled time series analysis are summarised in Table 2. The table is structured in four rows:
1. C as constant in the multivariate regression equation, reflecting the mean changes of a given parameter,
2. regressors in the model and their predictive value, which reflect multivariate influences,
3. influence of the setting as given by individualized, for each participant separately estimated, multiple regression coefficients, reflecting setting rhythms,
4. overall quality of the multiple regression model, given by standard, automatic quality-assessing model-identification criteria.

The columns represent the different multiple regression models as calculated for the four dependent variables: differences of cortisol D_{Cort}, mean cortisol level in sessions M_{Cort}, as well as differences of sIgA D_{sIgA} and mean sIgA M_{sIgA} values respectively in sessions. (Close attention has to be paid to the directions of signs of the multivariate predictors.)

Table 2: Multivariate predictors of sCortisol and sIgA in the analytic process

Indepenedent variables and model parameters	Dependent variables			
	sCortisol		sIgA	
	D_{Cort}	M_{Cort}	D_{sIgA}	M_{sIgA}
C	-2.18	9.24	3.02	9.44
Regressors				
D_{Cort}	xxx	xxx	-0.14	xxx
M_{Cort}	xxx	xxx	xxx	n.s.
Valence (pleas.=1 vs. unpleas.=5)	n.s.	-0.47	n.s.	-0.95
Arousal (high=1 vs. low=5)	n.s.	-0.57	-0.60	0.45
Dominance (low=1 vs. high=5)	n.s.	n.s.	0.77	-1.14
AR-parameters	1ar(2),	1ar(2), 2ar(1)	3ar(2), 4ar(2)	2ar(2), 3ar(1)
Setting: *Middle-of-the-week-sessions*				
Analyst 1	4.06	n.s.	n.s.	n.s.
Patient 1	3.89	n.s.	n.s.	n.s.
Analyst 2	n.s.	n.s.	14.37	-4.43
Patient 2	n.s.	n.s.	-7.10	n.s.
Model				
Adj. R-squ.	29%	94%	32%	61%
Durbin-Watson-Statistics	1.99	2.25	1.87	2.08
F=	2.71	66.89	1.89	7.29
p(F)<	0.004	0.0001	0.04	0.0001

Legend: C = constant, D = difference (values after - before sessions), M = mean (values before + after sessions / 2), Cort =salivary cortisol in ng/ml, sIgA = secretory immunoglobuline A in saliva in mg/dl, n. s. = not significant, Adj. R-squ. = alpha-adjusted R-square, AR = autoregressive parameter for: 1 = analyst 1, 2 = patient 1, 3 = analyst 2, 4 = patient 2 (No. of lags in parenthesis), p at least <0.05 for all coefficients given in the table.

The first multivariate model summarizes results concerning the differences "D_{Cort}" (Figure 2). The minus value of the constant C indicates that sCortisol fell on average in psychoanalytic sessions, taken all sessions and participants of the study together. It could be further shown that any dimension of the mood questionnaire SAM did not predict sCortisol differences. Only sCortisol values in participant 1 proved to be autocorrelated to lag 2, whereas all other participants showed no significant autocorrelation.

The psychoanalytic setting exerts an influence on patient 1 and analyst 1 with rising cortisol differences in session 2 and 3 ($p<0.001$), which is the middle phase of treatment within the therapeutic week. The total model accounts for 29% of the total variance (alpha-adj. R-squ.), a highly significant model with $F=2.71$, $p<0.004$ (Figure 10).

Looking at the mean values M_{Cort}, the results are displayed in the next column of Table 1. The positive C-constant indicates that sCortisol levels were significantly different from zero, being, with a value of 9.23 ng/dl, within normal ranges.

