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Temporal Dynamics of Arousal and Attention in 12-Month-Old Infants

ABSTRACT: Research from the animal literature suggests that dynamic, ongoing changes in arousal lead to dynamic changes in an individual's state of anticipatory readiness, influencing how individuals distribute their attention to the environment. However, multiple peripheral indices exist for studying arousal in humans, each showing change on different temporal scales, challenging whether arousal is best characterized as a unitary or a heterogeneous construct. Here, in 53 typical 12-month-olds, we recorded heart rate (HR), head movement patterns, electrodermal activity (EDA), and attention (indexed via look duration) during the presentation of 20 min of mixed animations and TV clips. We also examined triggers for high arousal episodes. Using cross-correlations and auto-correlations, we found that HR and head movement show strong covariance on a sub-minute scale, with changes in head movement consistently preceding changes in HR. EDA showed significant covariance with both, but on much larger time-scales. HR and head movement showed consistent relationships with look duration, but the relationship is temporally specific: relations are observed between head movement, HR and look duration at 30 s time-lag, but not at larger time intervals. No comparable relationships were found for EDA. Changes in head movement and HR occurred before changes in look duration, but not for EDA. Our results suggest that consistent patterns of covariation between heart rate, head movement and EDA can be identified, albeit on different time-scales, and that associations with look duration are present for head movement and heart rate, but not for EDA. Our results suggests that there is a single construct of arousal that can identified across multiple measures, and that phasic changes in arousal precede phasic changes in look duration. © 2016 Wiley Periodicals, Inc. *Dev Psychobiol* 58:623–639, 2016.

Keywords: infant; attention; arousal; dynamic; naturalistic; cross-correlation

INTRODUCTION

Arousal, understood as activity within the Autonomic Nervous System (ANS), is considered to be integrally related to attention (Broadhurst, 1957; Yerkes & Dodson, 1908). The arousal/alertness attentional subsystem, which is the first to become functionally mature (Johnson, 1990), is thought to be involved in mediating anticipatory

readiness, or alertness for incoming stimuli (Colombo, 2001). Sympathetic nervous system activity has neuromodulatory effects on frontal areas critical for attention and executive functions (Arnsten & Goldman-Rakic, 1984). Early abnormalities within this subsystem have been linked to cascade-like patterns of impaired development in other attentional subcomponents (Geva & Feldman, 2008; Geva et al., 2013).

Neural control of the ANS originates in the brain stem and hypothalamus. The hypothalamus, just above the brain stem, acts as an integrator for autonomic functions, and receives input from upstream cortical areas such as the insular cortex and limbic systems (Cechetto & Chen, 1990; Ulrich-Lai & Herman, 2009). Regulation of ANS function also involves homeostatic feedback loops involving endocrine as well as neural

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systems, such as the hypothalamic-pituitary-adrenal axis (Tsigos & Chrousos, 2002). Direct measurement of ANS activity, such as single cell recording from brainstem synapses, is common in animal research (Aston-Jones, Rajkowski, & Cohen, 1999; Usher, Cohen, Servan-Schreiber, Rajkowski, & Aston-Jones, 1999) but is not possible in humans. Almost all research with humans, therefore, has used one of several peripheral indices of ANS activity—such as heart rate, movement patterns, electrodermal activity (EDA), pupil size or EEG.

The ANS is in constant flux, contributed to by both endogenous factors on multiple time-scales (from circadian cycles through to temper tantrums), as well as exogenous factors (such as sudden loud noises) (Foote, Aston-Jones, & Bloom, 1980). In our previous research, we have explored dynamic changes in infant looking behaviors as predicted by neurobiological theories of attention and ANS activation (de Barbaro, Chiba, & Deák, 2011). More recently, we measured arousal using a composite of measures and showed that short-term variability in arousal associates with short-term variability in attention capacities (de Barbaro, Clackson, & Wass, in press). Using cross-correlations and linear mixed effects models we showed that short-term variability in arousal associates with short-term variability in attention capacities. Attention capacities were indexed by measuring look duration towards a continuous stream of novel visual information (de Barbaro et al., in press). These results were as predicted by the Aston-Jones model of attention, which states that at very low levels of arousal animals are relatively unresponsive to changes in external stimuli, whereas at high levels, animals are highly sensitive to peripheral change. At moderate levels of arousal, individuals can focus on a target stimulus, even in the presence of peripheral distractors (Aston-Jones & Cohen, 2005).

The Aston-Jones model, based on animal research, was derived by taking single cell recording from norepinephrine neurons in the Locus Coeruleus, a brainstem arousal nucleus (Usher et al., 1999). It remains unknown, however, whether the peripheral arousal indices used with human participants measure a single construct of arousal, as considered by the Aston-Jones model, or instead measure multiple, fractionable arousal subsystems. Of particular interest here is the question of sympathetic and parasympathetic subsystems within the ANS. Some peripheral indices of ANS function, such as EDA, are thought primarily to measure activity within the sympathetic nervous system (Shields, Macdowell, Fairchild, & Campbell, 1987), whereas others, such as heart rate, are thought to show contributions from both the parasympathetic and sympathetic subsystems (McCabe & Schneiderman, 2000).

In fact, surprisingly little previous research has investigated whether the different peripheral arousal indices conventionally used in human research co-vary with one another (Lacey, 1967; Loewenfeld, 1993; Quas et al., 2014; Sanders, 1983; Taylor & Epstein, 1967). Much research with human participants measures just a single ANS measure, and links it to behavior, leaving open the question of whether different peripheral arousal systems may be activated to different degrees independently of one another—and of whether each system has its own biological instantiation that results in different properties. This makes the task of interpreting results across different studies, that have used different measures, challenging.

In a recent study, Quas et al. (2014) looked at patterns of covariation in impedance cardiography, respiratory sinus arrhythmia, heart rate, and salivary cortisol in 664 4- to 14-year-olds in response to stress reactivity challenges. They used latent profile analyses to identify different patterns of covariation of change across measures in different children—differences that they linked to childrens' socioeconomic status, family adversity, and age. Although hugely informative, the approach used only examined static (time invariant) change, based on comparing the average response observed during the “stressor” with an average response observed during a baseline period. They do not look at patterns of covariance of change over time.

In a previous report, we examined tonic and phasic patterns of covariation between heart rate, EDA, pupil size, head movement velocity, and peripheral accelerometry in a cohort of 37 typical 12-month-old infants during the completion of a 20 min testing battery (Wass, de Barbaro, & Clackson, 2015). We analyzed co-variation of these autonomic indices in three ways: (i) correlations in tonic (baseline) arousal levels; (ii) co-variation in immediate phasic changes following the presentation of an attention-getting external stimulus; and (iii) patterns of co-variation in spontaneous changes during testing, relative to baseline. Across all three analyses, we found that heart rate, head velocity, and peripheral accelerometry showed strong positive co-variation. EDA showed no co-variation in tonic activity levels but did show phasic positive co-variation with other measures that appeared limited to sections of high but not low general arousal. Tonic pupil size showed significant positive co-variation, but phasic pupil changes were inconsistent.

However, three further, and vital, questions were not addressed in this previous work. The first is: do these different autonomic indices show different, or similar, patterns of association with attention? Previously, we found that EDA showed significant co-variation in patterns of spontaneous, phasic change with heart rate

and movement (albeit limited to sections of high, but not low, general arousal). However, when we examined change relative to the onset of a new stimulus (a previously unviewed picture), changes in heart rate and movement were detectable, but changes in EDA were not. Relatedly, it may be that different peripheral measures may show significant co-variation with *each other*, but not with changes in attention. For our measure of attention we used look duration, calculated as the length of time an infant spent looking at the screen (anywhere on the screen) before looking away from the screen, during the presentation of a testing battery consisting of a mixture of previously unviewed static and dynamic viewing materials (cf. Richards, 2004). Look duration is widely studied as an index of overt shifts of attention in infants, and considerable previous work has investigated the relationship between look duration and single indices of arousal, such as heart rate (e.g., Colombo et al., 2010; Richards & Casey, 1991; Richards & Gibson, 1997).

