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Dynamics of the human stress system in depression

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Temporal dynamics of physical activity and mood in depressed and non-depressed individuals

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ABSTRACT

Objective

The association between physical activity and affect found in longitudinal observational studies is generally small to moderate. It is unknown how this association generalizes to individuals. The aim of the present study was to investigate inter-individual differences in the bidirectional dynamic relationship between physical activity and affect, in depressed and non-depressed individuals, using time-series analysis.

Methods

A pair-matched sample of ten depressed and ten non-depressed participants (mean age = 36.6, sd = 8.9, 30% males) wore accelerometers and completed electronic questionnaires three times a day for 30 days. Physical activity was operationalized as the total energy expenditure (EE) per day segment (i.e. 6 hours). The multivariate time series (T=90) of every individual were analyzed using vector autoregressive modeling (VAR), with the aim to assess direct as well as lagged (i.e. over 1 day) effects of EE on positive and negative affect, and vice versa.

Results

Large inter-individual differences in the strength, direction and temporal aspects of the relationship between physical activity and positive and negative affect were observed. An exception was the direct (but not the lagged) effect of physical activity on positive affect, which was positive in nearly all individuals.

Conclusion

This study showed that the association between physical activity and affect varied considerably across individuals. Thus, while at the group level the effect of physical activity on affect may be small, in some individuals the effect may be clinically relevant.

INTRODUCTION

Physical activity or exercise is considered to be an effective treatment for depression (Ströhle, 2009; Ströhle et al., 2007; Dunn, Trivedi, Kampert, Clark & Chambliss, 2005). This proposition is appealing, because physical activity can be implemented easily and with relative low costs. However, the empirical evidence of the effectiveness of physical activity in alleviating depressive symptoms is not robust (Krogh, Nordentoft, Sterne & Lawlor, 2010; Cooney et al., 2013; Chalder et al., 2012). Similarly, observational studies have shown an inverse association between physical activity and depressive symptoms (Farmer et al., 1988; Strawbridge, Deleger, Roberts & Kaplan, 2002; Salmon, 2001; Dunn, Trivedi & O'Neal, 2001), with small to moderate effect sizes in different populations (Johnson & Taliaferro, 2011; Biddle & Asare, 2011). Although large cohort studies with a few measurements are useful to detect general patterns and traits in the population, they are not suitable for studying dynamic relationships between variables that fluctuate in daily life (Hamaker 2012; Hamaker, Dolan & Molenaar, 2005), which is the case for physical activity and depressive symptoms.

Some studies have adopted a more ecologically valid approach to investigate the association between depressive symptoms and physical activity. Ecological momentary assessment (EMA) studies address the dynamic nature of factors by investigating them repeatedly over time in participants' daily life. Depressive symptoms are characterized by increases in negative affect and decreases in positive affect (Clark & Watson, 1991). Improvement of depressive symptoms might therefore rely on lowering negative affectivity and increasing positive affectivity in depressed individuals. Physical activity, as explained earlier, seems to alleviate depressive symptoms, and such benefits might be due to a reduction in negative affect while also improving positive affect. Because slight changes in positive and negative affect might accumulate over time to result in depressed mood, it is important to investigate how physical activity influences daily affect levels (Rosmalen, Wenting, Roest, de Jonge & Bos, 2012). A recent literature overview of EMA studies investigating the relationship between physical activity and momentary affective states in daily life (Kanning, Ebner-Priemer & Schlicht, 2013) showed a generally consistent positive association between physical activity and positive affect across studies, which became stronger when only high-quality studies were included. In contrast, the influence of physical activity on negative affect, although observed in some studies (see for example LePage & Crowther, 2010; Dunton, Liao, Intille, Wolch & Pentz, 2011), was non-existent in the majority of studies reviewed (see Kanning et al., 2013).

The above EMA studies all used multilevel analysis to estimate dynamic associations. Although multilevel analysis allows for inter-individual differences when estimating the relationship between physical activity and mood, it is in principle a between-subject (group) approach; individual regression terms are averaged across the group and the same regression model is imposed on all subjects rather than modeling the dynam-

ic relationship for each subject individually. Only under strict conditions can findings at the inter-individual level be generalized to the intra-individual level (see Hamaker, 2012), and these conditions rarely apply to the study of dynamic psychological processes (Hamaker et al. 2005; Molenaar & Campbell, 2009). In addition, a within-subject time-series approach may be more suitable for investigating bidirectional relationships than multilevel analysis, because these models are built at the individual level and all variables in the model can be used as both predictors and outcomes (Brandt & Williams, 2007). The added value of such an approach was illustrated by a recent time-series study investigating the dynamic relationship between daily physical activity and depressive symptoms in four middle-aged male post-myocardial infarction patients with mild to moderate depression (Rosmalen et al., 2012). In spite of the relatively homogeneous study sample, this study indicated individual heterogeneity in the direction and strength of the association. E.g., for some individuals, previous depressive symptoms influenced the time spent on physical activity, while for others the direction and strength of the relationship was reversed. These individual differences, which have potential clinical relevance, would have gone unnoticed in a group design. This inter-individual heterogeneity observed should point to the fact that physical activity might be beneficial for some individuals with regards to depression but not to others.

