In infancy, it's the extremes of arousal that are 'sticky': naturalistic data challenge
homeostatic models of self-regulation

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Data availability: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Research highlights

- we recorded day-long spontaneous fluctuations in autonomic arousal in 12-month-old infants
- we found that both low- and high-arousal states were more long-lived than intermediate arousal states
- one possible explanation for these findings is that extreme arousal states have intrinsically greater hysteresis
- another is that, through ‘metastatic’ processes, small initial increases and decreases in arousal may become progressively amplified over time.

Abstract

Most theoretical models of arousal/regulatory function emphasise the maintenance of homeostasis; consistent with this, most previous research into arousal has concentrated on examining individuals’ recovery following the administration of experimentally administered stressors. Here, we take a different approach: we recorded day-long spontaneous fluctuations in autonomic arousal (indexed via electrocardiogram, heart rate variability and actigraphy) in a cohort of 82 typically developing 12-month-old infants while they were at home and awake. Based on the aforementioned models we hypothesised that extreme high or low arousal states would be more short-lived than intermediate arousal states. Our results suggested that, contrary to this, both low- and high-arousal states were more long-lived than intermediate arousal states. The same pattern was present when the data were viewed over multiple epoch sizes from 1 second to 5 minutes; over 10-15-minute time-scales, high-arousal states were more long-lived than low- and intermediate states. One possible explanation for these

findings is that extreme arousal states have intrinsically greater hysteresis; another is that, through ‘metastatic’ processes, small initial increases and decreases in arousal can become progressively amplified over time.

Keywords: self regulation, arousal, emotion regulation

Introduction

Animal research suggests that neural control of our arousal/regulatory systems involves regions from the brainstem (the medulla, pons (locus coeruleus) and midbrain) to the forebrain via both the hypothalamus and the thalamus (Pfaff, 2018), as well as neurotransmitter systems including noradrenaline (norepinephrine) (Aston-Jones & Bloom, 1981; Aston-Jones & Cohen, 2005; Aston-Jones, Rajkowski, & Cohen, 1999) and acetylcholine (Trofimova & Robbins, 2016). Although in recent years the fashion has been to emphasise the fractionation of different arousal/regulatory subsystems (Janig & Habler, 2000; Lacey, 1967; Schneirla, 1946; Trofimova & Robbins, 2016), there is also evidence that they operate at least partially as a unitary system (Calderon, Kilinc, Maritan, Banavar, & Pfaff, 2016; Pfaff, 2018). For example, behavioural animal researchers quantified three types of behaviour traditionally associated with arousal/regulatory systems: motor activity (distance travelled, total movement duration); sensory responses to external stimuli (e.g. auditory, vestibular, tactile and olfactory); and emotional responses (e.g. to conditioned fear paradigms) (Calderon et al., 2016; Pfaff, 2018). They applied Principle Components Analyses to high-throughput analyses of behaviour. Their results suggested that a significant Generalised Arousal component accounts for between 29 to 45% of the variance in behaviour across studies (reviewed (Calderon et al., 2016; Pfaff, 2018)). These three behavioural attributes also show unitary covariance in studies of selective animal breeding (Weil, Zhang, Hornung, Blizard, & Pfaff, 2010). In physiology, the different peripheral measures commonly used to measure arousal (including heart rate, heart rate variability, electro-dermal activity and movement), all show significant tonic and phasic covariance in infants (Wass, Clackson, & de Barbaro, 2016; Wass, de Barbaro, & Clackson, 2015), despite the fact that they are also thought to tap partially different systems (Cacioppo, Tassinari, & Berntson,

2000; Wass et al., 2015). Again, this merits the treatment of arousal as a construct that shows a single common factor as well as more fine-grained sub-factors.

The function of our arousal/regulatory systems is to perform reflexive, adaptive changes so that we can maintain stability in the face of changing environmental demands – a process known as allostasis (Walter B Cannon, 1929; Fiske & Maddi, 1961; Gunnar & Quevedo, 2007; McEwen & Seeman, 1999; Selye, 1951; Ulrich-Lai & Herman, 2009). To do this, they act over diverse time-scales and using diverse methods, including both slow-acting endocrine systems (such as the Hypothalamic-Pituitary-Adrenal (HPA) axis (Gunnar & Quevedo, 2007), and fast-acting neural systems (such as the Autonomic Nervous System) (Cacioppo et al., 2000). Contrary to Freud's early assumption that the central nervous system is "an apparatus which has the function of getting rid of the stimuli that reach it, or of reducing them to the lowest possible level" (Freud, 1915/1957b), current theoretical approaches suggest that reflexive arousal changes involve dynamically readjusting in order to maintain an 'optimal load' between over- and under-arousal (Gardner, 1995; Zuckerman, 1979). This can involve upregulating arousal under certain conditions, and downregulating it in others (Fiske & Maddi, 1961; Zuckerman, 1979) (see also (Gardner, 1995)).

However, our understanding of the mechanisms through which our arousal/regulatory systems respond to environmental influences has, historically, been held back by the fact that the majority of research (both human and animal) has taken place in laboratory settings. Laboratory settings, by definition, aim to remove or control for the influence of environment. To do this, the majority of studies take the same approach: they administer discrete experimental stimuli within a controlled laboratory setting, and measure regulation and reactivity by indexing the change between a baseline period and the stimulus (Wass, 2018).

This baseline-stimulus-baseline method may appear intuitive given approaches that emphasise the role of arousal/regulatory systems in allostasis. However, it has a number of fundamental limitations. First, the pattern of a discrete exogenous stimulus that suddenly appears and then disappears after a short interval only occurs rarely in the real world. Second, and relatedly, in the real world we continuously recalibrate, actively selecting what aspects of the social environment that we attend to from one second to the next. The fact that both the appearance of the stimulus, and its disappearance, are outside participant control in experimental settings again lacks ecological validity. Third, almost all research has used experimental stimuli intended to elicit increases in arousal, to examine how we downregulate following increased arousal; the question of how decreases in arousal (whether exogenously or endogenously triggered) are upregulated has been discussed (Fiske & Maddi, 1961) but rarely studied.

