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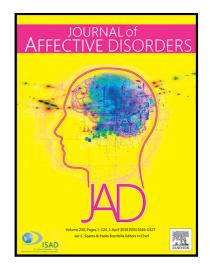
Ecological momentary assessment of mood and physical activity in people with depression

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Introduction

Depression is a widespread problem, with 300 million sufferers worldwide (World Health Organization, 2016). Common therapies for relieving symptoms of depression have drawbacks. Antidepressants may cause side effects such as headaches (NHS Choices, 2016), insomnia (NHS Choices, 2016) and emotional blunting (Price et al., 2009), and are often poorly adhered to (Byrne et al., 2006). Psychotherapies are prone to attrition (Hans and Hiller, 2013), particularly for those facing social or economic difficulties (Roseborough et al., 2016).

Physical activity has been shown to enhance mood, with the National Institute for Health and Care Excellence (NICE) recommending group based physical activity for individuals with persistent subthreshold, mild, or moderate depression (National Institute for Health and Care Excellence, 2009). Possible psychological mechanisms by which physical activity improves mood include increased self-efficacy and self-esteem through skill-development or social support (Cooney et al., 2013). Biological mechanisms include changes in levels of endorphins or monoamine neurotransmitters (Craft and Perna, 2004), and changes in levels of inflammation (Hamer et al., 2009). Increasing physical activity also reduces the risk of comorbid diseases associated with inactive lifestyles, such as diabetes and vascular disease, which are common in people with depression (Katon, 2011). Many patients also view physical activity as an acceptable adjunct or alternative treatment to current therapies, although they differ in what type and intensity of physical activity they perceive as beneficial for enhancing mood (Searle et al., 2011).

A Cochrane review reported moderate effectiveness of exercise for improving depression, finding it more beneficial than controls, and similar in effectiveness to pharmacological or psychological therapies (Cooney et al., 2013). The review however indicated uncertainty

regarding the optimum intensity of exercise for improving mood, and how long any benefits lasted after exercise (Cooney et al., 2013). Additionally, many of the interventions developed to date have used structured exercise classes, so it is unclear whether the benefits can be replicated by unstructured, lifestyle based physical activity.

Examining the temporal association between physical activity and subsequent mood in people who are depressed may help to suggest mechanisms by which they are associated, and generate hypotheses about dose and timing of physical activity that might be therapeutic for improving mood. This could ultimately help to develop more optimal prescription criteria for physical activity in people with depression. However, single administration questionnaires of mood used in aggregated research designs tend to sample only experiences averaged over time (typically one or two weeks), and do not capture the fluctuations of mood that occur in daily life (Wenze and Miller, 2010). Studies using ecological momentary assessment (EMA) repeatedly sample behaviours and outcomes in real time (Wenze and Miller, 2010), recognising that affective states are volatile and subject to change as a result of dynamic internal (e.g. hormones) and external (e.g. life events) influences (Schlicht et al., 2013). EMA can be powerful in measuring reactivity (change in one variable following change in another) (Wenze and Miller, 2010), providing a better indication of potential causal relatedness than cross-sectional or questionnaire based research designs (Hill, 1965). EMA has previously been used in mood disorders research to examine relationships between "daily hassles and uplifts" and subsequent affect (Peeters et al., 2003), or between pain and depression in people with chronic disease (Tennen et al., 2006).

EMA is now being increasingly used in studies examining the relationship between mood and physical activity in healthy populations. However, these studies frequently suffer from methodological flaws that can increase their risk of bias. Subjective reporting of physical activity, such as through diaries or questionnaires, tends to over-estimate physical activity

and has low-to-moderate correlations with more objective measures of physical activity such as accelerometery (Prince et al., 2008). Studies have shown that paper diaries can be prone to 'backfilling' (Stone et al., 2003). Delays in recording mood can also lead to recall bias, with easier recollection of memories that are congruent with their current affective state (Drace, 2013).

In recognition of these flaws, Kanning, Ebner-Priemer, and Schlicht (2013) highlighted the importance of more objective physical activity measurement and real-time mood measurement using electronic methods of data collection where responses can be time-stamped to ensure that data collection is compliant with the intended "in the moment" design of the study.