The second question, related, question is: how temporally specific are changes in each of these ANS measures, and attention? Traditionally, research into arousal has distinguished between *tonic* and *phasic* aspects. Tonic activation refers to shifts in the overall baseline of activity, whereas phasic activity refers to fluctuations over time, which may occur spontaneously or in response to an event. However, in practice, the distinction between tonic and phasic aspects of arousal activity is not clearly defined. Slow-moving trends in arousal activity that occur during the testing session can also be considered tonic shifts, and these slow-moving changes can systematically influence the degree of phasic changes relative to new stimulus events (Aston-Jones & Cohen, 2005). However, no clear cut-off exists between tonic and phasic shifts, and different approaches used during baselining may be confounding differences between studies. For example, some studies record a baseline at the start of the testing session, whereas others take the average over the entire session as the baseline. A third alternative is to take individual baselines immediately preceding each event to be analyzed. These differences may radically influence the results obtained. In order to examine an appropriate time-scale on which to measure changes in arousal and attention we wished to assess two aspects of our data: first, how fast-changing are the measures themselves (i.e., do they show a fast rate of change or a slow one?), and second, are relationships between measures, and with attention, observed on certain time-scales, but not on others?

A third, and again related, question is: do changes in one arousal index tend to occur before, or after, changes in another—and if so to what degree (Sforza,

Jouny, & Ibanez, 2000)? Our previous analyses used zero-lagged correlations to examine phasic associations between levels on measure and on another measure at that same moment in time (Wass et al., 2015). It is possible, however, that changes in one measure may tend temporally to precede changes in another—relationships that would not be detected using zero-lagged analyses. This is particularly the case if one measure (e.g., EDA) shows a slower rate of change than another (e.g., movement). Previous research has suggested that, whereas EDA increases following an arousing stimulus are slow and typically detectable on a scale of seconds (e.g., Kylliainen et al., 2012), changes in motor activity are detectable on a millisecond scale (e.g., Robertson & Johnson, 2009).

In the present study, we addressed these three questions. We recorded heart rate (HR), head velocity (HV), and electrodermal activity (EDA) data in 53 typically developing 12-month-old infants while they completed a testing battery that lasted approximately 20 min, and consisted of a mixture of novel (previously unviewed) infant-appropriate static and dynamic stimuli. Look duration was coded throughout the battery and treated as a continuous variable in the same way as our arousal measures.

Our previous analyses were based on “zero-lagged” correlational analyses. Thus, for example, we asked: “how does heart rate at a particular moment in time relate to EDA *at that same moment* in time?” Here, we introduce time-lags into the analyses, using techniques based on cross-correlations and auto-correlations. This allows us to ask, for example: “how does EDA at a particular moment in time relate to heart rate, just before, and just after, that moment?” We present three different analyses. Analysis 1 uses time-series analysis techniques to examine the temporal order of changes, within our arousal measures. Analysis 2 looks at how different arousal indices change relative to moments of particularly elevated arousal. Analysis 3 uses the same techniques as analysis 1 to examine how changes in our arousal indices relate to changes in look duration.

METHOD

Participants

The analyses presented in this paper are based on data collected from 53 typically developing infants. Volunteers were recruited from the volunteer participant pool for the Medical Research Council in Cambridge. The average age of participants was 12.3 months (mean age in days: 357, SD: 39, range: 315–501). The gender ratio was 27M/26F. Although detailed socio-economic or ethnic data were not collected as part of this study, it

should be noted that the recruitment area is a relatively wealthy, university town. Autonomic data collected from a subset of these infants (37) forms the basis for a previous paper looking at patterns of covariation between different autonomic measures (Wass et al., 2015). However, the present paper contains completely new analyses, addressing overlapping research questions, as described in detail in the Introduction.

Materials and Procedure

Equipment and Materials. Infants were seated on their caregivers' laps during recording. Viewing materials were presented using a Tobii TX300 eyetracker subtending approximately 30° of visual angle. Stimulus presentation was performed using Matlab, Psychtoolbox, and the Matlab Tobii SDK.

Electro-cardiogram (ECG) and EDA were recorded using a BioPac™ (Santa Barbara, CA) recording at 1,000 Hz. ECG was recorded using disposable Ag-Cl electrodes placed in a modified lead II position, on the right clavicle and the bottom of the left rib-cage. EDA was recorded using two EDA (isotonic gel) snap electrodes placed on the outer surface of the right foot (following the locations suggested in Ham & Tronick, 2008).

Head velocity data were derived from the head position estimates that are automatically calculated by

the eyetracker during heads-free eyetracking. Heads-free tracking is tracking in which the participant is not required to rest their head on a chin rest, but is allowed to move their head freely during recording. They were recorded by a Tobii TX300 eyetracker. The process used to extract this data are described by Wass et al. (2015).

In the original paper, data from pupil size and peripheral accelerometry were also included. In the present paper, we have omitted these measures. Pupil size was omitted because we were concerned that the unpredicted negative changes in pupil size values, we observed may have been attributable to the fact that some stages of the testing battery showed higher on-screen luminance than others, and that these sections may have been more arousing, thus confounding results. Peripheral accelerometry was omitted because results were, throughout, extremely similar to head velocity (as expected, given that both measures index body movement).

Testing Battery. Administration of the testing battery lasted approximately 20 min per participant. The battery consisted of a mixture of static images and infant-appropriate animations and TV clips (see Fig. 1). It was generally presented unbroken in one block, although on the rare occasions when an infant had become distressed a break was taken during testing and

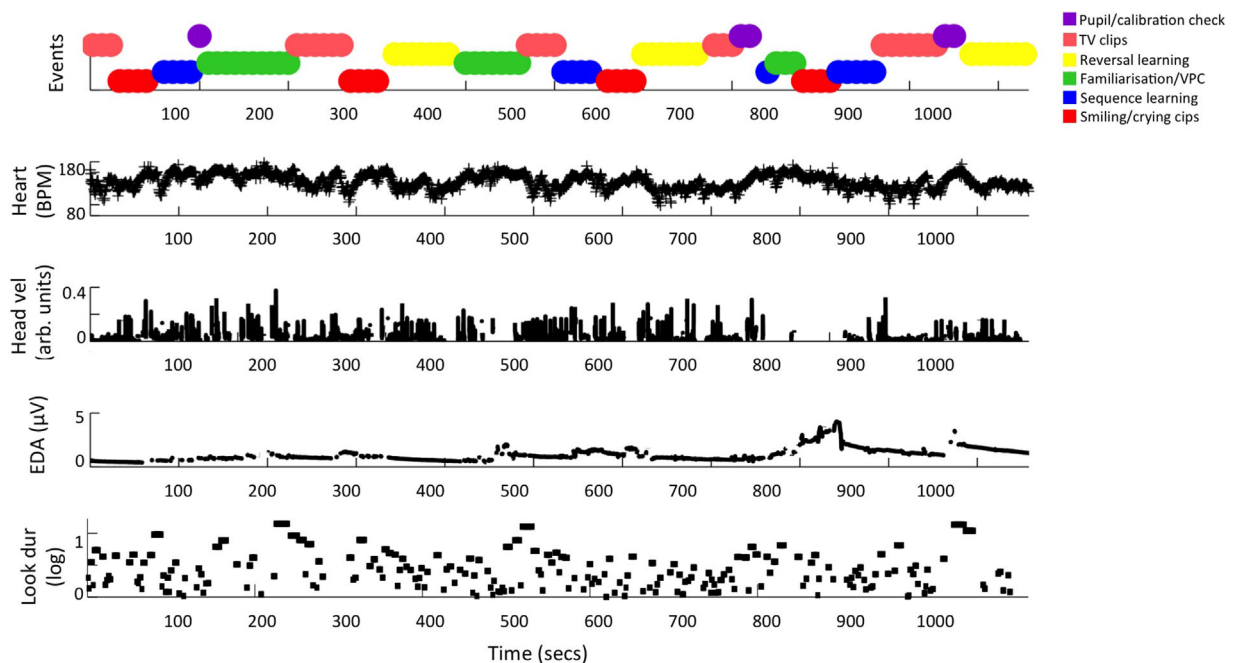


FIGURE 1 Raw data sample from an individual infant, showing the arousal measures recorded, prior to data reduction. From top to bottom: (i) events (the behavioural tasks presented); (ii) heart rate; (iii) head velocity; (iv) EDA; (v) look duration.

the battery re-commenced (never more than once during testing). On these instances data were not concatenated; rather the section of missing data were left blank, and excluded from all analyses. Viewing materials consisted of a mixture of photographs (such as pictures of another child's face, or hand-drawn images) and video clips (child-appropriate home movies and excerpts from children's television programs). The maximum length of each individual stimulus was 45 s, and most were less than 20 s. Calibration was performed prior to the commencement of the battery. The viewing battery, and the experimental protocols followed during its administration, were identical to that used in the previous study (Wass et al., 2015).

