

Title: New meanings of thin-skinned: the contrasting attentional profiles of typical 12-month-olds who show high, and low, stress reactivity.

Abstract: Previous research is inconsistent as to whether a more labile (faster-changing) autonomic system confers performance advantages, or disadvantages, in infants and children. To examine this, we presented a stimulus battery consisting of mixed static and dynamic viewing materials to a cohort of 63 typical 12-month-old infants. While viewing the battery, infants' spontaneous visual attention (looks to and away from the screen) was measured. Concurrently, arousal was recorded via heart rate, electrodermal activity, head velocity and peripheral movement levels. In addition, stress reactivity was assessed using a mild behavioral stressor (watching a video of another infant crying). We found that infants who were generally more attentive showed *smaller* heart rate increases to the stressor. However, they also showed greater phasic autonomic changes to attractive, attention-getting stimulus events, a faster rate of change of both look duration and of arousal, and more general oscillatory activity in arousal. Finally, four sessions of attention training were applied to a subset of the infants (24 trained, 24 active controls), which had the effect of increasing visual sustained attention. No changes in HR responses to stressor were observed as a result of training, but concomitant increases in arousal lability were observed. Our results point to two contrasting autonomic profiles: infants with high autonomic reactivity to stressors show short attention durations, whereas infants with lower autonomic reactivity show longer attention durations and greater arousal lability.

Keywords: Arousal; Attention; Reactivity; Infant

Introduction

The Autonomic Nervous System (ANS) serves as the fast-acting, neural substrate of the body's stress response (Cacioppo, Tassinary, & Berntson, 2000; Tsigos & Chrousos, 2002; Ulrich-Lai & Herman, 2009). The ANS is thought to operate primarily via norepinephrine and cholinergic neurotransmitters, and to be governed by a range of brain areas centered on the brainstem and hypothalamus (Amaral & Sinnamon, 1977; Arnsten & Goldman-Rakic, 1984). It acts through two complementary systems - the sympathetic (SNS) and parasympathetic (PNS) subdivisions - that have largely, but not exclusively, opposite effects (Berntson, Cacioppo, Quigley, & Fabro, 1994; Kolacz, Holochwost, Gariepy, & Mills-Koonce, 2016; Quas et al., 2014).

Like any dynamic, biological system, our levels of autonomic arousal are in constant flux. The ANS shows periodic oscillatory activity at multiple time-scales ranging from circadian rhythms (Aston-Jones, Gonzalez, & Doran, 2007; Silver & LeSauter, 2008) through to the sub-second scale (e.g. Mayer waves - Julien, 2006; see also Robertson, 1993; Robertson, Bacher, & Huntington, 2001). The ANS also responds reflexively in response to different types of external events: these include events that are unexpected, intense or threatening (Aston-Jones & Cohen, 2005; Usher, Cohen, Servan-Schreiber, Rajkowski, & Aston-Jones, 1999) as well as events that are nonthreatening and of moderate intensity (Sechenov, 1965). The ANS also shows random, stochastic patterns of change (Sawnani, Jackson, Murphy, Beckerman, & Simakajornboon, 2004; Surwillo & Quilter, 1965). Finally, it also shows other behaviours to maintain homeostasis, or allostasis – the re-establishment of equilibrium

following perturbation to the system (Davis, 1958; Karemaker & Strackee, 1987; Selye, 1951; Silver & LeSauter, 2008).

Early research in psychobiology (Yerkes & Dodson, 1908), consistent with later research based on animal models (Aston-Jones & Cohen, 2005), suggests that autonomic arousal and attentional behaviors covary. Individuals with high tonic ANS activity are more vigilant or stimulus-driven and show increased habitual responding, increased fear conditioning and memory consolidation, and more rigid, inflexible, attention behaviors. Mid-level tonic firing is associated with increased phasic responsiveness, together with superior working memory, superior selective attention, and increased attentional flexibility. Low-level tonic firing is associated with general inattentiveness, and reduced phasic responsiveness to sought-for stimuli (Aston-Jones, Rajkowski, & Kubiak, 1997; Rajkowski, Majczynski, Clayton, & Aston-Jones, 2004).