At present, studies examining the acute association between physical activity in daily life and subsequent mood have been conducted mostly in non-clinical samples. A systematic review (Liao et al., 2015b) found studies consistently concluded a positive relationship between acute physical activity and subsequent positive affect but not negative affect; less than half these studies used more objective measures of physical activity and electronic recording of affect. Other research examining acute associations using more objective methodologies together draw more inconsistent conclusions (Bossmann et al., 2013; Kanning et al., 2015; Liao et al., 2016a; von Haaren et al., 2013)

Currently there are few EMA studies have used more objective methods to measure the acute relationship between physical activity and mood in populations with depression. Stavrakakis et al. (2015) examined individual differences in the relationship between physical activity and affect in depressed individuals, this was conducted over a longer time period of 32 days but studied six hour windows of energy expenditure and so looked at a less acute temporal relationship. Kim et al. (2015) focused their analysis on the relationship between

intermittency of activity and subsequent depressed state, examining five to 60 minute windows either side of each mood measurement. Both Kim et al. (2015) and Stavrakakis et al. (2015) used accelerometers and electronic diaries, but only sampled small numbers of people with depression, and did not examine the effects of different intensities of physical activity.

This study used EMA methodology, with more objectively measured physical activity and electronic sampling of mood, to examine the temporal relationship between physical activity and mood in people with depression. Specifically, the study aimed to assess whether different amounts and intensity of physical activity over time periods of one and three hours predict subsequent mood.

It was hypothesised that the number of minutes of moderate-to-vigorous physical activity (MVPA) during the hour preceding mood measurement would predict subsequent mood score. National guidelines recommend moderate and vigorous intensities of physical activity as being beneficial for improving general physical health (NHS, 2018), yet it is unclear whether the benefits of these intensities extend to mental wellbeing. Given the existing lack of prior knowledge in the field about the relationship between activity intensity and activity duration and subsequent mood in depressed individuals, the study also aimed to conduct (a priori specified) secondary analyses to explore the association between mood and physical activity for different intensities of physical activity (light activity (LPA), and total PA (light plus moderate-to-vigorous activity (LMVPA)), and for a longer time window before the mood score (three hours). There is little consensus between studies as to the optimum time to measure physical activity prior to mood measure (Liao et al., 2015b), however one and three hours were chosen to provide a more acute and a longer period after physical activity, as the relationship might be mediated by different biological (Hearing et al., 2016) or psychological (Guérin et al., 2013) processes.

Methods

Participants

We recruited participants who were taking part in the eMotion pilot randomised controlled trial (ClinicalTrials.gov NC-T03084055). The eMotion study is described in detail elsewhere (Lambert et al., 2018). Briefly, the study piloted an online intervention (eMotion) that combines behavioural activation and physical activity promotion for reducing depressive symptoms in 62 people with moderate to severe depression. To be eligible for the eMotion trial, participants had to: be over 18 years old; have symptoms commensurate with moderate to severe depression as indicated by a score of between 10 and 24 on an eight-item Patient Health Questionnaire (PHQ-8) (Kroenke et al., 2009); be living in the community in the UK; have internet access; be able to walk independently for at least five minutes continuously (assessed by self-report); and provide informed consent. The current study was nested within the eMotion study. Participants taking part in the eMotion trial were informed of and consented to the use of their data for current study. A web-based consent form was used, where consent was indicated using a checkbox.

Measures

Physical activity: Physical activity was assessed using GENEActiv Original accelerometers worn continuously for seven days following baseline data collection for the eMotion study. Accelerometers were set to record at a rate of 100Hz for seven days, with acceleration recorded on three axes (x, y and z). Accelerometers were posted to participants, who were instructed to wear them on their non-dominant wrists. Files were considered valid if the wear criteria of 4 days with over 10 hours wear were available.

Ecological momentary assessment of mood: Mood was measured using a single-item SMS text message asking participants to rate their current mood on a 10-point scale, using the following wording:

"eMotion Trial: *Please rate your current mood on a scale of 1 to 10, where 1 = sad and 10 = happy*" (adapted from research by van Rijsbergen et al (2012)).