Data Reduction

All data reduction techniques were identical to those used previously (Wass et al., 2015). To summarize, briefly:

Heart Rate (HR). Automatic *r*-peak identification was performed by the Acknowledge commercial software package. Automatic artifact rejection was then performed by excluding those beats showing an inter-beat interval of <330 or >750 ms, and by excluding those samples showing a rate of change of inter-beat interval of greater than 80 ms between samples. In another paper by Wass et al. (2015), we report on a comparison of these cleaning techniques with traditional hand-coding which shows a close comparison between the two approaches. Finally, HR data were epoched into 1 s epochs and then z-scored. Epoching was performed by calculating the median value obtained within each epoch, and excluding epochs with greater than 80% of missing data for that epoch. Z-scoring was conducted by first calculating the mean and standard deviation obtained across the whole session for that individual and then calculating the distance of that epoch, in terms of standard deviations, from the mean. Epochs showing a difference of greater than \pm two standard deviations were capped at two.

Electrodermal Activity (EDA). Again, our approach was similar to that previously used with developmental populations (Ham & Tronick, 2008; Hernes et al., 2002). First, null values were removed from the data using a threshold of $.1 \mu\text{V}$. Second, data were log transformed to correct for positive skew in the data. Third, data were z-scored and epoched into 1 s epochs, as described above.

Head Velocity (HV). First, data samples showing a change in position of more than .025 screen units (2.5% of the total screen size) between 120 Hz iterations were excluded as being above the maximum possible threshold

at which head movement can take place and therefore likely to be artifactual. This level was set following visual comparison of the data obtained, compared across a range of individuals (see Wass, Forssman, & Leppanen, 2014). This threshold corresponds to 2.5% of the screen, representing approximately 1.25 cm in our set-up. Second, data were downsampled to 12 Hz by calculating a moving median window. Third, position data were converted to velocity data by taking the first derivative (calculating the change, in absolute values, between one sample and the next). Fourth, six data streams (three dimensions, two eyes) were collapsed to a single stream. Fifth, data were z-scored and epoched into 1 s epochs, as described above.

Look Duration. Traditionally, research based on look duration has measured the duration of looks to static (Colombo et al., 2010) or dynamic (Richards, 2004) images, generally presented on a computer screen. For the present paper, since we wished to analyze continuous looking data over a 20 min period, we have recorded a slightly different measure—namely the duration of all looks towards the screen during the presentation of the entire mixed testing battery (described above). Note that each look duration indicates how long the child looked at the screen (anywhere on the screen) before looking away from the screen, rather than the duration of each individual fixation. For comparison, in the Supplementary Materials we have also presented just the results obtained during a subsection of that battery, namely an infant-controlled habituation protocol. This protocol measures infant's looks toward a static image, in a way that is identical to that used in previous research (Colombo et al., 2010). Results obtained were highly similar across the two analyses. For the analyses presented in the main text, look duration was automatically coded based on the eyetracker footage recorded. Looks were treated as starting when the child first looked towards the screen, and ending when the child looked away from the screen. This was derived as the time interval between the moment when the eyetracker data first detected the child's gaze, and the moment where it ceased to detect it any more. Very short sections of missing data (<2 s) were interpolated, to cover short periods of missing data due to blinks and other artifactual causes (see further discussion of this in Wass et al., 2014). In the Supplementary Materials, we present results from a similar analysis based on hand-coded data.

Calculation of Cross-Correlation and Auto-Correlation

Our data consist of continuous time-series data, recorded over a 20 min testing session. First, these data

were time-synchronized and epoched, into 1 s epochs. A 1 s epoch duration was selected based on previous work, in which we perform systematic analyses to compare how relationships between measures change as a function of varying the epoch duration (Wass et al., 2015).

Two aspects of our data were of interest for the present analyses. Firstly, the extent to which two measures might be cross-correlated—that is, the degree to which they would show a relationship if a time-lag is introduced between them. This analysis would reveal how changes in one measure are temporally related to changes in another measure. Secondly, the extent to which each measure might be auto-correlated—that is, the degree to which each measure, considered individually, shows a relationship with itself if a time-lag is introduced. The auto-correlation essentially indicates whether a particular measure is fast- or slow-changing.

The procedure for calculating the cross-correlations between measures were as follows. First, we calculated the average correlation between values obtained for those measures across all epochs, using a Spearman's non-parametric correlation (since results obtained for some epochs were non-normally distributed). This correlation value was calculated independently for each participant, based on all epochs available for that participant (c.1,200 per individual). A single average correlation value was then calculated by averaging across participants. This average correlation value is shown as the value at Time 0. Next, correlations were calculated in the same manner at each time-lag by shifting one measure forwards and backwards in time, relative to the other.

Next, auto-correlations were calculated for each measure. These were conducted identically to the cross-correlations—except that instead of examining the relationship of two different measures at variable time intervals, the relationship of each measure *to itself* at variable time intervals was assessed. All measures will therefore have a correlation of 1 at Time 0. How steeply the graph falls off either side of this point indicates how fast-changing a measure is, or how much “momentum” it has: a sharper incline indicates a fast changing measure, and a shallower incline, a slower changing measure. In addition, if the auto-correlation function dips below zero at any point this can indicate periodicities in the data.

Calculating the significance levels of the auto-correlations is straightforward, and is based on the significance values of the Spearman's correlations conducted at each time interval. Calculating the significance levels of the cross-correlations is, however, non-trivial, since the values obtained for the cross-correlation (the degree to which the relationship between two measures is

present if a time-lag is introduced between them) is confounded by the degree of auto-correlation (the degree to which each measure, considered individually, is fast- or slow-changing) (Clifford, Richardson, & Hemon, 1989; Thiebaut & Zwiers, 1984). This potential problem in cross-correlations can be solved by first calculating the Effective Sample Size (Clifford et al., 1989; Thiebaut & Zwiers, 1984): at each time interval, the cross-correlation (i.e., the relationship between the two variables) was first calculated, and then the auto-correlation value for each variable (i.e. the relationship of that variable to itself, at that time-lag) was then calculated. The higher of these two values was used to calculate the Effective Sample Size, using the standard formula: $N^* = N (1 - \frac{r}{(1+r)})$, where N^* is the Effective Sample Size, N is the actual sample size and r is the higher of the two auto-correlation values obtained at that time interval for each of the two measures independently (Thiebaut & Zwiers, 1984). The significance level of the cross-correlation obtained was then adjusted based on the Effective Sample Size. In this way, we calculated the significance level of the relationship between two variables at a particular time-lag, *independent of the relationship of each variable to itself* at that time-lag. An alternative potential solution to this problem is to perform pre-whitening to remove auto-correlation in the data prior to analyzing the cross-correlation (Martens, Hoy, Wise, Bro, & Brockhoff, 2003).

Following this calculation, we also wished to estimate whether values obtained were significantly asymmetric around the zero time point. This calculation was conducted to assess whether changes in one measure reliably *preceded* changes in the other. For example, we examined whether the correlations observed between heart rate and head velocity at $t = -20$ (heart rate at one moment in time with head velocity 20 s *before* that moment) were larger than the correlations obtained at $t = +20$ (heart rate with head velocity 20 s *after* that moment). A paired-sample *t*-test was used to assess whether these two values differed significantly. A significant finding indicates that results were significantly asymmetric around zero. Where observed, this indicates that changes in one measure tended reliably to *precede* changes in another.