The present study aimed to further elucidate inter-individual differences in the bidirectional association between physical activity and affect. Adopting an intensive time-series approach, this study explored the dynamic relationship between directly measured physical activity (i.e., accelerometers) and affect in the daily life of pair-matched depressed and non-depressed individuals, and individual differences therein.

METHODS

Sample

The sample was part of the ‘Mood and movement in daily life’ (MOOVD) study, which was set up to investigate the dynamic relationship between physical activity and mood in daily life, and the role of several biomarkers therein. Participants (age 20-50) were intensively monitored in their natural environments for 30 days, by means of electronic diaries, saliva sampling, and continuous actigraphy. The multiple repeated measurements per individual ($T=90$) allowed assessing within-person temporal relationships between variables at the individual level. For the current study, 10 depressed and 10 non-depressed participants, who were pair-matched on gender, smoking status, age, and body mass index (BMI), were included (the first 20 participants that finished the study).

Depressed individuals were recruited from the psychiatry department of the University Medical Center Groningen (UMCG) and the Center for Integrative Psychiatry (CIP) in Groningen, the Netherlands. Non-depressed participants were recruited from

the general population by means of posters and advertisements in local newspapers. Participants were screened for depressive symptoms with the Beck Depression Inventory version 2 (BDI-II; Beck, Steer & Brown, 1996) and for several other health conditions with a general health questionnaire. Individuals with a BDI-II score of >14 (i.e., depressed group) and individuals with a BDI-II score of <9 (i.e., non-depressed group) were invited for the inclusion interview, according to the criteria proposed by Frank et al. (1991). Individuals with a BDI-II score between 9 and 14 were excluded in order to create a clear contrast between the depressed and non-depressed group. The inclusion interview covered the Composite International Diagnostic Interview (World Health Organization, 1990), and, if included, several questionnaires and a briefing in which the use of equipment and the electronic diary was explained. Depressed individuals were included if they met DSM-IV criteria for a Major Depressive Disorder (current episode or in remission for no longer than 8 weeks). Non-depressed individuals were included if they were free of mood disorders at the moment of inclusion. Individuals who reported chronic somatic illness or medication use that may directly influence functioning of the hypothalamic-pituitary-adrenal (HPA) axis or the autonomic nervous system (ANS) were excluded. Other reasons for exclusion were: pregnancy, significant hearing or visual impairments, alcohol and drug abuse, and having a current or recent (within the last two years) psychotic or bipolar disorder as assessed with the CIDI interview. Participants received a remuneration for participation (up to €100, dependent on compliance) and a personal report of their daily affect and activity patterns after the conclusion of the study. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The MOOVD study design was approved by the Medical Ethical Committee of Groningen and all participants gave written informed consent.

Ambulatory sampling

Participants completed questionnaires on an electronic diary, the PsyMate (PsyMate BV, Maastricht, The Netherlands; see Myin-Germeys, Birchwood & Kwapil, 2011) for a total of 32 days, with the first two days used to get familiar with the device. The PsyMate was programmed to generate beeps at three predetermined moments a day with equidistant intervals: in the morning (mean \approx 10:00 AM), six hours later in the afternoon (mean \approx 16:00 PM), and six hours later in the evening (mean \approx 22:00 PM). Three time points were chosen, in order to capture the major changes in affect during the day (morning, afternoon and evening) without sampling too often, because this compromises the total length of the study. This fixed interval design was chosen to allow the application of time-series analysis. To capture most of participants' daily life without intruding with their sleep habits, beeps were planned at the end of the morning, afternoon, and evening, with the exact time points depending on the individual participant's sleep-wake schedule. We used the Munich Chronotype Questionnaire (MCTQ; Roenneberg et al. 2007) to determine a subject's sleep wake rhythm. We determined the individual-specific sampling time using this information, such that

subjects filled out the diary about half an hour before their usual bedtime (and six and twelve hours before that). In addition, we asked about the time that an individual would go to bed if he/she would go to bed rather early. If this time deviated much from the usual bedtime, for practical reasons and compliance, we set the diary time somewhat earlier; 15-30 minutes earlier, depending on the specific answer.

After every alarm beep, participants were asked to fill out the electronic diary. They were instructed to do so immediately after the beep, but a time window of one hour was used for situations in which this was not possible. It took approximately three to five minutes for each participant to complete the electronic diary at each time point. Throughout the study period, participants wore the ActiCal® (Respironics, Bend, OR, USA), an omnidirectional water-resistant accelerometer, on the wrist of the non-writing arm. They were instructed never to remove the ActiCal except when entering a sauna or sunbed (high temperatures). The ActiCal recorded data over 1-min sampling intervals. For more details about the ActiCal, see (Heil, 2006).