The message was sent via the 'Text local' service twice daily for five days, using a predefined schedule (table 1) to ensure measurements were spread across weekdays and weekends, and throughout the day. Participants were not made aware of the schedule, or the time periods prior to prompts over which we were analysing physical activity. Each message prompted participants to respond by text with the number which best represented their current mood. The mood score was time stamped based on when the participant responded. Where responses gave a mood range (e.g. 3-4) the average value was recorded. Non-numerical responses, or numerical responses outside the allowed range (1 to 10), were treated as missing and excluded from analysis. Mood responses were regarded as invalid if they were returned the day after the prompt was sent.

Demographic data: Baseline data were collected (prior to any EMA assessment) on gender, age, ethnicity, employment status, education level, and whether the participant was receiving antidepressant medication or psychotherapy. Baseline depression was also measured using the PHQ-8 (Kroenke et al., 2009).

Data management: Data were stored on secure, encrypted university servers using anonymised file names, in line with UK data protection law.

Data Analysis

Physical activity data extraction and processing: Physical activity was extracted in one and three hour windows before the time each valid mood measure was returned. For each of these time periods, each minute of physical activity was categorised by intensity as MVPA, LPA or LMVPA. Data were extracted from the accelerometers using GENEActiv PC software into CSV files displaying total x, y, and z acceleration, and a single gravity-subtracted vector magnitude, the Euclidean Norm Minus One (ENMO), was created and aggregated over 1 second epochs.

ENMO (mg) =
$$\left(\sqrt{x^2 + y^2 + z^2}\right) - 1$$

The CSV files were processed in Microsoft Excel, where time spent in each activity intensity for each epoch was established using previously published cut-points reported in Esliger et al. (2011) that were adjusted for hand-dominance and converted into ENMO. These were, for left and right wrist respectively: between ≥45.2mg and <134.4mg, and between ≥80.4mg and <91.7mg for LPA; <134.4mg, and <91.7mg for MVPA; and <45.2mg and <80.4mg for LMVPA. We did not differentiate sleep time from inactivity.

Statistical analyses: Repeated measures of mood were considered to be clustered within each participant (Kanning and Schlicht, 2010) in that data values from within the same participant were more likely to be similar than values from different participants.

Multi-level statistical analysis was therefore used to account for intra-individual (level 1) and inter-individual (level 2) variation. An initial examination of the distribution of within- and between-person variance in mood items was carried out by examining the intraclass correlation (ICC) statistics from null multilevel models (no predictors).

Level-1 predictors were person-mean centred (i.e. assessment score minus person-mean) to test the within-person association and the person-mean scores were then centred by the grand

mean (i.e. person-mean minus grand mean) to test the between-person association. As recommended for all analysis of intensive longitudinal data, time of day was included as a fixed effect to control for any spurious effects due to time (Bolger and Laurenceau, 2013). Important covariates were also included in the model: age, gender, receipt of anti-depressive treatment (antidepressants or psychotherapy), and baseline depression (PHQ-8 score). We aimed to enter all Level-1 predictors as random effects to ensure maximal random effects (Barr et al., 2013); however, insufficient variance in the within-person effects led to model convergence problems and so the random effects were omitted. The formula of the random intercept model for the primary hypothesis was:

$$mood_{ti} = \beta_{00} + \beta_{10}MVPA_{ti} + \beta_{01}MVPA_{0i} + \beta_{20}Time_{ti} + \beta_{02}Age_{0i} + \beta_{03}Gender_{0i} + \beta_{04}Treatment_{0i} + \beta_{05}PHQ_{0i} + u_{0i} + e_{ti}$$

Where $mood_{ti}$ - the estimated mood for individual (i) at time-point (t) – is a function of the average intercept (β_{00}), the average within-person change in mood associated with a 1-minute positive deviation from person-mean MVPA (β_{10}), the average between-person change in mood associated with a positive 1-minute deviation in person-mean MVPA from the population grand-mean MVPA (β_{01}), the average change associated with of a 1-hour increase in time (β_{20}), the average change associated with a 1-year difference in age (β_{02}), the average change associated with a 1-year difference in age (β_{02}), the average difference between males (0) and females (1) (β_{03}), the average difference between males (0) and antidepressant treatment (1) (β_{04}), the average change associated with a 1-unit difference in PHQ-8 scored (β_{05}), plus individual-level residual variance in the intercept (u_{0i}) assessment-level residuals (e_{ti}).