RESULTS

Analysis 1—Cross-Correlation and Auto-Correlation

The first analysis examined three variables: HR, HV, and EDA. Figure 2a–c show the cross-correlations between each combination of variables. Figure 2d shows a

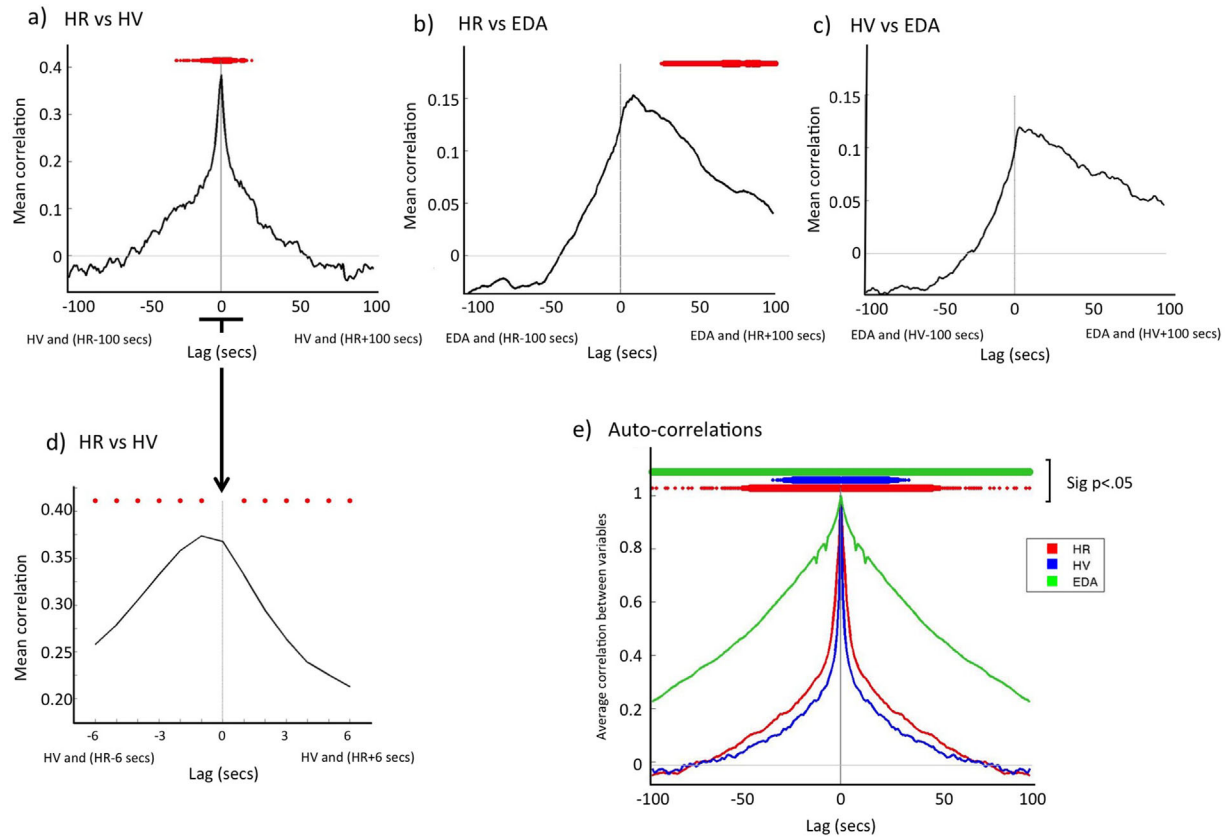


FIGURE 2 Results of cross-correlation and auto-correlation analysis, calculated as described in the text. Top (a–c)—the three pairwise cross-correlations calculated—(a) HR versus HV, (b) HR versus EDA, and (c) HV versus EDA. Y-axes show the mean correlation observed between that pair of variables. X-axes show the time-lags. Red dots above the plots show the significance levels of the analyses to examine whether a significant relationship was observed between the two measures at that moment in time, after correcting for effective sample size (small dot— $p < .05$, large dot— $p < .001$). Bottom (d)—magnification of the central section of figure a, showing the cross-correlation between HR and HV. (e) Results of auto-correlations, for HR, GSR, and HV. Coloured dots above the plot indicate whether a significant relationship was observed between that variable and itself, at each time-lag (small dot— $p < .05$, large dot— $p < .001$).

magnification of the central section of Figure 2a. Figure 2e shows the auto-correlations for each of the three variables.

We wished to examine four different questions in particular: first, how strong is the relationship between the variables at Time 0 (no lag)? Second, how rapidly does this association fall off when we increase the time intervals between the variables? Third, how asymmetric is this relationship around the Time 0 point (in other words, do changes in one measure tend generally to occur before, or after, changes in another)? Fourth, how fast-changing is each of the measures, when considered independently. In the discussion below, we discuss these four questions for each combination of variables: first, head velocity and

heart rate; second, EDA versus HR; third, EDA versus head velocity.

Head Velocity and Heart Rate. At Time 0 this is $r = .38$, suggesting a relatively strong relationship between the two measures (average $p < .001$) (Fig. 2a). Concerning our second research question, we found that at $-5/+5$ s lag the relationship is $.18/.21$, at $-10/+10$ s lag it is $.16/.14$, and at $-60/+60$ s lag it is $.007/.01$. The p -value of the correlations is significant at $p < .05$ between Time -30 and $+20$ s. This suggests that changes in the two measures are reliably associated within time-frames of 20–30 s.

Next, we considered the third question: given the strong associations between movement and heart rate,

do changes in movement tend to occur before, or after, changes in heart rate? To answer this, we can examine whether the cross-correlation plot shown in Figure 2a is asymmetric around the Time 0 point. Figure 2d shows a magnification of the central area in Figure 2a (time-lag -6 to $+6$) for heart rate and head velocity. Here, it can be seen that head movements tend to occur reliably slightly before heart rate changes: the plot is asymmetric around the zero time point, and the maximum correlation between heart rate and movement occurs between heart rate and movement one second earlier. Additional analyses, paired sample *t*-tests, were calculated to assess whether relationships observed were significantly asymmetric around the Time 0 point (as described in the Methods section above). Significant asymmetries were obtained from 8 s lag. This suggests that changes in movement tend reliably to precede changes in heart rate, but that this effect is only true within time frames of 8 s or less.

Our final question was: how fast-changing is each measure, considered independently (Fig. 2e)? Here, a value of, for example, .47 for heart rate (red line) observed at 5 s interval suggests that, across all epochs considered, the average correlation obtained between heart rate at one moment in time and heart rate 5 s after that moment is .47. Summary values from the auto-correlations for heart rate/head velocity are: 5 s lag: .47/.34; 10 s lag: .34/.26; 30 s lag: .18/.12; 75 s lag: $-.01/-.004$. Significant relationships were observed for heart rate at all time intervals up to 63 s lag, and for head velocity at all time intervals up to 34 s lag. This suggests that, in comparing heart rate and head velocity, heart rate is the slower-changing measure.

EDA and Head Velocity, and EDA and Heart Rate.

The relationships observed for EDA are markedly different. The green line on Figure 2e shows the results of the auto-correlation analysis conducted for EDA. Auto-correlation values obtained were: 5 s lag: .87; 10 s lag: .81; 30 s lag: .63. Significant relationships were observed at all time intervals measured. Although not shown on Figure 2e, the auto-correlation value of EDA does not reach 0 until 170 s. In contrast with heart rate and head velocity, it can be seen, therefore, that EDA has a much slower momentum (rate of change) than the other measures.

Next, we can examine, using cross-correlations, the relationship between EDA and both HR (Fig. 2b) and HV (Fig. 2c). In contrast to the relationship between HR and HV (Fig. 2a), it can be seen that the relations between EDA and both heart rate and head velocity are weaker, slower, and more asymmetric. First, the peak correlations observed between EDA and both HR (Fig. 2b) and HV (Fig. 2c) are markedly lower than

those observed between HR and HV (Fig. 2a). Second, whereas the relationship between HR and HV was found to be asymmetric around Time 0 only at shorter time intervals (Fig. 2d), the relationship of EDA to both HR and HV is much more asymmetric.

The red dots above Figure 2b show the significant results obtained for this analysis. Significant relationships were observed between HR and EDA at all time intervals between Time $+28$ and Time $+100$. Of note, significant correlations were not observed at the time intervals that showed the strongest correlations (Time $+5$ to $+27$) because the significance calculations correct for the degree of auto-correlation in those two measures independently at that time interval. The significance test therefore assesses the degree to which those two measures were associated with one another at that particular time interval, independent of their relationship with themselves (i.e., their degree of auto-correlation) at that same time interval. Relationships between HV and EDA were found to be similar to those between HR and EDA but, because the relationships are smaller and less consistent, these were found not to be significant.