Measures

The electronic diary questionnaire contained 60 items on mood, cognition, and daily activities. Positive and negative affect scores were computed from affect items adopted from Bylsma, Taylor-Clift & Rottenberg (2011), rated on a 7-point Likert scale, ranging from 1 (“not”) to 7 (“very”). The positive affect scale reflected the average of the items talkative, enthusiastic, confident, cheerful, energetic, satisfied, and happy; the negative affect scale of the items tense, anxious, distracted, restless, irritated, depressed and guilty. An example item is “I feel cheerful”. The affect items (‘I feel...’) were phrased in such a way as to capture how the participant felt at the moment of completing the diary.

Energy expenditure (EE) data from the ActiCal were used as a measure for physical activity. Each participant wore the ActiCal the whole day and night for the 30-day period of the study. This study focused on general physical activity during the day, which is defined as any type of EE resulting from bodily movements of skeletal muscles (Caspersen, Powell & Christenson, 1985). The ActiCal uses an in-built algorithm to calculate activity EE, using the raw activity monitor data. The process of creating this algorithm is described by Heil et al. (2006). For each participant, the amount of EE (kcal/min) across all sampling minutes over one day segment (i.e. 360 minutes per segment) was summed. This resulted in total EE per day segment (kcal/day segment).

Person characteristics including age, gender, educational level, smoking status, coffee and alcohol intake, and the average amount of exercise per week (min) were obtained from questionnaires filled out at the baseline assessment. BMI was calculated from the weight and height of each individual.

Statistical analysis

Missing diary data were imputed by means of Expectation-Maximization imputation

in IBM SPSS Statistics 20. For every participant, all variables used in the time-series model as well as auxiliary variables that were significantly associated with these variables were used as predictor variables in the imputation. On average, participants had 8 missing values ($sd = 6.7$, $range = 0 - 22$) on the diary variables (8.8%). Of the 20 participants, three participants had missing actigraphy data at the last 9 or 10 days of the study, because of technical problems. These relatively large periods without activity records were discarded and not imputed, leaving 60-63 valid data points for these three participants, which is still considered sufficient for the application of time-series analysis (Rosmalen et al., 2012; Lütkepohl, 2007).

The multiple time series of every individual were analyzed using vector autoregressive (VAR) modeling. A VAR model is a multivariate autoregressive model that consists of a set of regression equations for a system of two or more variables, in this case positive affect, negative affect, and EE (Brandt & Williams, 2007). All three variables in the system were treated as endogenous, which means that they could be both determinant and outcome. Each of the three endogenous variables was regressed on its own p lagged values and the p lagged values of the other variable. The errors of the VAR model should be serially uncorrelated but can be contemporaneously correlated. VAR analysis is especially suitable for investigating the dynamic relationships between two or more variables: inferences can be made about the temporal order of effects, which can involve bidirectional effects and feedback loops (Brandt & Williams, 2007). Moreover, by analyzing all variables in one system, the most important effects will be identified. For more details about VAR modeling and a non-technical introduction, see Brandt and Williams (2007) and Rosmalen et al. (2012), respectively.

The number of lags included in the models was a priori set to three, which is equivalent to a period of one day. A fixed number of lags was chosen to ease comparison of results for different participants. Considering the study's exploratory nature, a relatively high number of lags was chosen, allowing for the investigation of relatively long-term lagged effects (i.e. over 3 time intervals = 1 day). To account for structural lower morning values for total EE, compared to afternoon and evening values – participants spent part of the morning lying in bed – as well as diurnal rhythms in mood, dummy variables for morning and evening were included (afternoon served as a reference category). Variables for time and the square of time were included into the model if this was necessary to render the series stationary. Total EE was divided by 100 to accommodate the difference in scaling between EE and positive and negative affect. Maximum likelihood estimation with a degrees-of-freedom adjustment advocated for small samples was used for estimating the VAR coefficients (Lütkepohl, 2007).

VAR model assumptions, namely stability of the model, independence, homoscedasticity and normality of residuals, were assessed using diagnostic checks (Lütkepohl, 2007). If one of the tests indicated a violation of the model assumptions, models were adjusted, re-estimated, and re-evaluated, in an iterative model-building process, until

all assumptions were met. Outlier modeling was applied only if this was required to meet model assumptions, using the criterion of residual $SD > 3$ (stepwise lowering to $SD > 2$, if necessary; Field, 2009). Log transformation of the variables was applied if the residuals remained skewed. If scatterplots of skewed variables with other variables suggested curvilinear relationships, non-skewed variables were left untransformed. In other cases, all endogenous variables were log-transformed.

To assess the direct effect of EE on positive and negative affect, we examined the contemporaneous correlations between the variables, which can be retrieved from the residuals of the final models. These correlations represent the simultaneous correlations between the variables, i.e., between the scores at the same assessment point.

To assess the overall lagged effects of EE on positive and negative affect, and vice versa, the VAR regression coefficients of lags 1 to 3 were averaged into one joint coefficient, weighted by the inverse of their estimated standard error. Subsequently, the joint coefficients were standardized so that they could be compared across participants. The lagged effects represent the delayed effects of past day's EE on current positive and negative affect over time, and vice versa. To test the significance of the overall lagged effects the Granger causality Wald test was used. This is a test for the directionality of the influence between two time series, which tests the joined effect of previous lags of the predictor on the outcome variable, controlling for previous lags of the outcome variable (Lütkepohl, 2007; Granger, 1969). In view of the exploratory nature of the study, a significance level of 0.05 was used for all tests.