In previous research we took a different method: rather than taking an event-locked approach, we instead analysed spontaneous fluctuations in arousal during the presentation of age-appropriate (and not deliberately anxiogenic) static and dynamic viewing materials (Wass, Clackson, & Leong, 2018). Arousal was measured via a composite of peripheral measures of physiological arousal including electrocardiography (inter-beat interval), heart rate variability, electro-dermal activity and movement. We reasoned that if transitions in autonomic arousal are purely random, with deviations above and below the mean corrected for via allostasis, then arousal should be normally distributed across the session. In fact, we found that: 1) arousal was positively skewed, and 2) that increases in arousal had a lower extinction probability than decreases in arousal. We argued that our results suggested that increases in arousal might be intrinsically self-sustaining, even in the absence of identifiable

environmental stressors. Thus, for example, oppositional inter-personal interactions might be both a consequence, and a cause, of elevated arousal (Potegal, Carlson, Margulies, Gutkovitch, & Wall, 2009) – operating not as allostatic processes, but as ‘metastatic’ ones (from the Greek word meta, meaning ‘beyond’), in which small fluctuations become progressively amplified over time.

This previous analysis was, however, based on relatively small segments of data (c. 20 minutes per participant), collected during the administration of an attention battery in laboratory settings. Further, our analyses did not directly examine how the time series fluctuated, but merely examined the distributional properties of the dataset. Lastly, since during viewing parents were asked to keep their infant in a seat or on their lap, they also do not provide a good proxy for real-world settings, where infants are allowed to roam freely (Zubek & MacNeill, 1966).

Here, we examine for the first time how infants’ autonomic arousal spontaneously fluctuates in real-world, fully naturalistic settings, across day-long recordings. To measure this, we developed wireless miniaturised wearable autonomic monitors to record electrocardiogram (inter-beat interval), heart rate variability and actigraphy, along with cameras and GPS sensors to allow us to observe where the infant was and what they were doing. Experimenters visited participants’ homes in the morning to fit the equipment and returned in the evening to pick it up; otherwise, participants were encouraged to behave exactly as they would on a normal day. Because, when they were not home, infants were generally strapped into car seats or prams, which influenced their physiological recordings, we concentrated on segments where they were at home, and awake. During these periods infants were almost exclusively free-roaming. Motivated by previous research suggesting that arousal-behaviour interactions

are scale-free (Proekt, Banavar, Maritan, & Pfaff, 2012) we used the same approach to examine change across multiple time-frames, from 1-second through to 15-minute epoch durations (which was the maximum time interval that the quantity of available data would allow).

Specifically, we examined a question that builds on this previous research, but which has received relatively little attention in the literature: how the stability of infants' arousal varies contingent on their fluctuating levels of tonic (baseline) arousal, in naturalistic settings. In the absence of previous research that has looked at naturalistic arousal fluctuations we made the naïve prediction that, if spontaneous arousal fluctuations are random, with fluctuations above and below the mean corrected for via allostasis, then extreme high or low arousal states would be more short-lived than intermediate states.

Methods

Participants

Participants consisted of a socio-economically diverse cohort of 82 12-month-old infants recruited from the London, Essex, Hertfordshire and Cambridge regions of the UK.

Demographic details and exclusion criteria and are given in the Supplementary Materials (section 1.1, Table S1).

Experimental Protocol

Participating parents selected a day for which they would be spending the entire day with their child but that was otherwise, as far as possible, typical. The researcher visited the participants' homes in the morning (between 7.30 and 10am) to fit the equipment and explain its use, and then returned in the late afternoon (between 4 and 7pm) to remove it. Mean (*std*) recording time per day was 7.3 (*1.4*) hours.

The equipment consisted of two wearable layers (see Figure S1). A specially designed baby-grow was worn next to the skin, containing a built-in ECG recording device, Actigraph, GPS, and microphone. A T-shirt, worn on top of the device, contained a pocket to hold the microphone and a miniature video camera. The camera was commercially available (a Narrative Clip 2); the remaining equipment was specially manufactured for this study. The clothes were comfortable when worn and, other than a request to keep the equipment dry, participants behaved exactly as they would on a normal day.

Data pre-processing

Autonomic data. See Figure 1 for an example of the raw data recorded. Three peripheral (non-invasive) measures of autonomic arousal in humans were recorded ((Cacioppo et al., 2000; Wass, 2018; Wass et al., 2015):

- i) *electro-cardiography (ECG)*, from which heart rate measured as inter-beat intervals (IBI) in Beats Per Minute (BPM) was derived. ECG was recorded using three standard Ag-Cl electrodes, placed in a modified lead II position. Further details of how these data were recorded and parsed are given in the Supplementary Materials (section 1.2).
- ii) *Heart Rate Variability (HRV)*, which was derived from the IBI data. HRV was taken as the Root Mean Square of Successive Differences (RMSSD), although other frequency domain measures were additionally inspected and, as expected (Vest et al., 2018), showed highly similar results. Further details on recording and parsing are, again, given in the Supplementary Materials (section 1.2).
- iii) *Actigraphy* was recorded using a tri-axial accelerometer that was positioned approximately on the solar plexus of the infants, and held securely in place in the baby-grow. Movement data were low-pass filtered at 0.1Hz.

INSERT FIGURE 1 HERE

Our preliminary analyses suggested that the three autonomic measures showed strong patterns of tonic and phasic covariation, consistent with previous research (Wass et al., 2016; Wass et al., 2015). See further details, and discussion, in Supplementary Materials (SM) (section 1.2 and Figure S2). Motivated by this, and following previous work (Wass. et al., in press) we collapsed the autonomic indices into a single composite measure for Analysis 1.

This was done by calculating the natural logarithm of the actigraphy data, inverting the HRV data, calculating the z-score of each measure and then averaging the z-scores.

Awake/sleeping segments

Our analyses suggested that when infants were outside they were often strapped into a buggy or car seat, which strongly affected their autonomic data. Because of this, only segments of the data when infants were at home were included. Since all aspects of autonomic arousal differ markedly between waking and sleeping (see e.g. Figure 1), sections where infants were asleep were also excluded. Details of the criteria through which home/not-home and sleeping/waking segments were identified in our data are given in the SM (section 1.3).

Vocal affect.

Although our dependent measure was autonomic arousal, we also wished to consider the relationship between arousal and affect. The relationship between autonomic arousal and affect is complex and non-linear (Cacioppo et al., 2000; Walter Bradford Cannon, 1915; Kreibig, 2010; Pérez-Edgar, 2019); in order to examine their relationship in our data, all of the vocalisations recorded from the infant were hand-coded for two parameters: vocal affect, and vocal intensity. See further details for how this coding was conducted in the SM (section 1.4). We then examined how, across all samples collected, autonomic arousal co-fluctuated with vocal intensity and vocal affect (see SM Figure S3).