In summary, our results suggest that EDA shows a weak but significant pattern of co-variation with HR. Similar associations were found with HV, but these were weaker and non-significant. Relationships are also markedly asymmetric, with dynamical changes in HR and HV tending to precede changes in EDA. Finally, although *increases* in EDA appear to happen as fast as increases in other measures, *decreases* in EDA appear to take place more slowly than they do for head velocity and heart rate.

Figure 3 contains a sample of data obtained from a single individual that illustrates this point clearly. It can be seen that changes in arousal are often detectable across all three measures recorded. For example, at about 350 epochs, a sudden increase can be seen in values obtained from all three measures. For HR and HV, however, activity rapidly falls back down to normal levels. For EDA, however, the period of elevated arousal is much more long-lasting.

Analysis 2—Triggers for High Arousal Episodes

Next, we wished to examine similar questions using a different analytical technique, in order to ensure that the conclusions drawn from the first analysis were robust. For our second analysis we first identified moments of high arousal—defined as moments where one value first reached a value of 1.5 standard deviations above the average for the entire testing session. We then analyzed how our other measures changed relative to these moments of high arousal.

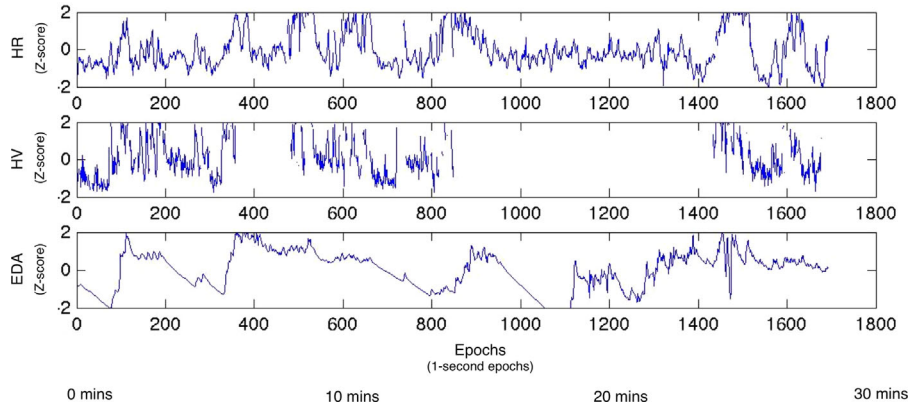


FIGURE 3 A sample showing data obtained from a single infant across a 27 min recording session. Data have been processed and epoched as described in the Methods section. From top to bottom, the plots show: heart rate (HR), head velocity (HV), and electro-dermal activity (EDA).

Figure 4 shows a demonstration of how this analysis was conducted. In this example, HR is the dependent variable. First, we looked for moments where the HR first exceeds 1.5 s.d. above mean—signalling the start of a period of particularly elevated HR. Second, we analyzed how our other measures, HV and EDA, changed relative to this point in time. As previously, we wished to understand whether moments of particularly elevated HR tend to precede, or to follow, moments of particularly elevated HV and EDA. We also wished to understand how rapidly the relationship between measures falls off when we increase the time interval between them.

In addition to comparing each variable with the other variables, the relationship of each variable to itself has also been plotted for comparison (see Fig. 5). In this way, we can examine: how does HR itself change, relative to onset of moments of particularly elevated heart rate? Do changes tend to build up, and to dissipate, suddenly or gradually? These can be compared to the auto-correlation functions, presented previously.

Of note, the number of instances of high arousal observed in our data varied both between participants and variables. For HV an average (std) of 41.1 (11.7) episodes was observed per participant, across the 20 min testing session. Each episode lasted on average (std) 3.8 (4.5) s. For HR an average (std) of 26.4 (10.8) episodes were observed per participant. Each episode lasted 4.0 (18.6) s. For EDA an average of 7.7 (7.1) episodes was observed, lasting an average (std) of 8.1 (18.5) s.

In analysis 1, the epoch-wise correlations were first averaged on a participant-by-participant basis, before being averaged again to create the final averages. In analysis 2, however, we were concerned that this

variable number of instances of high arousal available for different individuals might render this approach unreliable, since it would lead to data from some individuals (those with a higher number of high-arousal episodes) being over-sampled. Therefore, epoch-wise analyses were pooled together for all participants before averaging was performed, with one correlation calculated per group. This means that it was not possible to conduct similar statistical analyses to those shown in Figure 1. Of primary interest, therefore, for this analysis is to compare the relative heights and peaks of the graphs *between* different measures.

Figure 5 shows the results. Three separate plots show the analysis conducted with the three different possible dependent variables—HV, HR, and EDA. Thus, for example, Figure 5a examines the starts of high HV episodes, and looks at how HR, EDA, and HV change relative to those moments. Figure 5d shows the same comparison, but on a more fine-grained time-scale. Figure 5a–c show the relationships on a –80 to +80 s time-scale. Figure 5d–f show the same three relationships, but on a –8 to +8 time-scale.

Again, a number of points of interest can be noted in these data. As previously, we wished to find out: how slow- or fast-changing are our measures? And do changes in one measure tend to take place before, or after, changes in another?

In order to address the first question, we examined the relationship of each variable to itself. These are shown by the blue, red, and green lines on Figure 5a–c, respectively. For example, the green line in Figure 5c looks at the onset of periods of particularly elevated EDA, and examines how fast changes in EDA tend to build up, and to dissipate, relative to these moments. It can be seen that periods of elevated HV (Fig. 5a, blue line) tend to dissipate more rapidly than

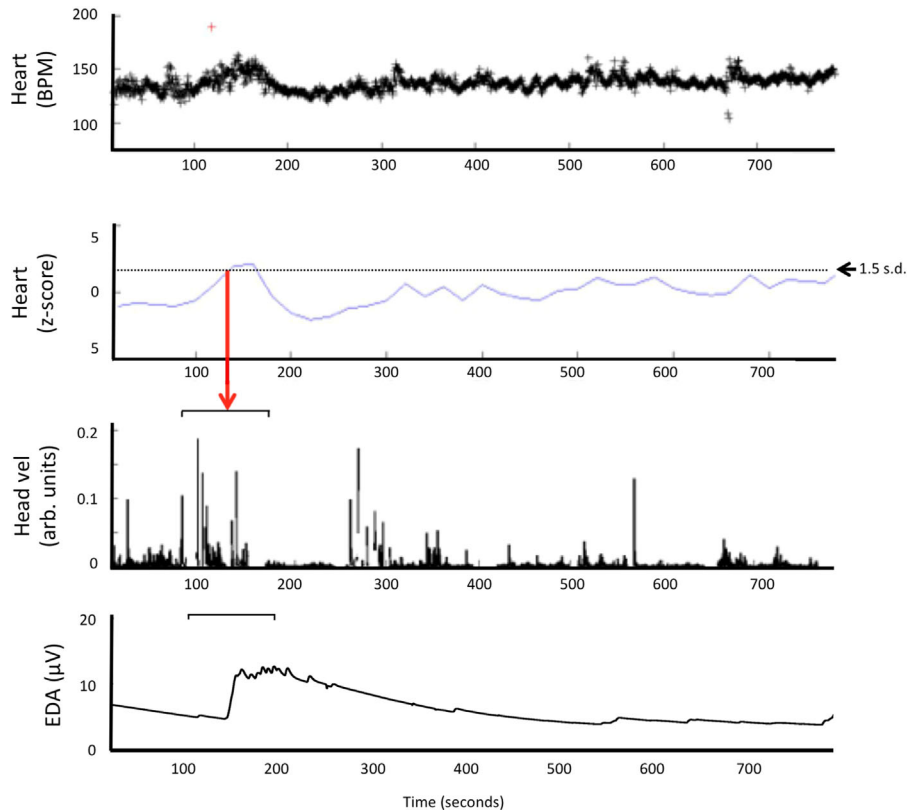


FIGURE 4 Demonstration of analysis 2. First, one measure (e.g., HR, indexed in beats per minute (BPM) as shown in the top panel) was processed, and converted epoch-wise into z-scores as shown in the second panel. Then moments we identified where the infant first entered into a high-arousal state (defined as a moment in which the HR values first exceeded 1.5 standard deviations above the average for that session). This threshold has been drawn as a dotted line on the second panel. Then, we examined how the other measures (head velocity and EDA) changed relative to this moment.

periods of elevated HR (Fig. 5b, red line). In turn, these tend to dissipate more rapidly than periods of elevated EDA (Fig. 5c, green line). This suggests that the patterns shown across the entire dataset in Figure 2e are also present in this analysis, which just examines moments of particularly elevated arousal.