We also assessed the relationship between physical activity and affective states using Cumulative Orthogonalized Impulse Response Function analysis (COIRF), to visualize the dynamic behavior of the system and to calculate dynamic effect sizes. Impulse response functions (IRFs) allow tracing out the dynamic impacts of changes in each of the endogenous variables over time. They do so by visualizing the influence of an isolated shock in one of the variables (i.e. an impulse of 1 SD in EE or affect) to the other variable(s), showing how this shock is fed through the system. This means that all effects in the VAR model (e.g. effects of different lags, feedback loops) are incorporated. Orthogonalized IRFs (OIRFs) take into account both the lagged and the contemporaneous correlations among the variables (Brandt and Williams, 2007). They assume a specific pre-defined ordering for the contemporaneous relationship. Because the EE scores covered the period directly before the affect measurement, we assumed the order EE \rightarrow affect for the contemporaneous relationship. The cumulative versions of the OIRFs (COIRFs) display the accumulated impact of a shock in one variable on the other variables over a certain time horizon, in our case 1 day (3 steps). We present these COIRFs, because in VAR analysis these are used as a dynamic effect size measure (Rosmalen et al. 2012; Brandt and Williams, 2007). Effect sizes were standardized by dividing them by the standard deviation of the response variable for every individual.

In order to assess between-group differences, dependent t-tests (pair matched t-test) and chi-square tests were performed to explore differences between the depressed and non-depressed groups with respect to the number of subjects having positive vs negative associations between EE and positive and negative affect. These were done for the direct associations, the lagged effects, and for the dynamic effect sizes. All analyses were done in STATA 11 using the suite of VAR commands (StataCorp. 2009).

RESULTS

Descriptives

The demographic and clinical characteristics of the depressed and non-depressed participants are presented in Table 1.

Table 1. Demographic and clinical characteristics for the depressed and non-depressed group

	Depressed group (n=10)				Non-depressed group (n=10)			
	Mean	SD	Min	Max	Mean	SD	Min	Max
<i>Demographics</i>								
Age	36.4	10.3	22	49	36.7	7.9	24	46
Gender (% male)	30.0	—	—	—	30.0	—	—	—
Anti-depressants (% users) ¹	60.0	—	—	—	0	—	—	—
Body Mass Index (BMI)	23.8	4.9	17.4	34.9	22.2	2.3	19.5	26.9
Educational level (0-3)	2.6	0.5	2	3	2.6	0.5	2	3
<i>Lifestyle</i>								
Coffee intake (per day)	2.2	2.5	0	8	1.8	1.4	0	4
Alcohol intake (per month)	10.8	14.5	0	40	8.4	14.4	0	48
Self-reported exercise frequency (per week)	1.7	1.5	0	4	2	1.5	0	4
Self-reported duration of exercise (min. per week)	83	89	0	240	133	109	0	240
Average EE over one day segment	233	77	126	385	258	69	120	369
<i>Mood and depressive symptoms</i>								
Pre-BDI-II	32.5	10	20	51	2.8	3.4	0	10
Post-BDI-II	25.9	15.8	2	47	4.4	4.6	0	13
Average PA (1-7)	3.1	1.3	1.1	4.5	4.6	1.3	1.7	6.1
Average NA (1-7)	3.6	1.2	1.4	5.3	1.6	0.6	1.0	2.8

Note: BDI-II = Beck Depression Inventory, EE = energy expenditure, PA = positive affect, NA = negative affect

¹ including quetiapine and St.Johns wort.

Short-term effect of physical activity on positive and negative affect

As depicted in Figure 1a, the majority of depressed (red bars) and non-depressed (blue bars) participants showed a positive contemporaneous association between EE and positive affect. As the EE scores covered the period directly before the affect rating, this can be interpreted as a direct effect of EE on positive affect. For five individuals (three non-depressed and two depressed) these positive associations were significant ($p < .05$). The size of the correlation coefficients (r) was small to moderate, according to the suggestions provided by Cohen (1992; <0.1 =small; <0.3 =moderate; <0.5 =large).

Figure 1b shows the direct association between EE and negative affect for depressed (red bars) and non-depressed (blue bars) participants. This can be interpreted as a direct effect of EE on negative affect. Seven of them showed a positive (non-significant) contemporaneous association between EE and negative affect, while ten participants showed a negative association, without any apparent differences between the groups (depressed and non-depressed). For two individuals (one depressed and one non-depressed) the negative association between EE and negative affect was significant ($p < .05$). The size of these correlation coefficients was again small to moderate.

The between-group analysis (chi-squared and dependent t-tests) showed no difference between the depressed and non-depressed groups with regards to the number of subjects showing a positive vs. a negative contemporaneous association between physical activity and positive affect ($X^2=.01$, $df=1$, $p > .05$; $t=.89$, $df=9$, $p > .05$) or negative affect ($X^2=.08$, $df=1$, $p > .05$; $t=.37$, $df=7$, $p > .05$).