Comparison of real data with control data

For our analyses, we wished to compare the dynamics of the observed arousal data with comparison time series that matched the original data as closely as possible, except for the parameter of interest – which, in this case, was the temporal interdependencies within the

time series. To do this, the mean and variance of the available data was calculated separately for each participant, and these parameters were used to generate a random time series with the same length, mean and variance as the original data using the ‘normrnd’ function in Matlab (see Figure 2a, 2b). Of note, one feature of the original data that this control analysis does not replicate is that the original data were generally mildly negatively skewed (see Figure 2b and SM section 1.5, Figure S4). However, we can see no way in which this feature of the data might have contributed to the observed results.

INSERT FIGURE 2 HERE

Analysis overview

Our aim was to examine how the stability of infants’ arousal varied contingent on their fluctuating levels of tonic (baseline) arousal. We hypothesised that, across all time scales, extreme high or low arousal states would be more short-lived than intermediate states. To test this, we conducted two analyses: Analysis 1 and Analysis 2.

Analysis 1: Data were downsampled using a median window into epochs of different sizes. The time scales used varied from 1 second epochs (i.e., examining change in arousal between consecutive 1-second epochs) through to 15-minute epochs (i.e., examining change in arousal between consecutive 15-minute epochs), in the following increments: 1 second, 10 seconds, 30 seconds, 60 seconds, 300 seconds, 600 seconds, 900 seconds. Based on the average total duration of 7.3 hours data per participant, and following exclusions to only examine segments while the infant was at home and awake, the mean (sterr) number of epochs included ranged from 13264 (691) for the 1-second epoch analysis through to 15.4 (0.8) for the 15-minute analysis.

Following downsampling using the variable epoch durations described above, data were binned into five equally sized epochs on a per-participant basis (see Figure 2c). First, we conducted exploratory analyses. Figure 2d shows an adapted Poincaré plot in which arousal bin at time t (x-axis) is plotted against arousal at time $t+1$ (y-axis). It can be seen that the most densely populated area is around the 1:1 line, indicating that the data show autocorrelation. Figure 2e is an autocorrelation plot which confirms this finding: even at +15/-15 minute time lag the mean level of autocorrelation present in the arousal data was 0.42, indicating that arousal shows a relatively slow rate of change over time. This finding is consistent with previous results (de Barbaro, Clackson, & Wass, 2016; Wass et al., 2016).

To address our primary research question we performed the following analysis. The results of this analysis are illustrated in detail using just one epoch duration (60 seconds) in Figures 2f-2j. Summary results based on the same analysis, but using variable epoch durations, are shown in Figure 3.

We calculated, separately for each arousal bin at time t , the likelihood of time $t+1$ being the same as time t . We then plotted this ‘change likelihood’ score against the arousal bin at time t . Figure 2e shows the results of this analysis for the real and the control data. It can be seen that, for the control data, this likelihood is flat at 0.2 – as expected given that the data are randomly distributed. In the real data, in comparison, two features can be seen:

The first is that, for all bins, the values for the real data appear greater than those for the control data. If true, this would reflect merely that the arousal show autocorrelation, as is already shown in Figures 2d and 2e. In order to test the significance of this, the values

obtained for each participant and for each arousal bin were compared between the real and the control data. Since the between-participant variance was not always normally distributed, the more conservative nonparametric Wilcoxon Signed Rank Test was used throughout. Multiple comparisons were corrected for using the Benjamini Hochberg False Discovery Rate (FDR) procedure (Benjamini & Hochberg, 1995). In the example shown (based on 60-second epochs), all bins of the real data are significantly ($p < .001$) higher than those for the control data.

The second feature of interest is that the extreme bins (bins 1 and 5) appear to show values that are higher than those in intermediate bins. This is the primary feature of interest in this paper. If true, this would reflect that extreme low- and high-arousal states tend to be more long-lived than intermediate arousal states. In order to test the significance of this, the values obtained for each participant and for each arousal bin were compared directly between bins; this was repeated pairwise for each possible combination of bins (bin 1 vs 2, 3, 4, 5; bin 2 vs 3, 4, 5 etc). Since not all results were parametrically distributed the more conservative Wilcoxon Signed Rank Test was used throughout, and multiple comparisons were corrected for using the Benjamini Hochberg False Discovery Rate (FDR) procedure (Benjamini & Hochberg, 1995). The significance of these tests is shown in Figures 2g and 2i. In this illustrative sample (based on 60-second epoch durations) in the real data (Fig 2g) all possible combination of bins differ, with the exception that bin 3 does not differ significantly from bin 4. No equivalent comparisons are significant in the control data (Fig 2i).

As an additional visualisation, Fig 2h and 2j show the likelihood of arousal at bin $t+1$ being less (Fig 2h) or greater than (Fig 2j) arousal at bin t . Given that the control data are randomly distributed, it is to be expected that at bin 5 the likelihood of the next sample being lower is

0.8, and that at bin 2 it is 0.2. In comparison, the real data show that, at bin 2, it is more likely than chance that the next sample will be lower; and that, at bin 5, it is less likely than chance that the next sample will be lower (Fig 2h). The opposite pattern of results is shown in Fig 2j. These results are consistent with the findings in Fig 2f, that both extremes show higher stability rates than expected.

INSERT FIGURE 3 HERE

Analysis 2:

In order to confirm the validity of the findings from Analysis 1, we also conducted a separate analysis to address the same question, by using vector plots. Instead of being based on a composite measure of arousal, this analysis examines patterns of change in the heart rate and the actigraphy measures both individually and in combination with one another. And instead of being based on analyses at multiple time-scales it is based just on one time scale (60 second epochs). As with Analysis 1, the analysis was conducted only on segments when the infant was at home and awake.

To calculate the vector plots, all heart rate and actigraphy data were averaged separately into 60-second epochs. Data were then concatenated across all participants; heart rate and actigraphy data were then separately divided into ten equally sized bins. In contrast to Analysis 1, in which the binning was conducted separately for each participant, in Analysis 2 the binning was, by necessity, calculated based on the entire concatenated data (see Figure 4a-c). Each epoch was then classified according to what bin it fell into for both heart rate and actigraphy. This is represented as a two-dimensional matrix – so all epochs that were bin 3 for heart rate and bin 4 for actigraphy are drawn at location $[x - 3, y - 4]$. The size of each blue

dot within the matrix indicates what proportion of the total available samples was located within each bin – so a larger blue dot at [3,4] than at [6,1] indicates that epochs at bin 3 for heart rate and bin 4 for Actigraphy were more commonly observed than epochs at bin 6 for heart rate and bin 1 for Actigraphy.