These results from animal work by Aston-Jones and colleagues are consistent with neuroimaging research into how stress affects attentional behaviors in adults. Temporarily elevated levels of stress are associated with down-regulation of areas such as the dorsolateral pre-frontal cortex that are involved in directed attention, together with up-regulation of areas including the hypothalamus, striatum, amygdala and occipital cortices involved in bottom-up, salience-driving orienting (Arnsten, 2009). At lower levels of stress (analogous to Aston-Jones' mid-level tonic arousal), frontal cortical areas show increased activity (Arnsten, 2009). Behaviorally this leads to a phenotype in which high stress is associated with decreased voluntary control of attention and increased oculomotor responsivity to salient peripheral targets, whereas lower stress is associated with increased voluntary control (Alexander, Hillier, Smith, Tivarus, & Beversdorf, 2007; Broadbent, 1971). However, the current models from cognitive neuroscience do not explore the neural correlates of hypo-arousal, as

predicted by the Yerkes-Dodson and Aston-Jones models. Presumably these would include globally decreased task-related activation.

Previous work with infants and children has robustly demonstrated that heart rate variability within the 0.2-1Hz range indexes Respiratory Sinus Arrhythmia (RSA), which is thought to measure PNS control (e.g. Porges, 2007). Increased RSA associates with increased visual sustained attention and superior general cognitive outcomes (Beauchaine & Thayer, 2015; DeGangi, Porges, Sickel, & Greenspan, 1993; Marcovitch et al., 2010; Rash & Aguirre-Camacho, 2012). In typical 4-6-month-old infants, greater RSA indexes greater sustained attention, as indexed using the interrupted stimulus method (Richards, 1985), along with reduced distractibility (Richards, 1987). In typical 3.5-year-old children, higher RSA is associated with better performance at a range of Executive Function tasks (Marcovitch et al., 2010).

Baseline RSA is also associated with the magnitude of HR decelerations to novel attention-getting stimuli, such that increased RSA is associated with increased decelerations (Richards, 1987; Richards & Casey, 1991). Increased decelerations to interesting, novel stimuli have also been shown to associate with enhanced neural processing (larger amplitude and more selective ERPs) (Guy et al., 2017; Richards, 2003; Xie & Richards, 2017) and reduced distractibility (Lansink & Richards, 1997; Richards & Gibson, 1997).

These findings can be contrasted with studies that have examined infants' HR reactivity to unexpected, negative stimulus events. Although fewer studies have addressed this question we recently reported that typical 12-month-old infants who show greater HR reactivity to a negative event (a stressor) show *shorter* attention durations, along with better visual recognition memory (de Barbaro, Clackson, & Wass, 2016b). This finding was, we argued, consistent with the adult and animal research

(Arnsten, 2009; Aston-Jones & Cohen, 2005; Yerkes & Dodson, 1908), such that temporary stress both increases distractibility and enhances processes dependent on subcortical structures such as basic memory consolidation, habit formation and fear conditioning (Cahill & McGaugh, 1996; Luethi, Meier, & Sandi, 2009). Also consistent with this, de Barbaro and colleagues found that infants who showed faster responses to brightly-colored videos were more distracted by peripheral stimuli and also showed more perseveration to the video stimuli over the course of multiple trials, also suggesting a lack of habituation (de Barbaro, Chiba, & Deak, 2011).

As yet, however, no research has reconciled the contrasting roles of lability within these previous research findings – in which increased arousal lability to unexpected ‘stressor’ stimuli is associated with shorter look durations, but increased arousal lability to interesting, sought-for events is associated with longer look durations. This was the aim of the present paper.

To examine this, we presented a stimulus battery consisting of mixed static and dynamic viewing materials to a cohort of 63 typical 12-month-old infants. To index attention we measured look durations. Individual differences in look durations toward static and dynamic stimuli show strong intra- and inter-individual stability at this age, meriting their use as an index of individual differences (Colombo & Mitchell, 2009; Wass, 2014). Previous research suggests that, at 12 months, which is the age of the infants tested here, looking behavior is beginning to be influenced by endogenous attention control (Colombo & Cheatham, 2006; Courage, Reynolds, & Richards, 2006; Richards, 2010).

Arousal was measured by recording heart rate, galvanic skin response, head movement and peripheral (foot) movement. Based on previous research that identified tonic and phasic covariation between these measures (Wass, Clackson, & de Barbaro,

2016; Wass, de Barbaro, & Clackson, 2015), these have been pooled into a single, composite measure. In the Supplementary Materials, the same results are presented separately for heart rate, head movement, foot movement and EDA.