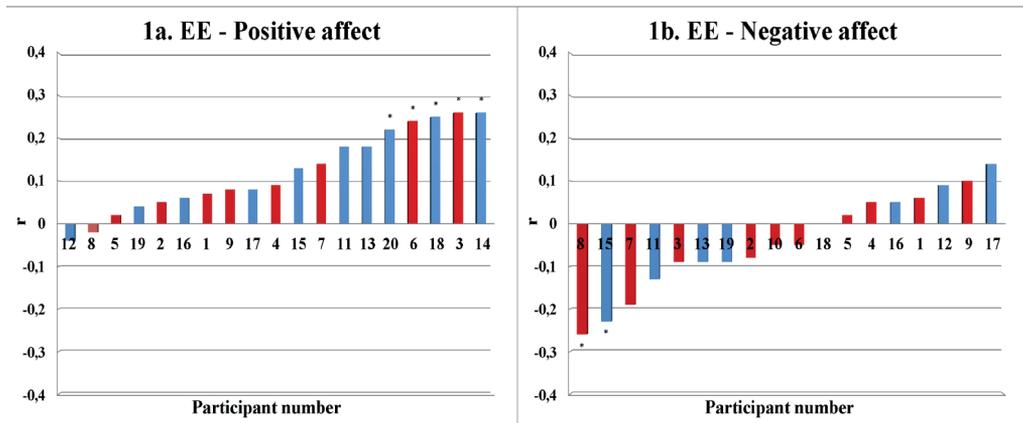


Figure 1a and 1b. Direct association between physical activity and positive (1a) and negative (1b) affect for the depressed (red / dark grey bars) and non-depressed (blue / light grey bars) individuals. * significant at the .05 level. Values on y-axis depict correlation coefficients (r).

Lagged effect of physical activity on positive and negative affect

The lagged associations between previous values of EE (i.e. the joint effects of lag 1, lag 2, and lag 3) and current values of positive affect varied greatly between individuals (Figure 2a). Seven participants showed a positive lagged effect of EE on positive affect, but only for two (one depressed and one non-depressed individual) this effect was significant. For the remaining 12 participants a negative lagged effect of EE on positive affect was observed, and for four individuals (all non-depressed) this effect was significant. Mixed effects (i.e. both positive and negative associations on different lags) were present in two of them (participant 15 and 16). Figure 2b shows the results for EE and negative affect. The majority of participants (eleven compared to seven participants) showed a negative lagged effect of EE on subsequent negative affect, which was significant in three participants (one depressed and two non-depressed). Overall, the effect sizes (i.e., beta) of the lagged effects of EE on positive and negative affect were small. Lagged effects indicate an effect of past day's EE on current affective states.

The between group analysis again showed no difference between the depressed and non-depressed groups with respect to the lagged effect of EE on positive affect ($X^2=.09$, $df=1$, $p>.05$; $t=-.03$, $df=8$, $p>.05$) or negative affect ($X^2=.011$, $df=1$, $p>.05$; $t=-.61$, $df=7$, $p>.05$).

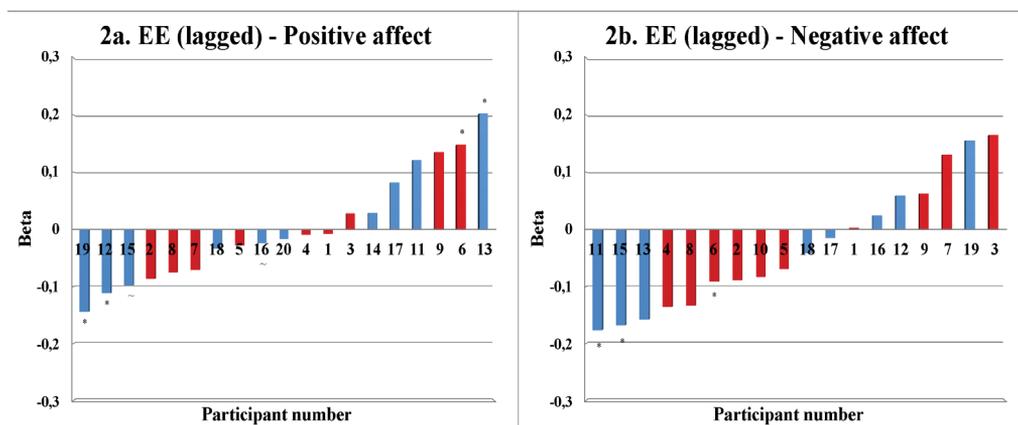


Figure 2a and 2b. Lagged associations between physical activity and positive (2a) and negative (2b) affect in the depressed (red / dark grey bars) and non-depressed (blue / light grey bars) individuals. * significant at the .05 level. ~ significant association with mixed sign of coefficients at different lags. Values on y-axis depict standardized regression coefficients (beta).