In addition, for each bin, we calculated the average change between all epochs in that bin, and the epoch immediately following. This change score is drawn on the vector plot as a red line. Thus, for the point located at [10,10] on the vector plot, which represents all epochs that were classified as in bin 10 for both heart rate and actigraphy, the vector extends -0.9 on the x-axis (representing change in heart rate), and -1.1 on the y-axis (representing change in actigraphy). This indicates that, across all epochs starting from [10,10], the average change to the next epoch was a reduction of 0.9 bins in heart rate, and 1.1 bins in Actigraphy.

Figure 4a-c gives an illustrative sample of three individual datasets to which this analysis has been applied. All data are grouped around the 1:1 equivalence line as heart rate and actigraphy are strongly correlated (see SM section 1.2). In addition, and because, as described above, binning was conducted on the entire concatenated dataset, it can be seen that participant #1 showed higher average levels for actigraphy and heart rate relative to other participants, that participant #3 showed lower heart rate but not lower actigraphy levels than other participants, and so on.

Our primary aim was to examine how, across the entire dataset, the change vectors for both heart rate and actigraphy varied as a function of bin. To assess this, we conducted a similar calculation as for Analysis 1: the change vectors obtained for each participant and for each bin were directly compared; this was repeated pairwise for each possible combination of bins

(bin 1 vs 2, 3, 4, 5; bin 2 vs 3, 4, 5 etc). Multiple comparisons were corrected for using the Benjamini Hochberg False Discovery Rate (FDR) procedure (Benjamini & Hochberg, 1995).

INSERT FIGURE 4 HERE

Results

Analysis 1

Figure 3a shows the results of the Analysis 1, conducted to examine how stability in arousal varies as a function of arousal. See Methods for details of how this analysis was conducted.

Figure 3b shows the results of the same analysis applied to the control data. Figures 3c and 3d show how the likelihood of decreases (3c) or increases (3d) in arousal varies as a function of arousal, relative to control data (drawn in grey). Figure 3e shows the results of significance tests, conducted as described in the Methods, to examine whether the results shown in Figure 3a differed significantly from the control analysis. Figure 3f shows the results of significance tests to examine how the results shown in Fig 3a differed pairwise between bins.

From these figures, the following conclusions can be drawn. First, results obtained at all epoch durations from 1 second to 300 seconds (Fig 3a) showed consistently higher stability in arousal than the control data (Fig 3b). This reflects the fact that, as shown in Figure 2e, autocorrelation is present, as expected (Wass et al., 2016). Second, arousal stability was higher at shorter epoch durations than at longer epoch durations. Again, this reflects the autocorrelation. Third, at longer epoch durations (600/900 seconds), less consistent differences in arousal stability between the real and control data are observed. Again, this reflects that autocorrelation would have a smaller influence on analyses based on longer epoch durations.

Of primary interest, however is the comparison between bins, which shows how arousal stability varies as a function of arousal. At epoch durations from 1 to 300 seconds, consistently significant differences between all bins were observed, such that bin

1>bin2>bin3<bin4<bin5 (Fig 3f). At shorter epoch durations (1 to 60 seconds), differences are observed between all bins; at 300 seconds, bins 1 and 5 (extreme high and low arousal) differ from other bins (bin 1>bins 2-4; bin 5>bins 2-4), but otherwise no significant differences are observed. At 600 and 900 seconds, bin 5 (extreme high arousal) shows higher stability than other bins (bin 5>bins 1-4). Overall, these results suggest that, when the data were viewed over multiple epoch sizes from 1 second to 5 minutes, both low- and high-arousal states were more long-lived than intermediate arousal states. Over 10-15-minute time-scales, high-arousal states were more long-lived than low- and intermediate states.

Analysis 2

Figure 4d shows the full vector plot for the control data; Figure 4e shows the full vector plot for the real data. Figure 4f shows arousal change as a function of arousal bin for the control data; Figure 4g shows the same plot for the real data. Figure 4h shows the results of pairwise bin comparisons to examine how arousal change varies as a function of arousal bin for the control data; Figure 4i shows the same plot for the real data.

From these plots the following points can be seen. First, the control plot shows long vectors pointing towards the centre of the plot. This indicates regression to the mean: the data have been randomly generated (see Method) and so it is likely that an epoch that is high will be followed due to random fluctuation by an epoch that is lower. Second, the fact that the vectors are shorter in the real data (Fig 4e) is because the real data show autocorrelation; the fact that they nevertheless radiate inwards shows that the real data also show regression to the mean. Third, the centre point of the inwards-radiating vectors is bin [6,6], rather than [5,5], which is because both measures show a mild negative skew (see SM section 1.5). Fourth, the slight swirling pattern in the data is because Actigraphy has a lower autocorrelation (faster

rate of change) than heart rate, and so that changes in actigraphy tend to anticipate changes in heart rate (Wass et al., 2016; Wass et al., 2015).

The key point of interest for the present paper, however, is how the change vectors vary as a function of bin. Fig 4f shows that, in the control data, these decrease linearly with increasing bin, due to regression to the mean: epochs where arousal is high are likely to be followed by a decrease in arousal, and epochs where arousal is low are likely to be followed by an increase in arousal. The significance plots (Fig 4h) indicate this as a highly significant pattern in the data (bin 1>bin 2>bin 3, etc). In the real data, in contrast (Fig 4g) the same overall pattern of regression to the mean is present in the data, but falls off at the extreme high and low bins. This is particularly true for lower bins: the significance plots indicate that, for both heart rate and actigraphy, bin 1 shows a significantly *lower* rate of change than some intermediate bins (bin 3/4) – a pattern not seen in the control data. The same pattern can also be seen in the higher bins: there is no significant difference between bins 9 and 10 in change scores for either actigraph or heart rate (Fig 4i), whereas there is in the control data. Overall, these results confirm our finding from Analysis 1, that extreme low- and high-arousal states were more long-lived than intermediate arousal states.