To address the second question, of whether changes in one measure tend to occur before, or after, changes in another, we examined whether results obtained were asymmetric around zero. In Figure 5d (red line) it can be seen, for example, that 2 s *before* the start of a high head velocity episode, the average heart rate is .2 s.d. above mean. 2 s *after* the start of a high head movement episode, it is .43 s.d. This suggests that moments of particularly elevated head velocity tend to show higher heart rate *after* that episode, than before it. In Figure 5e (blue line) it can be seen (albeit more weakly) that the opposite pattern can be seen: 2 s *before* the start of a high HR episode, HV is .69 s.d. above mean, but 2 s after the start of the episode, it is .58

above mean. This suggests that moments of particularly elevated heart rate tend to show higher head velocity before that episode than after it.

In Figure 5a,b it can be seen that 10 s *before* instances of elevated heart rate and movement, average EDA values are .04/.11 for HV/HR. Whereas 10 s *after* they are higher: .12/.21. This suggests that changes in EDA appear to happen *after* changes in other measures. Furthermore, 80 s *after* a moment of elevated heart rate or movement, EDA values remain high: .12/.22. This suggests that EDA tends to be a slow-changing measure; consistent with the findings shown in Figure 2e.

Overall, the following conclusions can be drawn from Analysis 2. First, moments of particularly elevated head velocity tend to show higher heart rate *after* that episode, than before it. Second, moments of particularly elevated heart rate tend to show higher head velocity before that episode, than after it. Third, changes in EDA tend to occur after the starts of episodes of particularly elevated

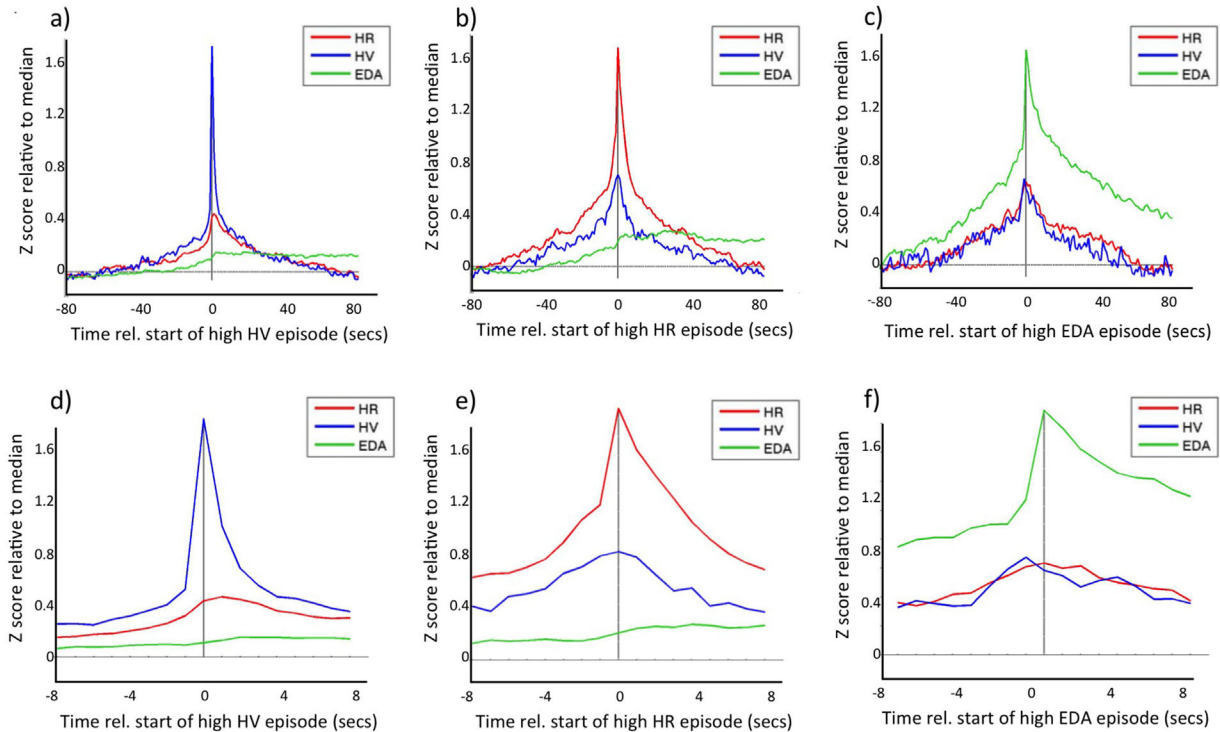


FIGURE 5 Results of analysis 2 (a–c) show results on a large time-scale (± 80 s). (a) shows analyses with HV as the dependent variable (DV); (b) HR as DV; (c) EDA as DV. For each analysis, moments where the DV rises above 1.5 standard deviations above the mean were identified, and we examined how the behaviour of the three other remaining variables changes relative to the DV. (d–f) show results of the same analysis, on a smaller time-scale (± 8 s). (d) HV as DV; (e) HR as DV; (f) EDA as DV.

head velocity and heart rate. Fourth, increases in EDA tend to dissipate more slowly than increases in either head velocity or heart rate.

Analysis 3—Relation of Arousal Measures to Look Duration

Analysis 3 was based on look duration data obtained across the 20 min testing battery (see Supplementary Materials for an alternative analysis based on look duration during a short portion of the battery). Continuous look duration data were epoched into 1 s epochs, with each epoch assigned the duration of the look in which it occurred. Sections that occurred between looks were excluded from analysis, and lagged correlations were not calculated across sections of missing data. The procedures for the calculation of the cross-correlations and auto-correlations was identical to those used in Analysis 1.

As previously, our questions were: first, how strong is the relationship between look duration and each of our arousal variables at Time 0 (no lag)? Second, how rapidly does this association fall off at increasing time

intervals? We consider this relationship for each of our three arousal measures—head velocity, heart rate, and EDA.

At Time 0, a negative correlation is observed between head velocity and look duration (avg $r = -.25$) (Fig. 6a). This indicates that higher head velocity is associated with *shorter* look duration. At $-5/+5$ s lag it is $-.20/-.19$, at $-10/+10$ s lag it is $-.16/-.16$ and at $-60/+60$ it is $.01/.01$. Significantly negative associations (correcting for effective sample size) are consistently observed from time-lag -32 to $+16$. This suggests that head velocity relates significantly to look duration, and that relationships observed are fairly specific in time (Significant relationships are not observed at time delays of greater than 30 s).