Lagged effect of positive and negative affect on physical activity

The majority of the participants (n=14) showed a positive association between lagged values of positive affect and current values of EE (Figure 3a). For two participants (both depressed) this association was significant. Five participants (three depressed and two non-depressed) showed a non-significant negative association. Figure 3b shows the results for negative affect and EE. The majority of participants showed a positive lagged effect of negative affect on subsequent EE (eleven compared to

seven participants). For only one (depressed) participant this effect reached statistical significance ($p < .05$). Overall, the effect sizes (i.e., beta) of the lagged effects between positive and negative affect and EE were small. Lagged effects indicate an effect of past day's affective states on current EE.

The between group analysis showed no difference between the depressed and non-depressed groups with respect to the lagged effects between positive and negative affect and EE ($X^2 = 1.01$; $df = 1$, $p > .05$; $t = .39$, $df = 8$, $p > .05$ and $X^2 = 1.57$, $df = 1$, $p > .05$; $t = -.55$, $df = 7$, $p > .05$ respectively).

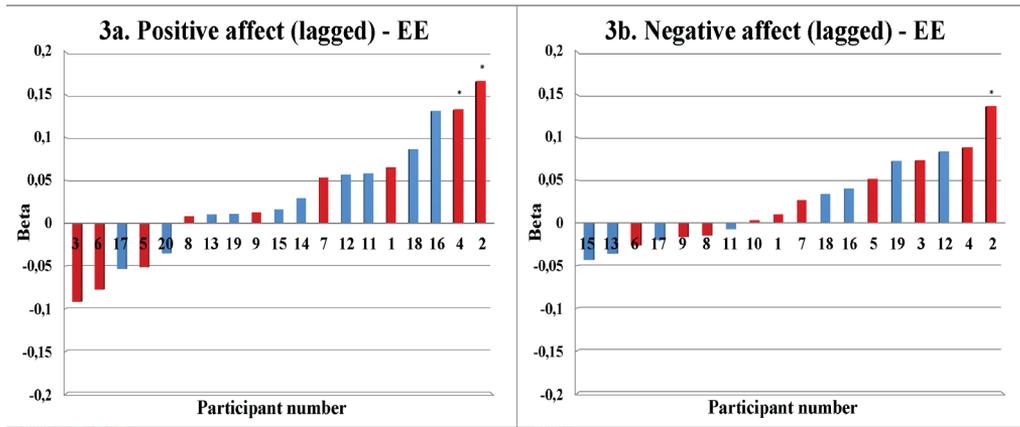


Figure 3a and 3b. Lagged associations between positive (Figure 3a) and negative (Figure 3b) affect and physical activity in the depressed (red bars) and non-depressed (blue bars). * significant at the .05 level. Values on y-axis depict standardized regression coefficients (beta).

Direction of the relationship

None of the individuals showed a significant bidirectional relationship between physical activity and positive or negative affect. Six participants showed a significant lagged effect of EE on positive affect, while two participants showed a significant lagged effect of positive affect on EE. Three participants showed a significant lagged effect of EE on negative affect, while one participant showed a significant lagged effect of negative affect on EE.

Dynamic effect sizes (COIRFs)

The dynamic effect over a 1-day horizon of an impulse of 1 SD in EE on positive affect ranged from -0.38 to 0.78 (see Table 2). For the majority of participants, the effects were positive (13 out of 19). The effects were significant for five individuals with a positive effect. Furthermore, the dynamic effect of an impulse of 1 SD in EE on negative affect ranged from -0.59 to 1.04, and it was negative for 10 out of 19 participants. A significant positive effect was found for one participant, and a significant negative effect was found for two participants. In the other direction, the dynamic effect of an impulse of 1 SD in positive affect on EE ranged from -0.34 to 0.31, and the majority had a positive sign (13 out of 19). There was a positive significant effect

for three individuals, and a negative significant effect for one individual. Finally, the dynamic effect of an impulse of 1 SD in negative affect on EE ranged from -0.10 to 0.24, and it was positive for 12 out of 18 individuals. The effect was positive and significant for three individuals.

Table 2. Dynamic cumulative effect size over a 3-step horizon

ID	EE (impulse) – PA (response)	EE (impulse) – NA (response)	PA (impulse) – EE (response)	NA(impulse) – EE (response)
1	0.02	0.04	0.15	0.01
2	-0.24	-0.25	0.21	0.23
3	0.18	0.20	-0.25	0.11
4	0.09	-0.15	0.36	0.26
5	-0.03	-0.13	-0.12	0.06
6	0.11	-0.17	-0.19	-0.06
7	0.05	-0.03	0.11	0.07
8	-0.11	-0.13	0.08	-0.02
9	0.09	0.18	0.02	-0.05
10		-0.17		0.05
11	0.04	-0.12	0.15	0.00
12	-0.29	0.24	0.10	0.29
13	0.64	-0.42	0.13	-0.07
14	0.18	0.19	-0.17	
15	-0.04	-0.29	0.14	-0.17
16	0.02	0.03	0.36	0.10
17	0.12	0.00	-0.14	-0.01
18	0.14	0.00	0.41	0.15
19	-0.14	0.03	0.09	0.20
20	0.10		-0.07	

Note: Impulse = one standard deviation in the impulse variable. Bold effect size indicates that zero does not lie in 90% confidence interval. EE = Energy expenditure, PA = Positive affect, NA = Negative affect.