Discussion

We recorded spontaneous fluctuations in autonomic arousal across day-long data segments in naturalistic settings. Our participants were 12-month-old infants from mixed demographic backgrounds (see Table S1). Only segments of the data when the infant was at home and awake were analysed. In the absence of any previous data on how infant arousal fluctuates in naturalistic settings we made the naïve prediction that, if transitions in arousal are random, with deviations above and below the mean corrected for via allostasis, then extreme high- and low-arousal states would be more short-lived than intermediate states. In fact, we found the opposite: consistently across two separate analyses, we found that extreme high and low states were more long-lived than intermediate states. The same pattern was observed at multiple time-scales, from 1-second to 5-minute epochs (Nakamura et al., 2007; Proekt et al., 2012), although at longer epoch durations (10- and 15-minute) only extreme high arousal states were more long-lived than intermediate and low arousal states. Our supplementary analyses indicate that high and low arousal states are not limited to particular valence emotions, but that both extremes of arousal included a mixture of both positive and negatively valenced emotions (see SM section 1.4, Figure S3) (Pérez-Edgar, 2019).

One possible artifactual cause for our finding could be that the raw arousal data are from a Gaussian distribution, but divided into five equal-sized bins. In a Gaussian distribution, between-samples variance would naturally be greater in the extreme bins; it is plausible that this might cause our finding that extreme high and low states are more long-lived. However, the control analysis is designed to preclude this possibility, as the control data also come from a Gaussian distribution with matched variance (although see SM section 1.5).

Previously we found that, when infants are sitting on their parents' lap watching an experimental test battery, with the parents asked to restrain the infant if they try to get down, then only high arousal states are more long-lived than expected (Wass et al., 2018). Our findings are consistent with this, but suggest that, in naturalistic home settings, both low- and high arousal states are more long-lived than expected. Indeed, of the two extremes, low arousal states seemed even more stable than high arousal states (Fig 4g, 4i).

There are two possible explanations for our finding. The first is that extreme arousal states are intrinsically slower-decaying – or show different hysteresis. This possibility has certainly been acknowledged – for example, Hobson and Steriade noted that “a transition from a motorically activated state (waking) to a motorically inactivated state (sleep) is always slower than the reverse: thus the ascending limb of the rest-activity cycle is steeper than the descending limb” (Hobson & Steriade, 1986). Once achieved, sleep is naturally a more stable arousal state than others; although sleeping sections were excluded from our data in this study, it is possible that other arousal states (including both extreme high and low states) may also show differing intrinsic hysteresis.

An alternative possibility is that both extreme low and high arousal states may lead to changes in how we interact with the external environment and with people - changes that may in turn lead to extreme arousal states becoming progressively amplified over time. Adult research into emotion regulation offers several models from adult psychopathology for how processes such as rumination or attention biases (Gross & Feldman Barrett, 2011; Pine et al., 2005) can lead to ‘metastatic’ processes, in which small fluctuations in arousal may become progressively amplified over time (Wass et al., 2018). Thus, for example, an infant in a low state of arousal might engage in fewer interpersonal interactions, and seek out less

stimulation from the environment; and a child in a high state of arousal might engage in more interpersonal interactions, including oppositional behaviours; and seek out more stimulation from the environment. Both of these processes might show small initial increases and decreases in arousal becoming amplified over time.

Another, partially complementary, possibility is that our susceptibility to external influences fluctuates systematically contingent on our tonic arousal. For example, in animals, tonic activity in the Locus Ceruleus predicts phasic, stimulus-evoked responsiveness, with greatest phasic responsiveness observed at intermediate tonic activity (Aston-Jones & Cohen, 2005; Aston-Jones et al., 1999). Broadly consistent results have been observed with humans (Wass, 2018), suggesting that phasic autonomic responsiveness to attention-eliciting stimuli is greatest in infants and young children at intermediate states of tonic autonomic arousal. This relationship has, however, only been observed for attention- and not for emotion-eliciting stimuli (Wass, 2018). Furthermore, it has only been demonstrated for phasic responsiveness over the second-by-second scale, and not across the multiple time-scales we used here. However, the suggestion that sensitivity to the external environment is greatest at intermediate arousal, and that both extreme high and low arousal shows less sensitivity to external stimuli, could be consistent with our present findings.

Future research should use more sophisticated approaches to differentiate between these two possibilities: a) that extreme high and low arousal states show different intrinsic stability and b) that extreme states trigger different environmental and interpersonal interactions that then take on a self-sustaining character. Understanding this will help us to enrich our understanding of self-regulation. Instead of relying solely on approaches that minimise environmental influences using an experimenter-controlled baseline-stimulus-baseline

approach, we can instead recognise that self-regulation involves ongoing, dynamic interplay between exogenous and endogenous factors, which operate via a process of continuous, dynamic recalibration. Such an approach may offer new insights into how arousal and self-regulation develop over time, from infancy into adulthood, as well as how these processes develop atypically in developmental psychopathology.

Figures

Figure 1: Data sample illustrating the raw data collected from a single participant. Six and a half hours' data is presented (see time axis at the bottom). From top to bottom: the inter-beat intervals derived from the electro-cardiography recording, indexed as Beats Per Minute (BPM); the heart rate variability (indexed as the Root Mean Square of Successive Differences (RMSSD)); actigraphy (indexed as micro-Volts); the results of coding for of the microphone data (see SM section 1.4).

Figure 2: a) example data segment from a single participant showing (top) 14596 samples (=4.05 hours) of real infant arousal data at 1Hz and (below) an equivalent number of samples of Control surrogate data, generated as described in the Methods). b) histograms showing the distribution of real and control datasets shown in Figure 2a (see also SM section 1.5 and Figure S4). c) example excerpt of data from a single participant after data were binned into 5 equally sized bins, based on arousal data downsampled to 60-second epochs. d) Exploratory visualisation of an adapted Poincaré plot in which arousal bin at time t is plotted against arousal bin at time $t+1$, based on arousal data downsampled to 60-second epochs. e) Exploratory auto-correlation plot, based on arousal data downsampled to 60-second epochs. Thick red line shows average autocorrelation; coloured lines show autocorrelation plots for individual participants. f) plot based on arousal data downsampled to 60-second epochs which shows, separately for each arousal bin at time t , the likelihood of

time $t+1$ being the same as time t . Red line shows the real data; grey the control data. Shaded areas show Standard Error of the Means. g) and i): results of pairwise significance comparisons between bins for real (g) and control (i) data – yellow squares indicate a significant difference between bins, blue indicate no significant difference. h) plot based on arousal data downsampled to 60-second epochs in which the likelihood that: (bin at time $t+1$) < (bin at time t) is shown (y-axis) against bin at time t (x-axis). j) plot based on arousal data downsampled to 60-second epochs in which the likelihood that: (bin at time $t+1$) > (bin at time t) is shown (y-axis) against bin at time t (x-axis).