Figure 6b shows the relationship between heart rate and look duration. A similar pattern is observed as for head velocity, but relationships are weaker. Again the correlations are generally negative, suggesting that higher HR is associated with shorter look durations, consistent with previous findings (de Barbaro et al., under review). At $-5/+5$ s lag the relationship is $-.12/-.09$, at $-10/+10$ s lag it is $-.13/-.08$, and at $-60/+60$ s lag it is

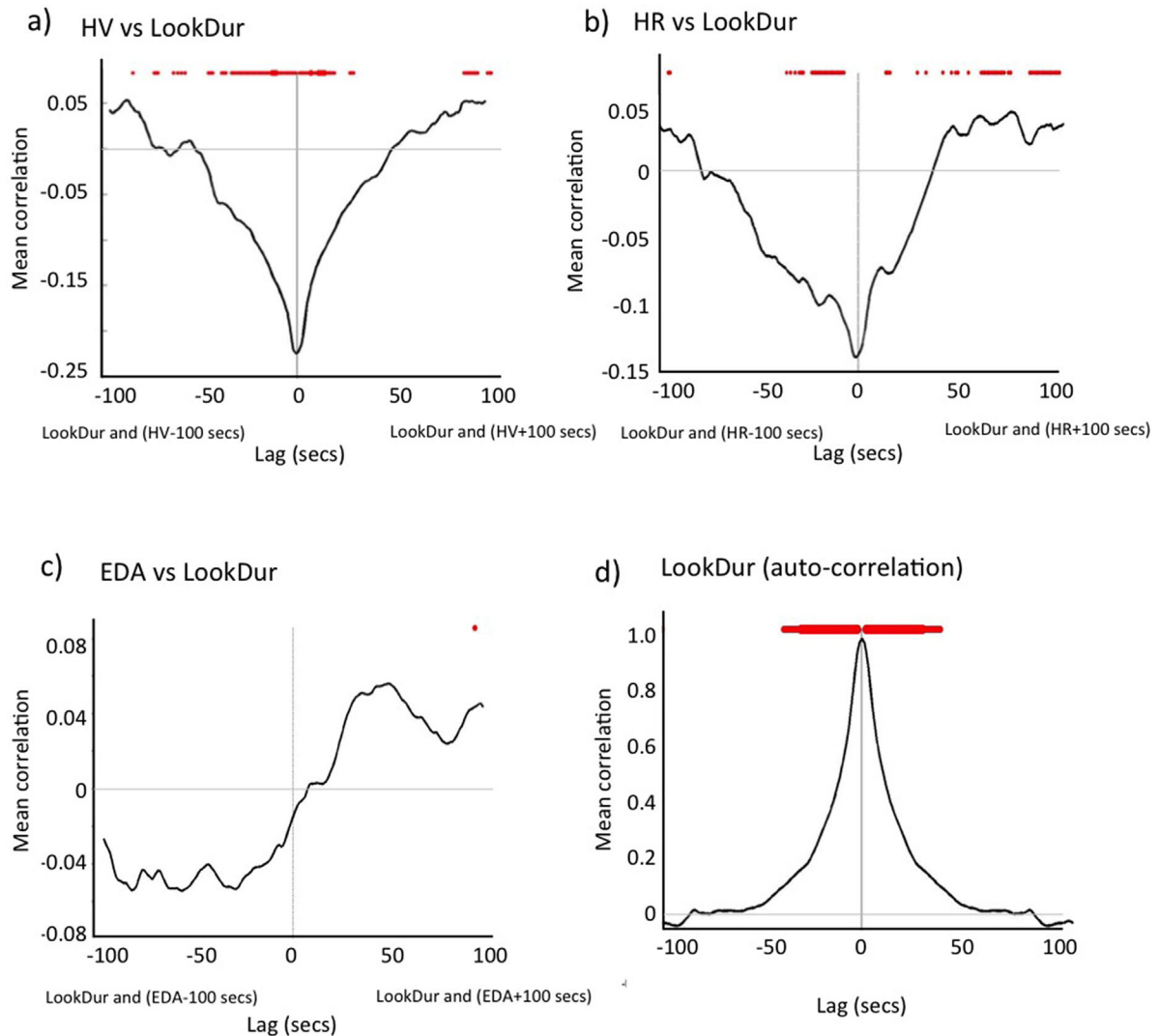


FIGURE 6 (a–c) Results of cross-correlation analyses conducted to examine the relationship between look duration and our arousal measures. (a) HV versus look duration; (b) HR versus look duration; (c) EDA versus look duration. Red dots above the plots show whether a significant relationship was observed between the two measures at that moment in time, after correcting for auto-correlation (small dot— $p < .05$, large dot— $p < .001$). (d) Results of auto-correlations on the look duration data. Red dots above the plot indicate whether a significant relationship was observed between look duration and itself, at each time-lag (small dot— $p < .05$, large dot— $p < .001$).

-.02/.01. Significant relationships are observed between HR and look duration from Time -30 to -2. This suggests that HR and look duration are significantly negatively associated over these time frames. Of note, significant *positive* associations are also observed at larger positive time-lags—a pattern that is also present, albeit more weakly, in the HV data. This is discussed further in the Discussion section.

Figure 6c shows the relationship between EDA and look duration. This shows a similar pattern to that seen

in Figure 2b,c: relationships appear consistent, and are heavily lagged. However, no significant relationships were observed between EDA and look duration.

Next we examined: do changes in our arousal measures tend to take place before, or after, changes in look duration? To assess this, we examined the degree to which relationships were found to be significantly asymmetric around zero. Stronger asymmetries were found for HR than for HV. For HR, relationships with look duration were significantly asymmetric at all time

intervals greater than 59 s. For HV, the first significant asymmetry occurred at a time-lag of 24 s. For EDA the relationship was asymmetric around zero for all time intervals greater than 60 s lag. However, the effect size of the relationship between EDA and look duration is markedly smaller than those observed for HV and HR, and correlations were found not to be significant.

Overall, the results from Analysis 3 suggest that significant negative relationships can be observed between HV and HR. These relationships appear to be consistently observed at shorter time intervals, but to disappear when increasing time delays are introduced. For EDA, in contrast, although results were consistent with previous analyses, no significant results were observed. Finally, we found that changes in both head velocity and heart rate tend to take place significantly *before* changes in look duration.

DISCUSSION

These analyses were conducted to examine the dynamics of peripheral arousal indices, and their relationship to attention in infants. Our research questions were threefold: first, do changes in one arousal index tend to occur before, or after changes in another? Secondly, how temporally specific are changes in each of these arousal measures? Third, to what degree are changes in different autonomic indices associated with changes in attention? Analyses 1 and 2 presented two complementary approaches to addressing the first two of these questions. Analysis 3 addressed the third research question.

The Aston-Jones model of attention, derived from animal research, predicts how dynamic, ongoing changes in arousal should associate with dynamic changes in attention capacities (Aston-Jones & Cohen, 2005). However, it treats arousal as a unitary construct. To what degree are similar patterns observed across different, peripheral indices of arousal?

Encouragingly, and despite the fact that different analytical strategies were used to address these questions, our results were highly consistent across analyses. Four principal conclusions can be drawn: (i) strong associations are found between HR and HV, with changes in head velocity consistently anticipating heart rate changes; (ii) electrodermal activity (EDA) changes are consistent with changes in HR and HV, but on a markedly longer time-scale; (iii) HR and HV show consistent relationships with look duration, with changes in both measures temporally preceding changes in look duration; (iv) relationships between EDA and look duration are inconsistent. We will now consider each of these conclusions in more detail:

Strong Associations Are Found Between Heart Rate and Head Velocity, With Head Velocity Consistently Anticipating Heart Rate

In previous research, we examined tonic and phasic co-variation between the same three indices of arousal—heart rate, head velocity, and EDA (Wass et al., 2015). We found that heart rate and head velocity showed strong patterns of association—both in terms of tonic (baseline) levels, and in phasic changes (response to an attention-getting stimulus event). Here, we built on these findings to show that: (i) this relationship has a relatively high level of temporal specificity, and falls off at time intervals of greater than 15 s (Figs. 2a and 5a,b,d,e); and (ii) that changes in head velocity tend reliably to precede changes in HR by a few seconds (Figs. 2d and 5d,e).

Porges et al. (2007) measured co-variation in heart rate and motor activity recorded via an actigraph attached to the wrist in 3–6-year-old children and found consistent (but non-significant) relationships between activity and heart rate even during baseline periods ($r = .20/.18/.13/.18$) that were significant during periods of exercise (see Byrne & Smithmartel, 1987; O'Sullivan & Berthier, 2003). However, they did not examine the temporal dynamics of change. In the previous study, we examined how HR and HV change relative to an externally defined event (the presentation of a previously unviewed stimulus). We found that both HR and HV decrease following the change of stimulus, but that HV changes tended to occur more rapidly than HR changes—a pattern consistent with the present findings (Wass et al., 2015—see also Byrne & Smithmartel, 1987).

Direct and indirect relations between movement and heart rate are plausible given the underlying physiology. The heart is controlled both directly via the autonomic nervous system and also by a number of homeostatic endocrine feedback mechanisms that control the increase in heart rate required as more blood is needed to take oxygen to the muscles following movement (Silver & LeSauter, 2008). It seems plausible, therefore, to ask, based on our findings: if heart rate changes consistently occur after changes in movement, are these changes taking place in *response* to changes in movement? It could be, however, that the heart is merely a slower-responding system than the motor system, and that both are regulated by a central control (Cechetto & Chen, 1990). Additional, more computationally advanced techniques, such as Granger Causality, can be used to unpack these relationships further (Eichler, Motta, & von Sachs, 2011). There is also a distinct risk that non-linear relationships between variables may subsist in

our dataset—which would not be detected using the correlational techniques that we used here.