DISCUSSION

To our knowledge, this is the first study to use a within-subject time-series approach to investigate the dynamic relationship between physical activity and affective states in depressed and non-depressed individuals. The associations found were not consistent across individuals. For some individuals, physical activity was positively related to positive affect and negatively related to negative affect, while for others the sign of the relationship was opposite. Additionally, in some individuals changes in phys-

ical activity were followed by changes in affective states, while in others changes in affective states were followed by changes in physical activity, and in another group of individuals no temporal effects were found at all. An exception was the direct association between physical activity and positive affect, which was positive in nearly all individuals, albeit with varying effect sizes.

A positive relationship between physical activity and positive affect has also been found in the majority of group-based EMA studies (for example see Wichers et al., 2012; Giacobbi, Hausenblas & Frye, 2005; Schwedtfeger et al., 2010). Schwedtfeger et al. (2010), showed a relationship between EE and positive affect, where increases in bodily movements of varying intensity were associated with increases in positive affect. Wichers et al. (2012) showed that increases in physical activity resulted in increases in positive affect. These increases in positive affect were shown to last up to 3 hours later. However, the lagged effect of physical activity on positive affect was not consistently found in our current study; in some individuals it was positive, while in others it was negative. Furthermore, the strength of the lagged relationship was small to negligible for most individuals. Thus, the results suggest that physical activity enhances positive affect directly while only in some individuals there is also a delayed effect, contrary to the findings by Wichers et al. (2012).

The increase in positive affect following physical activity did not seem to differ between depressed and non-depressed individuals as the between-group analysis showed. However, the small sample size used in this study is not optimal to draw strong conclusions regarding between-group differences. Wichers et al. (2012) showed that the effects of physical activity on positive affect did not differ between people who scored high versus low on the continuous depressive symptom scale. However, they did find that for individuals with a history of depression this effect lasted a shorter period of time. Another EMA study, comparing patients with a depressive disorder and non-depressed controls (Mata et al., 2012), showed similar improvements in positive affect after physical activity in both groups. Hence, physical activity seems to (directly) improve positive affect in individuals regardless of their depression status.

While the direct association between physical activity and positive affect was quite consistent across individuals, this was not the case for negative affect. Both positive and negative associations between physical activity and negative affect were observed, though the strongest effect sizes were negative. A similar pattern emerged for the lagged effects of physical activity on negative affect. In some individuals there was a negative effect of physical activity on negative affect, but in most individuals this relationship was weak or non-existent. When aggregating data of individuals with opposing effects of physical activity on negative affect, the group-level effect will be small and inconsistent across different study samples. Hence, individual differences may explain inconsistent results in EMA studies regarding the relationship between physical activity and negative affect (Kanning et al., 2013).

Observational (between-subject) studies have found a reciprocal relationship between physical activity and depressive symptoms (Lindwall, Larsman & Hagger, 2011; Jerstad, Boutelle, Ness & Stice, 2010; Stavrakakis, de Jonge, Ormel & Oldehinkel, 2012). The available EMA studies also suggest that there are reciprocal relationships between affective states and physical activity (Giacobbi, Hausenblas & Frye, 2005; Hawkey et al., 2009). Wichers et al. (2012), however, could not find evidence that increases in positive affect resulted in increases in physical activity. The present study extends the above findings by showing that in some individuals changes in positive affect were followed by changes in physical activity levels, while in others it was the other way around. Interestingly, none of the individuals showed a noticeable bidirectional relationship. If these data were aggregated, a bidirectional relationship at the group level might have been concluded, while in all individuals the relationship was unidirectional, albeit in different directions.

The strength of the effects (correlation coefficients and standardized regression coefficients, which can be interpreted as effect sizes; Cohen, 1992) was generally small, but considering the non-experimental daily-life design and the short intervals between the measurements this could have been expected (Wichers et al., 2012). Nonetheless, small effects can accumulate over time and become larger, because of the way these changes are disseminated through the system and mutually enhanced through possible feedback loops. This was nicely illustrated by the results of the Impulse Response Function analysis, which examines exactly this process. The dynamic effects were generally larger than the individual lagged and contemporaneous effects. If physical activity becomes a daily habit, for instance through regular sport participation, this could result in systematic long-term improvements in positive affect. Future research using intensive time-series designs should explore this putative accumulating effect in more detail, in order to elucidate whether the short-term benefits of physical activity on affect can accumulate into larger benefits over time, and if so, in which individuals.

Clinical Relevance

Two findings from the current study might be of interest to clinicians. First, these results suggest that physical activity might benefit positive affect in the short-term. A recent meta-analysis of randomized controlled studies showed evidence of a short-term benefit of physical activity on depression (Krogh et al., 2010). The results from the present study support and extend this finding by showing that these short-term benefits might be acting through an elevation of positive affect rather than through a decrease in negative affect for the majority of individuals. However, this short-term effect was significant in only a few individuals and therefore the conclusion that physical activity can elevate individuals' positive affect is tentative. The mechanisms behind this putative short-term benefit of physical activity on positive affect are currently not understood. Some hypotheses have been proposed implicating the endorphin system (Thoren, Floras, Hoffmann & Seals, 1990; Dishman & O'Connor, 2009) and increases in self-efficacy (Bodin & Martinsen, 2004), but future research is

needed to explore these in more depth.