The primary analysis tested the study hypothesis relating MVPA over a one-hour time period to mood. Secondary analyses were then used to explore the relationships between different intensities of physical activity measured over three hours and subsequent mood. Multilevel

linear regression models were generated with SPSS (IBM Corp, 2017. IBM SPSS Statistics for Windows, Version 25. Armonk, NY: IBM Corp), using the 'mixed' command, and full maximum likelihood estimations. A linear relationship between the outcome and predictor variables was assumed. Like linear regression models, multilevel models assume that outcome variables are normally distributed. This assumption was assessed visually using histograms.

For all tests of statistical significance, the alpha level was set at 0.05. Bonferroni corrections were not applied to the secondary analyses, as these analyses were deemed to be exploratory (and to be interpreted accordingly). Coefficients are presented as change in mood for every minute of activity.

Ethics

This study received ethical approval from the University of Exeter Sports and Health Sciences Research Ethics Committee (AM160316-21 151021/B/03).

Results

Descriptive statistics

Participant demographics from the 43 people who consented to take part and returned both accelerometer and mood data are reported in Table 2. Participants had a mean baseline depression score (as measured by the PHQ-8) of 14.5 (standard deviation (SD) = 3.1), where a score of 10 - 14 is indicative of moderate depression, and 15 - 19 of moderately severe depression (Kroenke et al., 2009). The analysis included 388 pairs of matched mood and physical activity data. Participants responded to a mean of 9 out of 10 text prompts (90%), with 36 text prompts not answered, three consisting of spoilt or non-numerical data, and three which were discounted as mood scores were returned the following day.

Average physical activity levels during the one and three hours preceding mood measurements over the whole week of the study are presented in Table 3. All physical activity data were non-normally distributed, so medians and interquartile ranges are presented. Across all observations, participants had a mean mood score of 5.44 (SD = 1.98) on a 10-point scale (ICC = 0.42), and completed a median of 0.4 mins (interquartile range = 0.1 - 1.8) of MVPA in the hour preceding each mood score (ICC = 0.22).

Primary hypothesis

Table 4 shows the coefficients relating physical activity and mood for all the primary and secondary analyses. Within-persons, no statistically significant relationship was found between the amount of MVPA completed over the hour preceding mood measurement and subsequent mood (β_1 coefficient = 0.05, confidence interval (CI) = -0.008 – 0.099, p = 0.095).

Secondary data analysis

There was no statistically significant within-person association between MVPA and subsequent mood over the three-hour time window (β_1 coefficient = 0.045, CI = -0.026 – 0.115, p = 0.217), or between LPA and subsequent mood over either one-hour (β_1 coefficient = 0.023, CI = -0.004 – 0.048, p = 0.094) or three hour (β_1 coefficient = 0.032, CI = -0.005 – 0.071, p = 0.091) windows.

However, engaging in more physical activity of any intensity (LMVPA) than usual was associated with a 0.023 increase in mood for each additional minute of activity in the previous hour (β_1 coefficient = 0.023, CI = 0.001 – 0.045, p = 0.037). This means 10 minutes more LMVPA than usual would equate to an increase in 0.1 standard deviations of mood (weak effect size (Cohen, 1988)) A 0.028 increase in mood was associated with engaging in more LMVPA than usual over the previous three hours but the relationship was not statically

significant (β_1 coefficient = 0.028, CI = -0.001 - 0.058, p = 0.062). No between-person effects of activity on mood were evident.

Discussion

Summary of findings

No significant relationship was found between mood and minutes of MVPA completed in the hour preceding mood measurement. However, the median amount of MVPA detected in the one hour time window (0.4 minutes) was very small, and it is therefore hard to draw firm conclusions about the association between MVPA and subsequent mood given the low variability in this dataset. It is possible that this relationship might have reached significance in a larger dataset, with more participants and more mood measures taken per participant.

Our secondary analyses showed a statistically significant positive relationship between mood and combined activity (i.e. LMVPA) over the hour preceding mood measurement. Ten minutes of LMVPA would equate to a change of 0.1 standard deviations in mood, suggesting a weak effect size (using Cohen's criteria) (Cohen, 1988). Additionally, increasing inactive time showed a statistically significant negative association with mood over the hour preceding mood measurement; this association was of the same magnitude as that of the positive relationship between LMVPA and subsequent mood.