Figure 3: a) Results of analysis 1, examining how stability in arousal varies as function of arousal. Analysis was conducted as described in the Methods. Different coloured lines show the different epoch durations used. Shaded areas show the Standard Error of the Means (SEM). b) Results of identical analysis to a, but conducted on control data. See Methods for description of how this was generated. c) and d): Results of analysis 1, showing how the likelihood of a decrease (c) or an increase (d) in arousal varies as a function of arousal. Different coloured lines show the different epoch durations used. Grey line shows the control data; for clarity, only one epoch duration for the control data is shown (60 seconds). Shaded areas show the SEM. e) Results of analysis to compare the observed values within each bin to chance. f) Results of pairwise significance analyses to compare the observed results between bins. For both plots, yellow squares indicate a significant difference between bins, blue indicate no significant difference.

Figure 4: Vector plots conducted for analysis 2. See detailed description in the Methods of how these were calculated. a) to c): sample dataplots for three individual participants. d) Vector plot for entire control dataset. e) Vector plot for the entire real dataset. f) and g): Scatterplots showing how arousal change (equivalent to the length of the vectors in the vector plots) varies contingent on arousal. Purple dots show change in actigraphy (the x-dimension of the vectors on plots d and e). Green dots show change in heart rate (the y-dimension of the vectors on plots d) and e)). h) and i): Results of pairwise significance analyses to assess how arousal change (as shown in figures f and g) differs between bins. Green indicates no difference; red and blue indicate significant differences (blue – x axis bin < y axis bin; red – x axis bin > y axis bin).

References

- Aston-Jones, G., & Bloom, F. E. (1981). Activity of norepinephrine-containing locus coeruleus neurons in behaving rats anticipates fluctuations in the sleep-waking cycle. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 1(8), 876-886.
- Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function: Adaptive gain and optimal performance. *Annual Review of Neuroscience*, 28, 403-450. doi:10.1146/annurev.neuro.28.061604.135709
- Aston-Jones, G., Rajkowski, J., & Cohen, J. (1999). Role of locus coeruleus in attention and behavioral flexibility. *Biological Psychiatry*, 46(9), 1309-1320. doi:10.1016/s0006-3223(99)00140-7
- Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the royal statistical society. Series B (Methodological)*, 289-300.
- Cacioppo, J. T., Tassinary, L. G., & Berntson, G. G. (2000). *Handbook of Psychophysiology* (2nd ed.): Cambridge University Press, Cambridge, UK.
- Calderon, D., Kilinc, M., Maritan, A., Banavar, J., & Pfaff, D. (2016). Generalized CNS arousal: an elementary force within the vertebrate nervous system. *Neuroscience & Biobehavioral Reviews*, 68, 167-176.
- Cannon, W. B. (1915). Bodily Change in Pain. *Hunger, Fear and Rage, appleton and Company, New York*.
- Cannon, W. B. (1929). Organization for physiological homeostasis. *Physiological reviews*, 9(3), 399-431.
- de Barbaro, K., Clackson, K., & Wass, S. V. (2016). Infant attention is dynamically modulated with changing arousal levels. *Child Development*, 88(2), 629-639. doi:10.1111/cdev.12689
- Fiske, D. W., & Maddi, S. R. (1961). Functions of varied experience.
- Gardner, J. M., Karmel, B.Z. (1995). Development of Arousal-Modulated Visual Preferences in Early Infancy. *Developmental Psychology*, 31(3), 473-482.
- Gross, J. J., & Feldman Barrett, L. (2011). Emotion generation and emotion regulation: One or two depends on your point of view. *Emotion review*, 3(1), 8-16.
- Gunnar, M., & Quevedo, K. (2007). The neurobiology of stress and development. *Annu. Rev. Psychol.*, 58, 145-173.
- Hobson, J. A., & Steriade, M. (1986). Neuronal basis of behavioral state control. *Comprehensive Physiology*.
- Janig, W., & Habler, H. (2000). Specificity in the organization of the autonomic nervous system: a basis for precise neural regulation of homeostatic and protective body functions. *Progress in brain research*, 122, 351-368.
- Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: A review. *Biological Psychology*, 84(3), 394-421.
- Lacey, J. I. (1967). Somatic response patterning and stress: Some revisions of activation theory. In M. H. Appley & R. Trumbull (Eds.), *Psychological stress*: New York: Appleton-Century-Crofts, 1967.
- McEwen, B. S., & Seeman, T. (1999). Protective and damaging effects of mediators of stress: elaborating and testing the concepts of allostasis and allostatic load. *Annals of the New York Academy of Sciences*, 896(1), 30-47.