Our first method for defining lability was taken from our previous research (de Barbaro et al., 2016b). Infants were shown a mild behavioral stressor, a video of another infant crying, while their HR changes were monitored. In addition, we used four novel ways of characterizing lability. First, in the frequency domain, we analysed the total amount of oscillatory activity in the 0.1-2Hz range (Analysis 1). We measured oscillatory activity in HR, for which activity at c.0.5Hz is thought to index RSA (Porges, Stamps, & Walter, 1974); we also examined oscillatory activity in EDA and two measures of movement that are not known to covary with the respiration cycle in the same way. This was done in order to assess whether any associations observed between attention and autonomic lability were specific to RSA/PNS-associated changes, or whether they represented a more general feature. Second, in the time domain, we examined the rate of change of spontaneous modulation of arousal and look duration across the session, by calculating the auto-correlation function. These analyses examine the rate of change of arousal (Analysis 2) and look duration (Analysis 3), irrespective of stimulus events, during the presentation of our mixed, continuously changing testing battery. Third, we examined the change in arousal observed relative to new, attractive, attention-getting stimuli (clips from baby TV programs). Spectrograms were used to examine change in the frequency domain, as a function of time. This approach is similar to previous research that examines changes in mean HR relative to new stimulus events (e.g. Pempek et al., 2010).

Based on previous research we predicted that look duration would associate negatively with HR change to stressor (longer look duration associated with smaller

HR change to stressor) (de Barbaro et al., 2016b). Based on other previous research (Richards, 1985, 1987; Richards & Casey, 1991) we predicted that positive associations would be observed between look duration and oscillatory activity in arousal. We also predicted that look duration would associate positive with the phasic, event-related change in arousal observed relative to attractive, attention-eliciting stimulus events. Of note, these contrasting relationships have not, to our knowledge, previously been tested within a single cohort.

The above observations are all correlational, leaving open the possibility that observed relationships are not due to any underlying causal associations between the two variables, but merely due to shared variance attributable to some unobserved third factor. Therefore, to examine causal mechanisms, we administered targeted attention training, that previous research suggests leads to significant increases in habituation speed and visual sustained attention, as well reductions in resting salivary cortisol (Wass, Cook, & Clackson, in press). Here, we examined for the first time whether training-related changes in attention were accompanied by concomitant changes in arousal lability. Based on previous correlational findings (de Barbaro et al., 2016b; Richards & Casey, 1991; Rueda, Posner, & Rothbart, 2005) we predicted that training attention would lead to increased general arousal lability, but decreased HR changes to a mild experimental stressor.

Methods

Participants

Cross-sectional study (Analyses 1-5). 63 infants participated in the cross-sectional study from a volunteer research participant pool at the MRC Cognition and Brain Sciences Unit in Cambridge. The recruitment area for this study, Cambridge, UK, is a wealthy university town and participants were predominantly Caucasian. No participating families reported any major psychiatric or other clinical conditions within the immediate family. Of the 63 infants who participated in the cross-sectional study, data collection was impossible for 6 of the infants due to equipment malfunction. In total, therefore, usable data were collected from 57 infants. The average age of the infants who contributed usable data was 12 months (mean age in days: 377, SD: 40); the sample comprised 30 males and 27 females.

Training study (Analysis 6). Of the 63 participants in the cross-sectional study, 48 were randomly allocated to participate in the training study. This selection was done at random, and prior to the participants' first contact with the research team. Following recruitment, and prior to their first contact with the experimental team, the 48 infants were randomly allocated to one of two groups: the trained group (N=24) or a control group (N=24). Participants' mean (S.E.M.) age at visit 1 was: trained group - 360 (23), control group - 361 (23) days. The gender split was 11/24 male for the trained group, 9/24 male for the control group.

Protocol – cross-sectional study (Analyses 1-5)

All procedures involved in the study received ethical approval from the Cambridge University Psychology Research Ethics Committee. The title of the

approved study was ‘Using targeted training to investigate attentional control in typically developing 12-24-month-olds.’

Infants were seated on their caregivers’ laps during recording. Caregivers were requested not to talk during recording, but otherwise no explicit instructions were given. The stimulus battery, which is described in more detail in the Supplementary Materials (see Figure S1) constituted a mixture of three different types of stimulus: photographs (pictures of other children’s faces), mixed static/dynamic animations and shapes (e.g. a cartoon monkey face moving between two rectangles) and video clips (excerpts from popular children’s television programs). Different types of stimulus were presented in rotating order. No one type of stimulus was presented for more than 1-2 minutes before a change. Although the blocks were presented in consistent order, the selection of which stimuli was presented within each block was counterbalanced between participants. The exception to this were the two videos presented at the start of the session, that were used as the baseline for the analysis examining reactivity to stressor. These were always presented at the start of the session. They were a) a clip from the children’s television program *Abadas* and b) a baby video taken from *YouTube*. Overall, all participants viewed all materials once during the testing session.