Second, in some individuals high levels of positive or negative affect were associated with subsequent increases in physical activity in the current study. Feeling good might increase the level of physical activity engagement, but apparently also feeling bad might have such an effect in some individuals. This concurs with the suggestion that physical activity might be perceived as an efficient strategy to repair negative affect, i.e., ‘walking off’ negative affectivity (Clark & Isen, 1982). The present study cannot address this hypothesis properly, but suggests inter-individual differences in the way affect influences subsequent activity levels that need to be taken into account.

Strengths & Limitations

This study has several notable strengths. First, the time-series design allows the investigation of the associations at the individual level, thanks to the multiple repeated measurements over time, and also allows for the exploration of temporal patterns and the direction of the relationship. Second, although obtaining multiple repeated measurements can be troublesome, time-consuming, and demanding, especially for participants with depression, the compliance of the participants did not seem to deteriorate significantly in this study. There was no indication that the participants were unable or found it difficult to comply with the study protocol, and any systematic missing values were due to technical problems with the accelerometers. Even in these cases the number of obtained measurements per individual (>60) was still adequate to perform time-series analysis. Finally, in this study the sample was matched on four important variables, and this should help to explore inter-individual differences in a relatively homogeneous sample of depressed and non-depressed individuals. Ideally, the sub-groups should be matched on other important variables (e.g., occupation, disability status, socioeconomic status and personality) as well. However, for practical reasons, this was not possible.

The results from this study should be interpreted with some caution due to several limitations. First, the generalizability of within-subject studies to the population at large is limited, and this is the trade-off that comes with the increased specificity of within-subjects time-series studies. Therefore, a combination of within- and between-subject approaches is warranted in order to improve our understanding of the complex relationship between physical activity and daily affect. Second, the models applied in this study assume that the relationship between physical activity and affect is linear. It is possible that the relationship between the two is curvilinear and a specific threshold (i.e., frequency, duration or intensity) of physical activity is needed to benefit individuals with regards to their affect, while exceeding this threshold might result in negative consequences. However, a post-hoc t-test comparison showed that there were no significant differences in the relationship between physical activity and affective states between individuals who were relatively active throughout the month, compared to individuals who were relatively inactive (see Supplementary Table A). Another potential limitation is that the strength of an association depends on the

degree of variability in the data. Therefore, it is possible that for some individuals the variability between the measures was not large enough to detect an association. Moreover, this study did not take into account the nature of physical activity and the different contexts in which activities are done. It is reasonable to expect that different types of activities (e.g. exercise, shopping, household) will have different effects on affect. Furthermore, this study considered the temporal ordering of the contemporaneous associations to be from physical activity to affect, given the fact that physical activity covered each time period as a whole and affect was assessed at the end of each time period. It is possible that reverse effects (affect to physical activity) were acting here as well, which might have introduced bias in the interpretation. However, due to the design of the study this eventuality was not assessed. Finally, the contemporaneous and lagged associations were separated in the VAR models of this study, to distinguish the dynamic from the simultaneous part of the model (Brandt & Williams, 2007). An alternative approach may be the unified SEM approach developed by Gates, Molenaar, Hillary, Ram and Rovine (2010), which integrates the estimation of contemporaneous and lagged relationships.

Conclusion

In conclusion, inter-individual differences in the magnitude and direction of the relationship between physical activity and positive and negative affect using a within-subjects time-series design were explored. The findings provided evidence that the strength and direction of the relationship between physical activity and affect differs across individuals. Future time-series studies in larger groups could identify subgroups that benefit from physical activity, which could subsequently be subtyped using multiple predictor variables (e.g. genetic makeup, personality). Otherwise, time-series approaches could be directly implemented in clinical care (e.g. while on a waiting list), using automated time-series analyses and personalized feedback, which are already available for research purposes (Emerencia et al., 2014). Prediction models as well as automated feedback could both aid the clinician in the decision whether to implement physical activity interventions for depressed mood or not.

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SUPPORTING INFORMATION

Table A. T-test for high- versus low-active groups

Relationship	T (df)	p-value	Mean difference	St. Error difference	95% CI
EE (lagged) - PA	0.370 (17)	0.716	0.017	0.455	-0.079 – 0.113
EE (lagged) - NA	-0.142 (16)	0.889	-0.008	0.054	-0.123 – 0.107
PA (lagged) - EE	0.475 (17)	0.641	0.159	0.034	-0.055 – 0.087
NA (lagged) - EE	1.072 (16)	0.300	0.026	0.024	-0.025 – 0.076
EE (direct) - PA	-2.073 (18)	0.053	-0.083	0.040	-0.167 – 0.001
EE (direct) - NA	1.628 (16)	0.123	0.085	0.052	-0.026 – 0.195

Abbreviations: EE, Energy expenditure; PA, Positive affect; NA, Negative affect; CI, confidence interval.