EDA Changes Are Consistent With Changes in HR and HV, But on a Markedly Slower Time-Scale

For heart rate and head velocity, significant relationships were only found within time-lags of 30 s or less. For EDA, in contrast, although widely significant associations are found, these relationships show markedly less temporal specificity. Thus in Figure 2b, for example, significant correlations between HR and EDA were observed (after correcting for effective sample size) at all time intervals after +28 s. (Of note, all analyses were z-scored and therefore looked at phasic changes relative to the average EDA levels across the whole session.) Figure 3 shows a raw data sample to illustrate this point. It can be seen that changes in heart rate and head velocity occur, and then return to baseline levels, fairly rapidly. Peaks in EDA, in contrast, return to baseline less rapidly.

The other aspect of interest is that of whether changes in EDA tend to occur before, or after, changes in head velocity and heart rate. Here, again, encouragingly consistent results were observed across analyses. In Figure 2b it can be seen that the maximum association between HR and EDA occurs between HR and EDA +11 s, indicating a time-lagged relationship between the two measures. Similar results were observed in Figure 2c, and also in Figure 5a,b (green lines), which look at changes relative to the onset of particular, high arousal, moments. These findings, which suggest that long-lasting changes in EDA tend to occur after change in heart rate and head velocity are, to our knowledge, novel. Kahneman, Tursky, Shapiro, and Crider (1969) observed consistent changes in heart rate and skin resistance during information intake and processing in typical adults, but no research has investigated this question in infants. These findings are discussed in more detail below.

HR and HV Show Consistent Relationships With Look Duration, With Changes in Both Measures Temporally Preceding Changes in Look Duration

Previous research has suggested that, in general, lower arousal associates with longer look duration (Lansink, Mintz, & Richards, 2000; Richards, 1985). Here, we replicate this finding, and extend it in three ways. First, we show that the relationship holds when movement is used to index arousal, just as it does for heart rate (cf. O'Sullivan & Berthier, 2003). Second, we show that this relationship has a relatively high degree of

temporal specificity: relationships are consistently observed between, for example, movement and look duration at 30 s time-lag, but not at 90 s lag. Third, we show that changes in movement and heart rate consistently precede changes in look duration, by small periods. Although the present results were obtained based on continuous look duration recorded during the administration of a mixed testing battery, we also found highly similar results when look durations were measured relative to static stimuli in an infant-controlled habituation protocol (see Supplementary Materials).

It is conceivable that we could have found movement and heart rate to be strongly associated (Fig. 2a), but that while heart rate relates to look duration, movement does not. The fact that we found consistent relationships suggests that the two measures show a similar relationship to look duration.

All of our analyses were conducted on data that were first normalized, by z-scoring, on a per-participant basis. This z-scoring controls for baseline differences across the whole session. Our findings therefore suggest that temporary changes in arousal are associated with temporary changes in look duration—aside from baseline differences. The challenge is to reconcile this finding with previous research that has examined these areas from the point of view of static (i.e., stationary) individual differences—such as information processing models, in which infants' encoding speed is treated as a static, non-varying construct (Sokolov, 1963; see Richards, 2010). Future work should examine this in more detail. Intriguingly, in Figure 6a,b, we observed positive correlations at larger time intervals (± 80 s), in contrast with the negative correlations observed at shorter time intervals. This is not directly attributable to normalizing effects, as our z-scoring was conducted on larger, 20 min, data segments. It may therefore represent some kind of periodic change in arousal and attention (cf. Bacher & Robertson, 2001; Robertson, Bacher, & Huntington, 2001), that may be detectable more clearly using frequency-based analyses, based on larger data segments.

We also found that changes in movement and heart rate tend to occur before changes in looking behavior. Again, this is a finding that we believe may be of some theoretical interest. In particular, research into self-regulatory behaviors in infants suggests that infants look away from particular objects in order to calm themselves (e.g., Rothbart, Ellis, Rueda, & Posner, 2003; Sheese, Rothbart, Posner, White, & Fraundorf, 2008)—whereas we found that changes in movement and heart rate tend to precede changes in looking. Future work should examine how this relationship changes contingent on context, and when different types of looks are considered (Aston-Jones & Cohen, 2005).

Relationships Between EDA and Look Duration Are Inconsistent

In sharp contrast to the findings shown in Figures 2 and 5, where consistent patterns were noted in relationships between EDA and both movement and heart rate, in Figure 6c we showed no significant relationships between EDA and look duration. This is consistent with our previous findings where, we examined phasic changes to an attention-getting new stimulus (a new image of an infant's face) and found that, whereas heart rate and movement both showed significant phasic change, EDA did not (Wass et al., 2015).

Relatively little research has used EDA to index arousal in infants. Hellerud and Storm (2002) looked at EDA changes to nociceptive (heel prick) and tactile (routine nursery handling) stimulation in newborn infants. They found that preterm infants had significant increases in skin conductance variables during both tactile and nociceptive stimulation, but in term infants, the postneonatal group only showed significant increases to nociceptive stimulation. Ham and Tronick (2008) showed significant phasic changes in 5-month-old infants in response to a hand-clap procedure. In previous research, we reported that spontaneous changes in EDA tended to co-occur with changes in other measures only when general arousal levels were high; at lower levels, predicted co-variation did not occur (Wass et al., 2015). It may be, then, that EDA is sufficiently sensitive a measure to reliably detect change at high general levels of arousal (as induced by a heel prick), but not a lower levels of arousal (as induced by an attention-getting stimulus). Alternatively, it may be that EDA measures sympathetic nervous system activity, whereas heart rate and movement index the parasympathetic as well as sympathetic nervous systems—and that the contributions previously noted between heart rate/movement and attention are attributable to the former, and not the latter. Further research, involving other putative sympathetic nervous system indices such as impedance cardiography (Alkon et al., 2006) is necessary to distinguish between these possibilities.

Directions for Future Work

The present analyses have shown, for the first time, how different peripheral indices of arousal interact with each other over time. Our results have shown that changes in movement consistently occur before changes in heart rate, and that changes in electrodermal activity (EDA) are consistently observed following changes in heart rate and movement—but on a much larger time-scale. We have also shown that look duration consistently relates to heart rate, and head velocity, with changes in the arousal indices consistently preceding changes in look duration.

In contrast, consistent relationships of look duration to EDA were not observed.

Future work should investigate in more detail how changes in arousal relate to changes in other aspects of behavior. Of particular interest here, from a theoretical perspective, is to investigate how the influence of arousal on look duration changes contingent on context. Work with animals by Aston-Jones and Cohen (2005), has suggested, for example, that mid-level arousal may be associated with an ability to shift between high focused attention (long look durations) and a more open attention states (shorter look durations) contingent on setting. In contrast, individuals with hyper-arousal may only show shorter look durations, and individuals with hypo-arousal may show longer look durations (cf. Rose, Feldman, & Jankowski, 2002). It would be interesting to investigate the predictions of these results with human infants.

A second potential area for future research is to investigate how the relationships that we documented here change as a function of age. Look durations change extensively with increasing age (Colombo, 2001), but little previous research has investigated how arousal patterns change with age (although see e.g., Richards, 1985). It is currently unknown, for example, how the lability of arousal changes with increasing age (a question that could be addressing using the auto-correlation analyses presented here), and how the strength of the relationship between arousal and attention changes with age (a question that could be addressed using cross-correlation analyses).

Our finding that short-term changes in arousal associate with short-term changes in look duration—even controlling for baseline differences—may be seen as a challenge to other researchers. Many researchers assume that the factors that determine look duration are generally static (time-invariant, equivalent to a tonic approach) (Colombo & Mitchell, 2009). Future work should investigate in more detail the degree to which individual differences are better conceptualized in static (tonic) or temporary (phasic) terms. Work using cross- and auto-correlations to investigate relations between arousal and other aspects of attention and learning, can, we believe, go some way towards addressing these questions.

NOTES

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