At two predefined moments during the experimental battery a mild experimental stressor was presented. These were 30-40-second videos, presented with sound, showing young infants crying. Parents were warned that these videos would be presented before the start of the experiment. If infants showed strong or persistent negative affect (such as crying) during the presentation of the videos, the experiment was curtailed. This occurred less than 5% of the time; the vast majority of the infants observed both videos in full.

Exactly the same stimuli were presented to all infants. Materials were presented

using Matlab (Mathworks, Inc) and Psychtoolbox. Breaks were permitted during testing if the child became agitated or the parent requested it. This occurred only rarely (<10% of cases). In these cases, recording and stimulus presentation were discontinued and only recommenced when the infant was in an alert and interested state.

Protocol - attention training study (Analysis 6)

Visit 1 consisted of the pre-assessment battery, which was the same protocol as for the cross-sectional study, described above. This was then followed immediately by a training or control (T/C) session 1; visits 2-4 consisted of dedicated T/C sessions; visit 5 consisted of the post-assessment tasks (identical to pre-assessment tasks). Visits 5 took place within mean 17 (sd 8) days of visit 1.

Training materials consisted of a battery of gaze-contingent eyetracker tasks intended to train the voluntary control of attention, by targeting a combination of interference control, short-term memory and focused attention. These are described in more detail in the Supplementary Materials (see Figure S2). The control group attended the same number of sessions but watched non-contingent infant-appropriate animations and TV clips on the eye-tracker for a matched amount of time.

Of 48 infants initially recruited, 8 withdrew between visits 1 and 5 (4/4 for T/C), due either to the child or a member of their family falling ill during the initial two week-phase, meaning that they could not complete the sessions within the allocated time (N=4), or to infant fussiness (N=4). In a separate report we reported in detail on the changes in behavior as a result of testing (Wass et al., in press). Specifically, we found that training led to increases in visual sustained attention, to faster habituation speeds and improved sequence learning. We also found that training led to a significant decrease in salivary cortisol (Wass et al., in press).

Data analyses

Behavioral measure. Visual attention was indexed by recording the durations of infants' looks to and away from the screen. Episodes were treated as starting when the child first looked towards the screen, and ending when the child looked away from the screen. This measure was automatically coded based on eyetracker footage recorded. Short sections of missing data (<2 seconds) were interpolated, to cover data loss due to blinks and other artifactual causes.

Arousal measures. In humans, autonomic arousal is measured by recording peripheral ANS indices such as heart rate, electrodermal activity, movement and pupil size. Some of these, such as heart rate, are thought to be influenced by both the SNS and PNS (McCabe, Schneiderman, & Field, 2000), whereas others, such as EDA, are thought to be primarily influenced by SNS (Shields, Macdowell, Fairchild, & Campbell, 1987). However previous research has pointed to significant tonic and phasic covariation between these peripheral indices, consistent with the idea that the SNS and PNS operate largely (albeit not exclusively) in opposition (Kahneman, Tursky, Shapiro, & Crider, 1969; Wass et al., 2016; Wass, de Barbaro, et al., 2015).

Electro-cardiogram (ECG), electro-dermal activity (EDA) and triaxial accelerometry were recorded using a 1000Hz BioPac™ (Santa Barbara, CA) device. ECG was recorded using disposable Ag-Cl electrodes in a modified lead II position. EDA was recorded with EDA (Isotonic Gel) snap electrodes on the plantar surface of the foot (Ham & Tronick, 2008). A triaxial accelerometer 5G was used, and head velocity data was derived from eyetracker data using a method described previously (Wass, de Barbaro, et al., 2015).

i) Heart rate (HR). Automatic r-peak identification was performed using the Acknowledge commercial software package. Automatic artifact rejection was then performed by excluding those beats showing an inter-beat interval of <330 ms or >750 ms, and by excluding those samples showing a rate of change of inter-beat interval of greater than 80ms between samples. In the Supplementary Materials, we report on a comparison of these cleaning techniques with traditional hand-coding which shows a close agreement between the two approaches. Finally, HR data were z-scored and epoched into one-second epochs.

ii) Electrodermal activity (EDA). First, null values were removed from the data using a threshold of $0.1\mu\text{V}$. Second, data were log transformed to remove positively skewed values. Third, data were z-scored and epoched into one-second epochs.