Relationship to other literature

Mata et al (2012) showed that a clear positive association between activity dose (intensity and duration) and subsequent positive affect in people with depression. This may be due to the greater number of participants who were sampled more frequently in Mata et al (2012). However, Mata et al. (2012) used self-reported physical activity (in bouts of activity of at least five minutes) which could have been influenced by the participants current mood states

(Drace, 2013). Bouts of physical activity may also have a different relationship with mood than overall activity (as measured in the present study) and could be another explanation for the stronger relationship.

Stavrakakis et al. (2015) and Kim et al. (2015) both used accelerometers to record physical activity in people with depression. Stavrakakis et al. (2015) examined individual differences in the relationship between total energy expenditure in the six hour period preceding affect measurement in depressed and non-depressed individuals. A positive relationship between energy expenditure and positive affect was found in the majority of depressed participants, but was only significant in two out of 10 depressed individuals. The small median effect sizes for depressed individuals was comparable to that of LMVPA in the present study despite the longer time frame of activity sampled prior to mood measurement.

In the present study, the analysis was focused on defined physical activity intensity cut-offs to aim to further characterise the relationship between physical activity and mood. This study struggled to capture instances of MVPA, which is not unexpected in this population, and has been seen in other studies with inactive samples (von Haaren et al., 2013). Other studies using more objective physical activity data collection protocols in people with depression (Kim et al., 2015; Stavrakakis et al., 2015) and other low activity adults such as inactive students (Bossmann et al., 2013) and older people (Kanning et al., 2015) do not examine different intensity cut offs. As such, their reported total energy expenditure or activity counts may include small instances of activity that would not have met the threshold for LPA in the present study. Short sampling periods (one to three days) and narrow activity analysis windows before mood measurement (10 to 15 minutes) used by Kanning et al. (2015), von Haaren et al. (2013), and Bossmann et al. (2013) may make it more challenging to sample higher intensity physical activity if it is already rarely occurring. Moreover, these studies offer contradictory conclusions as to which dimensions of affect show a significant

relationship with physical activity. There therefore remains scope for further investigation into the relationship between difference activity intensities and subsequent affect.

Strengths

The strengths of the study were the more objective measurement of physical activity using accelerometers, and the electronic time-stamped EMA methodology, as recommended by Kanning et al (2013). There were also very little missing data, suggesting high internal validity and a low participant burden. The simple text-based service used is cost-effective, and compatible with a wide range of participants' phones. There are however several limitations that need to be acknowledged.

Limitations

Our sample was 81% female; this is common within EMA research (Liao et al., 2015b), but may limit the generalisability of the findings to males, especially as there is evidence suggesting that optimal physical activity intensity may differ by gender (Asztalos et al., 2010). Mood measures were time-stamped based on when they were returned by text. It was assumed that participants were reporting their mood at the time of completing the measure, and not recalling to when the text was sent. In future studies, the question wording and study information should clearly instruct participants to record their mood at the time when they are responding. Our study did not use a random prompt design, which may have led to participants anticipating prompts and adjusting their physical activity behaviour accordingly. However, the prompt schedule varied for each day of data collection, and the schedule and physical activity windows analysed prior to prompts was not made known to participants in advance.

The present study used a single item measure of mood. This continuous 10-point scale was based on the visual analogue scale used by van Rijsbergen et al. (2012), that has been able to predict relapse in people with depression, but has not been validated against other measures of mood (van Rijsbergen et al., 2012). It does also not separate out positive and negative affect dimensions of mood, as captured in measures such as the Positive and Negative Affect Scale (Watson et al., 1988). In the present study we were interested in capturing the overall mood state, in such that "happy" would encompass the high pole of positive affect, and the low pole of negative effect (and vice versa for "sad"). However, different dimensions of mood may have a different distinct relationship with physical activity that would not be captured in our results. Other EMA studies have captured mood using validated multiple item questionnaires, such as the Positive and Negative Affect Schedule (20-item) or the Multidimensional Mood Questionnaire (MDMQ) (30-item). However, these longer measures would have been relatively burdensome for taking frequent repeated measurements from participants in the present study, who were taking part in a wider trial, and would have been difficult to administer using the "text local" service that was employed.