The parameter M_{Cort} could be predicted, in the multivariate model, by valence (unpleasant feelings connected with low cortisol excretion and vice versa, $p<0.02$) and by arousal (high arousal predicts high cortisol excretion, $p<0.001$, notes that the negative sign is due to direction of scale). Mean cortisol M_{Cort} was autocorrelated in patient 1 and analyst 1 (the first analytic dyad, with significant parameters for lag 2 in analyst 1 and lag 1 in patient 1). On an average, the patients had lower cortisol levels in the middle sessions 2 and 3, whereas the analysts tended to display higher cortisol levels in these sessions, an effect, however, which failed to be significant. The total

model accounted for 94% of the total variance (alpha-adj. R-squ. F=66.89, p<0.0001).
Concerning the sIgA differences D_{sIgA} (cf. Table 1 and see Figure 3), a significantly positive constant c indicates an increase of sIgA on average in the psychoanalytic sessions, if we take all participants and all sessions together. Secretory IgA differences D_{sIgA} could be predicted by varying concentrations of cortisol in saliva (negative relationship: high sCortisol correlates with low sIgA, p<0.02), by the arousal SAM dimension (high arousal predicts high sIgA secretion, p<0.001) and by the dominance dimension of the SAM (positive relationship, high dominance predicts high sIgA levels, p<0.05). Serial dependency of the sIgA differences existed in participants 3 and 4.
In patient 2, D_{sIgA}-values were lower in the middle part of the week (p<0.0001), whereas his corresponding analyst displayed higher D_{sIgA}-values in these same sessions (p<0.001). The total model accounted for 32% (alpha-adj. R-squ.) of the total variance (Figure 11).
Looking at the sIgA mean levels M_{sIgA}, the constant c with a value of 9.44 mg/dl shows that mean sIgA levels are significantly different from zero and within normal ranges of sIgA concentrations in samples. High sIgA levels were predicted by pleasant feelings (p<0.001), by low arousal (p<0.03) and low dominance (p<0.05).
In sessions 2 and 3 of the week, analyst 1 had higher sIgA levels than in sessions 1 and 4 (trend with p<0.07, n. s.), whereas patient 1 had lower sIgA levels in sessions 2 and 3 of the week (trend with p<0.08, n.s.). Analyst 2 had lower sIgA levels in these middle phase sessions (p<0.03), and his corresponding patient 2 showed insignificant higher sIgA levels in the middle phase of the week. The total model accounted for 61% of the total variance for the alpha-adjusted R-square.

Discussion

The study evaluates in some detail how a "standard" analytic setting is mirrored by changes in salivary cortisol and sIgA. Concerning sCortisol variations, the analytic hour is paralleled by a decrease of sCortisol (-1,04 ng/ml considering all participants and all sessions together, cf. Table 1). In one therapeutic dyad, an increase of this parameter could be observed in the middle, "hot" part of the therapeutic week. These findings where in line with previous observations [65]. The mean level of sCortisol was predicted by pleasant or highly aroused moods, which possibly could reflect therapeutically intensive moments of the psychoanalytic process.
In general, a significant increase of mean sIgA levels within the analytic session (+4,75 mg/dl considering all sessions and all participants together, cf. Table 1) could be observed. Changes in sIgA were predicted by sCortisol (increase of sCortisols predicts decrease of sIgA), by high arousal and high dominance, so that the feeling of dominance and affective stimulation were connected with an increase of immune defense. Mean sIgA levels in sessions were predicted by pleasant, lowly aroused and submissive feelings, a set of moods, which can be best interpreted by the passive strivings of regression. The influence of the setting was heterogeneous. In the second psychoanalytic dyad, a divergent pattern could be observed with higher sIgA levels in the middle part of the therapeutic week on the side of the therapist, being accompanied by decreases of this parameter on the patient's side. This observation may be interpreted as a "complementary" counter-transference situation, in which the patient feels "under pressure" during the "hot" part of the analytic week, a phase, which is paralleled by a decrease of sIgA. His analyst, in contrast, feels more at ease and has higher sIgA values in these sessions. In patient 2, in a quite literal sense, the four-hour setting of analysis undermined his immune competence. This corresponds to his clinical symptomatology of the patient's fear of "too much intimacy" with his analyst in context with the tight schedule of the four-hour analysis. The first couple showed only insignificant increases of the parameter for both parties, thus reflecting a more relaxed attitude towards the psychoanalytic process in these "intense", middle-of-the-week sessions. Psychoanalysis, after all, tends to have an immune stimulating effect on both, patient as and analyst alike, perhaps by initially stimulating both parties in terms of positive stress.
With regard to the shortcomings of this study, the time period of five weeks resulting in 20 data points must be regarded as an absolute minimum to assess the psychotherapeutic process. In future research it might be necessary to study longer processes, since a period of five weeks is insufficient to allow for general conclusions concerning the (psychobiological) interplay between analyst and patient. Even though our findings have, in terms of statistical significance, been well established, a clinical point of view requires longer periods of studying psychoanalytical processes to better understand some of the dynamics in the transference and counter-transference going on between patient and analyst. Secondly, we studied only two analytic couples, which make our results more applicable to case studies than to generalisations (for single case design in psychosomatic research cf. [81], [82], [83]). This study can therefore certainly be just the starting point for further research on this topic. To give a number, at least 10 samples of psychotherapeutic processes under study would meet the criteria of evidence-based medical research.
One crucial methodological problem of our study was that the sessions of the two analyses we had compared were set in slightly different time frames. Future studies should try to avoid this complication and, instead, should attempt to compare to each other only sessions placed in exactly the same time frame. It would be of some interest to study afternoon sessions because of the reduced natural variation of cortisol. If saliva cortisol is found to be reduced over a period of one hour in morning sessions, it might be at least partly due to the circadian rhythm of cortisol with its well-known morning decreases. Moreover, *increases* of this parameter in the morning hours would be even more remarkable, since we expect a natural de-