iii) Head velocity (HV). First, data samples showing a change in position of more than 0.025 screen units between two consecutive samples (recorded at 120Hz) were excluded. Second, data were downsampled to 12Hz by calculating a moving median window. Third, position data were converted to velocity data by taking the first derivative. Fourth, six data streams (three dimensions, two eyes) were collapsed to a single stream by taking the average. Fifth, data were z-scored and epoched into one-second epochs.

iv) Peripheral accelerometer (PA). First, data were filtered to remove high-frequency noise using a Butterworth filter with a cut-off of 0.5Hz. Second, three-dimensional movement data were summed to create a one-dimensional estimate of total movement. Third, median windowing was performed.

Following data reduction, data were downsampled to a sampling frequency of 4Hz, that was consistent across all four arousal measures. Short (<4 second) segments

of missing data were linearly interpolated, and Z-scores were calculated by comparing results across all participants. Following previous research that identified tonic and phasic covariation between these measures (Wass et al., 2016; Wass, de Barbaro, et al., 2015) they were collapsed into a single composite, by averaging the z-scores. However, in addition, in the Supplementary Materials, we also present results of the measures singly.

Analysis 1 - HR reactivity to stressor. This was calculated using an identical procedure to previously (de Barbaro et al., 2016b). In brief, the average HR (in beats per minute (BPM)) was calculated during the stressor videos and compared with two baseline videos presented at the start of the session. Stress reactivity was indexed as (HR during stressor videos) – (HR during baseline videos). We also tested for relationships between baseline HR and HR to stressor as predicted by the Law of Initial Values (Richards, 1980).

Our new measures of arousal lability were calculated in the following way:

Analysis 2 - Calculation of Short-Time Fourier Transform (STFT). The STFT converts a signal from its original domain (time) to a representation in the frequency domain (Chatfield, 2004). Prior to calculating the STFT, data were detrended to ensure stationarity. This was performed by computing the least-squares fit and subtracting the function from the data. As determined by the sampling frequency of our data (4Hz) we reported on fluctuations up to 2Hz, and down to 0.1 Hz. Analyses were then averaged across the time domain to index the total amount of oscillatory activity at each frequency band across the entire sample.

Analysis 3/4 - Calculation of Auto-Correlation function (ACF) and Partial Auto-Correlation function (PACF). The ACF indexes the cross-correlation of a measure with itself at different lag-intervals in time (Chatfield, 2004). It indexes the similarity

between observations as a function of the time-lag between them. The PACF also indexes the cross-correlation of a measure with itself at different time lags, but at each time lag k it controls for the effect of previous autocorrelations from lag 1 to $k-1$ (Chatfield, 2004). Prior to calculating the ACF and PACF a linear detrend was conducted by computing the least-squares fit and subtracting the function from the data.

Analysis 5 - Calculation of spectrograms. Spectrograms quantify how the frequency content of a dataset changes over time (Muthuswamy & Thakor, 1998). Spectrograms were calculated by applying a short-time Fourier Transform in non-overlapping 1000 ms windows. Results were rescaled by dividing results by the average power observed at that frequency across all trials. Our analyses examined how oscillatory activity at each frequency changed, relative to stimulus events, across time.

Results

Figure 1A shows the experimental set-up and Figure 1B shows a sample of the continuous semi-processed data that was used in our analyses.

INSERT FIGURE 1 HERE

Visual sustained attention, indexed via look duration, was treated as the main dependent variable. The median ([range], *standard deviation*) look duration observed was 22.9 ([5.2-43.5], 9.1) seconds.

Analysis 1 – look duration to HR change to stressor

First we examined the bivariate relationship between HR change to stressor and look duration across the entire testing battery. Kolmogorov-Smirnov (KS) tests showed that both variables were normally distributed. Consistent with previous results (de Barbaro et al., 2016b) we found that HR to stressor showed a negative association with look duration $r(56)=-.33$, $p=.02$ (Figure 2D). Also consistent with previous results, we found no relationship between tonic HR (calculated as the mean HR across the entire testing session) and HR change to stressor $r(56)=-.11$, $p=.42$ (de Barbaro et al., 2016b).