As with other studies of low-active adults (von Haaren et al., 2013), there were difficulties when sampling from a relatively inactive population. The inactive nature of our sample made it harder to sample periods of MVPA in particular, as this occurred infrequently. This may have reduced the sensitivity of our analysis to detect associations between MVPA and mood. Our twice-daily sampling protocol was relatively infrequent compared to other studies, which have measured mood up to 12 times a day (Liao et al., 2015b). Sampling more frequently in the day may however may have made the study less acceptable and reduce the response rate to mood requests, as participants taking part in this sub-study were also part of a wider trial and overall burden had to be considered. It is also difficult to compare response rate to other studies as this is often poorly reported (Liao et al., 2015b; Liao et al., 2016b). However, given

the high 90% response rate, a more frequent sampling protocol could be adopted in future studies.

It is possible that mood scores may have been predicted by previous mood rather than previous physical activity. However, a lagged analysis was not possible in present study due to the number of data points. Due to the relatively low sample size, the models would not converge with random slopes included. This meant we were unable to detect the extent to which people varied in the observed within-person effect, which is an important limitation that must be addressed in future research.

Whilst a strength of the study is the use of objectively measured physical activity, accelerometry does have a number of limitations. Whilst the present study used a minimum wear time of 4 days with 10 hours for a valid day (Trost et al., 2005), it is acknowledged that longer wear periods provide more precise estimates of physical activity (Price et al., 2018), yet may result in a smaller sample and selection bias if low adherence to wear time is observed (Price et al., 2018). In addition, there is still some activities which accelerometers are unable to capture (e.g. cycling) which is a known limitation (Mannini et al., 2013).

Finally, it is worth noting that our method of extracting data from the accelerometery records could not differentiate inactivity from sleep time. This may be an issue (particularly for analyses relating to the three-hour time window) as sleep time may have a different relationship with mood than inactivity. However, if sleep time were affecting the data substantially, we would expect the responses to the earliest (9 am) data request to be the most affected. No such pattern was seen in the data and time of day was not a significant covariate in any of the models, even with a 3-hour time window (see Supplementary File). Nevertheless, future studies of this type should consider including methods for identification of sleep time in the protocol for data collection and analysis.

Future directions

In order to address the limitations of this study, further research is needed to explore the dynamics of the relationship between mood and physical activity in depressed populations, using well-powered studies with more objective measures of physical activity and well-validated (and brief) mood scales, as well as methodologies that can maximise the detection of (relatively infrequent) bouts of MVPA.

As highlighted above, better characterisation of the dynamics of the temporal relationship between physical activity and mood could help guide strategies for alleviating low mood in people with depression. More research with larger samples and more intensive measurement regimes is required to further characterise the boundaries relationship between activity patterns, bout length and subsequent mood. This could help to specify optimal time periods to sample physical activity before or after mood measurement, as well as furthering investigation into individual differences in the relationship between physical activity and mood, which must be addressed in order to aid future prescription of exercise for optimizing mental health.

An alternative approach for detecting activity in inactive samples is interactive multimodal ambulatory assessment (Ebner-Priemer et al., 2012). This uses an algorithm to monitor physical activity continuously and participants are prompted to complete mood measures when activity surpasses a threshold, in addition to random sampling during inactive periods (Ebner-Priemer et al., 2012). Ebner-Priemer et al report that this method detects bouts of physical activity four times as frequently as random sampling alone (Ebner-Priemer et al., 2012). This approach could be useful in examining samples where activity rarely occurs, and for use in shorter time windows where capturing activity is more difficult.

It may also be worth investigating the mediating effects of other determinants on the relationship between mood and physical activity, including baseline fitness, enjoyment of physical activity (including experiences of side effects such as fatigue or muscle ache), type of physical activity, perceived autonomy (Deci and Ryan, 2000), and the environmental (White et al., 2016) and social context in which physical activity occurs (Dunton et al., 2015; Liao et al., 2015a).

To conclude, no association was found between the amount of MVPA in the hour preceding mood measurement and subsequent mood. However, our secondary analyses found that overall time spent engaging in any level of physical activity (light, moderate or vigorous) was significantly associated with improved mood one hour later, and that time spent inactive was associated with subsequent negative mood, of the same magnitude. These data are only exploratory however and further research is needed to more clearly define the dynamics of the relationship between physical activity and low mood.

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