- Nakamura, T., Kiyono, K., Yoshiuchi, K., Nakahara, R., Struzik, Z. R., & Yamamoto, Y. (2007). Universal scaling law in human behavioral organization. *Physical review letters*, 99(13), 138103.
- Pérez-Edgar, K. (2019). Through the Looking Glass: Temperament and Emotion as Separate and Interwoven Constructs *Handbook of Emotional Development* (pp. 139-168): Springer.
- Pfaff, D. (2018). *How Brain Arousal Mechanisms Work: Paths Toward Consciousness* (Vol. 1): Cambridge University Press.
- Pine, D. S., Mogg, K., Bradley, B. P., Montgomery, L., Monk, C. S., McClure, E., . . . Kaufman, J. (2005). Attention bias to threat in maltreated children: Implications for vulnerability to stress-related psychopathology. *American Journal of Psychiatry*, 162(2), 291-296.
- Potegal, M., Carlson, G., Margulies, D., Gutkovitch, Z., & Wall, M. (2009). Rages or temper tantrums? The behavioral organization, temporal characteristics, and clinical significance of angry-agitated outbursts in child psychiatry inpatients. *Child Psychiatry Hum Dev.*, 40(4), 621-636.
- Proekt, A., Banavar, J. R., Maritan, A., & Pfaff, D. W. (2012). Scale invariance in the dynamics of spontaneous behavior. *Proceedings of the National Academy of Sciences*, 109(26), 10564-10569.
- Schneirla, T. C. (1946). Problems in the bio-psychology of social organization. *The Journal of Abnormal and Social Psychology*, 41(4), 385.
- Selye, H. (1951). The Physiology and Pathology of Exposure to Stress. *The Journal of Bone and Joint Surgery*, 33-A, 818-819.
- Trofimova, I., & Robbins, T. W. (2016). Temperament and arousal systems: a new synthesis of differential psychology and functional neurochemistry. *Neuroscience & Biobehavioral Reviews*, 64, 382-402.
- Ulrich-Lai, Y. M., & Herman, J. P. (2009). Neural regulation of endocrine and autonomic stress responses. *Nature Reviews Neuroscience*, 10(6), 397-409. doi:10.1038/nrn2647
- Vest, A. N., Da Poian, G., Li, Q., Liu, C., Nemati, S., Shah, A. J., & Clifford, G. D. (2018). An open source benchmarked toolbox for cardiovascular waveform and interval analysis. *Physiological measurement*, 39(10), 105004.
- Wass, S. V. (2018). How orchids concentrate? The relationship between physiological stress reactivity and cognitive performance during infancy and early childhood. *Neuroscience & Biobehavioral Reviews*.
- Wass, S. V., Clackson, K., & de Barbaro, K. (2016). Temporal dynamics of arousal and attention in infants. *Developmental psychobiology*, 64, 1-17. doi:DOI 10.1002/dev.21406
- Wass, S. V., Clackson, K., & Leong, V. (2018). Increases in Arousal are More Long-Lasting than Decreases in Arousal: On Homeostatic Failures During Emotion Regulation in Infancy. *Infancy*.
- Wass, S. V., de Barbaro, K., & Clackson, K. (2015). Tonic and phasic co-variation of peripheral arousal indices in infants. *Biological Psychology*, 111, 26-39.
- Wass., S. V., Smith, C. G., Clackson, K., Gibb, C., Eitzenberger, J., & Mirza, F. U. (in press). Parents mimic and influence their infant's autonomic state through dynamic affective state matching. *Current biology*.
- Weil, Z. M., Zhang, Q., Hornung, A., Blizard, D., & Pfaff, D. W. (2010). Impact of generalized brain arousal on sexual behavior. *Proceedings of the National Academy of Sciences*, 107(5), 2265-2270.

Zubek, J. P., & MacNeill, M. (1966). Effects of immobilization: Behavioural and EEG changes.
Canadian Journal of Psychology/Revue canadienne de psychologie, 20(3), 316.

Zuckerman, M. (1979). *Sensation seeking*: Wiley Online Library.

1 Supplementary Methods

1.1 Demographic details

Exclusion criteria were: complex medical conditions, skin allergies, heart conditions, parents below 18 years of age, and parents receiving care from a mental health organisation or professional. We also excluded families in which the primary day-time care was performed by a male parent, because the numbers were insufficient to provide an adequately gender-matched sample.

Table S1: Demographic details for the sample

Infant age (days) – mean		351.9
- SE		4.6
Gender (% male)		39.3
Infant Ethnicity (%)	White British	51.9
	Other white	11.4
	Afro-Caribbean	8.9
	Asian, Indian & Pakistani	10.1
	Mixed - White/Afro-Caribbean	2.5
	Mixed - White/Asian	7.6
	Other mixed	7.6
Household Income (%)	Under £16k	30.4
	£16-£25k	29.1
	£26-£35k	11.4
	£36-£50k	12.7
	£51-£80k	8.9
	>£80k	7.6
Maternal education (%)	Postgraduate	34.2
	Undergraduate	49.4
	FE qualification	2.5
	A-level	3.8
	GCSE	5.1
	No formal qualifications	2.5
	Other	1.3

Figure S1: photographs of: a) equipment used b) a child wearing the equipment

1.2 Autonomic data parsing and calculation of the autonomic composite measure

Electro-cardiography (ECG). ECG was recorded at 250Hz. Analysis of the Inter-Beat Intervals (IBIs) was performed using custom-built Matlab scripts that operate via a combination of adaptive amplitude and velocity thresholding, along with application of max/min IBI and rate of change of IBI criteria (Wass, de Barbaro, & Clackson, 2015). Data were verified *post hoc* via visual inspection. Due to technical problems with the ECG recording leads (N=9) and to problems with the placement of the ECG recording electrodes (N=2), the ECG data were unavailable for 11 of the participants tested.

Heart-Rate Variability (HRV) was calculated using the PhysioNet Cardiovascular Signal Toolbox (Vest et al., 2018). In these scripts, which performed a completely separate analysis of the ECG data, a 60-second window with an increment of 60 seconds was implemented, and the default settings were used with the exception that the min/max inter-beat interval was set at 300/750 ms for the infant data and 300/1300 ms for the adult data. The Root Mean Square of Successive Differences (RMSSD) measure was taken to index Heart Rate Variability, but other frequency domain measures were additionally inspected and showed highly similar results, as expected.

Actigraphy. Actigraphy was recorded at 30Hz. To parse the actigraphy data we first manually inspected the data, then corrected artifacts specific to the recording device used, then applied a Butterworth low-pass filter with a cut-off of 0.1 Hz to remove high-frequency noise, and then collapsed from three dimensions into one. Actigraphy data were available for all participants tested.

Arousal composite. In previous research we have shown significant patterns of tonic and phasic covariation between different autonomic measures collected from infants (Wass, Clackson, & de Barbaro, 2016; Wass et al., 2015). Here, we include plots showing that the present dataset replicated and extended these results. The plots only show the sections of the data when participants were at home, comparing sections in which the infants were awake and asleep. Figure S2a shows cross-correlation plots examining the relationship between heart rate and movement. In both waking and sleeping sections the zero-lag correlation is 0.5. Figure S2c shows how these zero-lagged correlations vary on a per-participant basis. S2b shows an illustrative sample from a single participant. Sleeping sections show very low movement levels and lower heart rate. Of note, heart rate and movement do still inter-relate during the sleeping

sections of the data (Figure S2c), albeit that the variability in heart rate and movement is lower. Figure S2 d)-f) show similar relationships between heart rate and heart rate variability, illustrating the strong and consistent negative relationships that were observed between these variables, as predicted.

Figure S2: Illustrating the relationship between the individual physiological measures included in the composite measure. a) Cross-correlation of the relationship between HR and Movement. b) Scatterplot from a sample participant. Each datapoint represents an individual 60-second epoch of data. c) Histograms showing the average zero-lagged correlation between 60-second epochs, calculated on a per-participant basis and then averaged. d)-f) Equivalent plots for Heart rate and Heart rate variability.