crease, due to biological rythmicity within these hours. In any event, caution is needed in ascribing the effect only to a postulated impact of the hour, in the sense of a "relaxing" effect. Taking afternoon sessions as objects of study, this problem would be partly avoided. However, afternoon sessions are burdened by the fact that protein-rich midday meals also have an (elevating) effect on cortisol concentration in saliva [84]. In order to overcome the problem of daytime variations of cortisol a second psychobiological parameter was introduced to the design. Secretory IgA proved to be a more reliable and dependable psychobiological parameter in terms of absent diurnal variations. Due to its broad intraindividual and interindividual variation, the parameter is not without problems either. From a pragmatic viewpoint, however, it can be stated that sIgA is used, despite its slight methodological problems, in field settings with some success [85]. Most of the authors regard sIgA still as a fairly reliable parameter, even if the saliva flow rate is not controlled (which is almost impossible in a natural clinical context).

One additional major criticism addresses the problem, that the biological effect of the analytic *hour*, as shown by the study, is not necessarily motivated by the psychoanalytic *process*. No one disputes, advocates of this line of critique would possibly argue, that lying on a couch may have a positive psychoimmunological effect in terms of relaxation. But, following this line of interpretation, has it anything to do with psychoanalysis as a psychotherapeutic setting or with the content of the hour? One important argument against this line of interpretation lies in the fact, that the study shows an overall effect of the four-hour setting with different effects of sessions 2 and 3 of the week compared to sessions 1 and 4. A closer look to the psychoanalytic process notes could even give additional information about the interactions between process and psychobiological data [23], ([62], "first dream"-session).

In conclusion, it seems a likely prospect that the study of psychobiology in a psychoanalytic setting will contribute to the clarification of emotional reactions during psychoanalysis and may also contribute to the empirical foundation of the schedule of a regular four-hour psychoanalysis as a psychotherapeutic device. Seen under the paradigm of alexithymia with its disorders of affect regulation [68], (cf. also [86], [87]), the reported findings may contribute to a theory basis in the treatment of alexithymic patients. Clinically, it seemed obvious, that the closeness and intimacy of a classical psychoanalytic setting found a "resonance" in the somatic realm and that the data support the view that intensive psychodynamic psychotherapy may contribute to a "loosening" of "alexithymic" defences.

To draw a conclusion, psychoanalysis may have a gradual impact on the immunological competence of both, patients and analysts. Moreover, intensive psychoanalytic work may help a patient to loosen his "alexithymic" defences. Patients who fear, in contrast, "too" close relationships may experience in psychoanalysis a kind of immune depressing stress, which is paralleled by a decrease of immunoglobulins.

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