Extensive previous research has identified fractionation, and differentiation, within our autonomic response systems (Janig & Habler, 2000; Kreibig, 2010; Lacey, 1967; Levenson, 2014; Quas et al., 2014) – suggesting, for example that the sympathetic and parasympathetic subdivisions operate, to an extent, in a non-additive manner (Samuels & Szabadi, 2008). Although indubitable, these findings should be seen as rendering incorrect our treatment here of autonomic arousal as a one-dimensional construct. Like many other arguments concerned with general versus specific factors, the question is rather one of the relative proportions of variance that can be accounted for by a single common factor in comparison with the variance accounted for by the sum of specific factors (Graham & Jackson, 1970) (see also (Calderon, Kilinc, Maritan, Banavar, & Pfaff, 2016)).

As a result of these considerations, the three autonomic measures were collapsed into a single composite measure for Analysis 1. This was done by calculating the natural logarithm of the actigraphy data, inverting the HRV data, calculating the z-score of each measure and then averaging the z-scores.

1.3 Home/Awake coding

Home/not home. Coding of when participants were at home was performed using the GPS monitors built into the recording devices. The position of the participant's home was calculated based on the postcode data that they supplied, and any GPS samples within a 50m area of that location were treated as Home (corresponding to the accuracy of the GPS devices that we were using).

Sleeping/waking. To identify samples in which infants were sleeping, parents were asked to fill in a logbook identifying the times of infants' naps during the day. This information was manually verified by visually examining the actigraphy and ECG data collected, on a participant by participant basis. Actigraphy, in particular, shows marked differences between sleeping and waking samples (see Figure 1 in main text), which allowed us to verify the parental reports with a high degree of accuracy. N=4 of the participants recorded did not sleep during the day that we were recording.

1.4 Relationship of vocal affect to autonomic arousal

Vocal affect coding. For reasons of bandwidth, the microphone recorded just a 5-second snapshot of the auditory environment every 60 seconds. *Post hoc*, trained coders listened to each recording to identified samples in which the infant was vocalising, and those in which the parent was vocalising to the infant, and those in which the parent was vocalising to another adult. In order to assess inter-rater reliability, 24% of the sample was double coded; Cohen's kappa was found to be 0.89, which is high (McHugh, 2012). The infant vocalisations were also coded for vocal intensity on a scale from 1 (least intense) and 9 (most intense), and for affect on a scale from 1 (fussy and difficult) to 9 (happy and engaged). In order to assess inter-rater reliability, 24% of the sample was double coded; Cohen's kappa for this coding was 0.60, which is acceptable (McHugh, 2012). All coders were blinded to all intended analyses.

Figure S3: Top: stacked bar-chart illustrating the proportion of samples by vocal intensity, sorted by arousal z-score. Yellow colours indicate the most intense vocalisations, and blue colours indicate least intense vocalisations. Bottom: stacked bar-chart illustrating the proportion of samples by vocal affect, sorted by arousal z-score. Yellow colours indicate positive affect vocalisations, and blue colours indicate negative affect vocalisations.

Figure S3 shows the distribution of hand-coded vocal intensity (top) and hand-coded vocal affect (bottom) by autonomic arousal. Vocal intensity showed a relationship such that greater intensity was observed at higher autonomic arousal. Intense negative affect was more commonly observed at high arousal, but intense positive states were equally common throughout.

1.5 Skew in original data

One feature of the original data that our control analysis does not exactly replicate is that the original data showed a consistent mild negative skew (see Figure S4). This is because the data were z-scored using all of the data available per participant, per day. The present analyses, however, only examine segments of the data while the participants were at home and awake. Because the sleeping segments that were excluded showed markedly lower overall arousal, the remaining z-scored data showed mean values consistently greater than 0, with a negative skew. We have not replicated this feature of our data in the control analysis, which uses data with the same mean and variance as the original data, but with no skew. However, we cannot see how this feature of our data may have contributed to the observed results.

Figure S4: Violin plot showing mean skew in original data, sorted by epoch bin size.

References

- Calderon, D., Kilinc, M., Maritan, A., Banavar, J., & Pfaff, D. (2016). Generalized CNS arousal: an elementary force within the vertebrate nervous system. *Neuroscience & Biobehavioral Reviews*, 68, 167-176.
- Graham, F. K., & Jackson, J. C. (1970). Arousal systems and infant heart rate responses. *Advances in child development and behavior*, 5, 59-117.
- Janig, W., & Habler, H. (2000). Specificity in the organization of the autonomic nervous system: a basis for precise neural regulation of homeostatic and protective body functions. *Progress in brain research*, 122, 351-368.
- Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: A review. *Biological Psychology*, 84(3), 394-421.
- Lacey, J. I. (1967). Somatic response patterning and stress: Some revisions of activation theory. In M. H. Appley & R. Trumbull (Eds.), *Psychological stress*. New York: Appleton-Century-Crofts, 1967.
- Levenson, R. W. (2014). The autonomic nervous system and emotion. *Emotion review*, 6(2), 100-112.
- McHugh, M. L. (2012). Interrater reliability: the kappa statistic. *Biochemia medica: Biochemia medica*, 22(3), 276-282.
- Quas, J. A., Yim, I. S., Oberlander, T. F., Nordstokke, D., Essex, M. J., Armstrong, J. M., . . . Boyce, W. T. (2014). The symphonic structure of childhood stress reactivity: patterns of sympathetic, parasympathetic, and adrenocortical responses to psychological challenge. *Dev Psychopathol*, 26(4 Pt 1), 963-982. doi:10.1017/s0954579414000480

- Samuels, E. R., & Szabadi, E. (2008). Functional neuroanatomy of the noradrenergic locus coeruleus: its roles in the regulation of arousal and autonomic function part I: principles of functional organisation. *Current neuropharmacology*, 6(3), 235-253.
- Vest, A. N., Da Poian, G., Li, Q., Liu, C., Nemati, S., Shah, A. J., & Clifford, G. D. (2018). An open source benchmarked toolbox for cardiovascular waveform and interval analysis. *Physiological measurement*, 39(10), 105004.
- Wass, S. V., Clackson, K., & de Barbaro, K. (2016). Temporal dynamics of arousal and attention in infants. *Developmental psychobiology*, 64, 1-17. doi:DOI 10.1002/dev.21406
- Wass, S. V., de Barbaro, K., & Clackson, K. (2015). Tonic and phasic co-variation of peripheral arousal indices in infants. *Biological Psychology*, 111, 26-39.