INSERT FIGURE 2 HERE

Analysis 2 – look duration to general oscillatory activity in arousal

Figure 2 shows the results of the FFTs calculated for the composite arousal measure. Figure S4, in the SM, shows the equivalent plots for the individual arousal

measures. Data have been split using a median split by look duration (Figure 2). Shaded error bars show the 95% CIs observed within each group. A RM ANOVA examining the relationship between Frequency (18 levels) x Group (High vs Low sustained attention) identified a significant main effect of Group ($F(1,56)=16.9$ $p=.0001$). Next, the relationship between total average arousal power (summed across the frequency range) and average look duration was examined (Figure 2C). KS tests showed both variables to be normally distributed. A significant bivariate relationship was observed $r(56)=.47$, $p<.001$. This suggests that individuals with longer average look durations tend to show higher arousal total power (i.e. more total oscillatory activity). An identical analysis identified no relationship between tonic HR and total arousal power $r(56)=.19$, $p=.17$.

Next, we examined the relationship between total oscillatory activity in arousal and HR change to stressor (the measure used in Analysis 1) (Figure 2E). KS tests showed both variables to be normally distributed. Pearsons' correlations showed a negative relationship between the two variables: $r(56)=-.30$, $p=.005$. This suggests that individuals who showed a higher HR change to stressor showed less arousal total power (i.e. less total oscillatory activity).

The stressor videos were embedded within the stimulus battery (see Figure S3). Therefore, in addition to the main analyses, that were conducted on data obtained across the entire stimulus battery, we also wished to examine whether our results were directly attributable to differences in behavior around the stressor video. To examine this, the sections of data between the start of each of the two stressor videos and 3 minutes after the end of the stressor videos were excerpted, and an identical analysis was repeated based on the remaining data. The relationship between arousal power and look duration was still present $r(56)=.47$, $p<.001$. This suggests that the relationship between arousal

power and look duration was not directly attributable to differences in behavior around the stressor video.

Analysis 3 - do infants with higher visual sustained attention show increased general modulation of arousal, irrespective of looks?

The auto-correlation function (ACF) of a time-series indexes the rate of change of that time-series relative to itself (Clifford, Richardson, & Hemon, 1989; Thiebaut & Zwiers, 1984). Essentially, a faster fall-off in ACF values indicates a more rapidly changing measure. Figure 4 A-C shows an illustrative example. The partial auto-correlation function (PACF) indexes the cross-correlation of a measure with itself controlling for values of the time series at all shorter lags (Chatfield, 2004).

Group results were split using a median split into 'high visual sustained attention' and 'low visual sustained attention' and the ACF functions of arousal were compared for each group. Figures 3D and 3E show the ACF and PACF results split by visual sustained attention. The PACF showed a sharp drop-off after lag 1 suggesting that the data show a strong first order auto-regressive tendency. Statistical analyses therefore were therefore conducted on the first lag value of the PACF.

K-S tests showed that results were not normally distributed, so a non-parametric Wilcoxon rank sum test was used to assess the significance of group differences. The PACF function showed a significant difference at lag 1 $Z=2.07$, $p=.039$. This indicates that the group with higher visual sustained attention showed a more rapidly changing profile of arousal.

The second order lag term was also marginally significant in both groups. However the Wilcoxon rank sum test indicated no significant group differences on this term $Z=1.49$, $p=.30$.

One possible explanation for the difference observed on the lag 1 term is that infants with greater endogenous attentional control (or interest) would show both longer look durations and increased look-related arousal decelerations. We conducted a number of analyses to examine this possibility, as we present in the Supplementary Materials. The evidence that we obtained suggested that, in our cohort of 12-month-olds and with our experimental set-up, there was only relatively weak evidence for arousal decelerations on a look-by-look basis. Thus, increased look-related arousal decelerations are unlikely to be the explanation for the results observed.

INSERT FIGURE 3 HERE

Analysis 4 - do infants with higher visual sustained attention show more increased general modulation of look durations?

Next we wished to examine: does the high visual sustained attention group show a faster *rate of change of look duration* than the low visual sustained attention group? To assess this, we again calculated auto-correlations (see Figures 4A-4C for illustrative examples). The group was split using a median split into ‘high visual sustained attention and ‘low visual sustained attention’ and the ACF functions for look duration were compared. The ACF and PACF are shown in Figures 4D and 4E. Again, the PACF showed a sharp drop-off after lag 1 suggesting that the data show a strong first order auto-regressive tendency, and so statistical analyses concentrated on the first lag value of the PACF.

K-S tests showed that results were not normally distributed, so a non-parametric Wilcoxon rank sum test was used to assess the significance of group differences. The PACF function showed a significant difference at lag 1 $Z=2.26$, $p=.024$. This indicates

that the group with higher visual sustained attention showed a faster-changing profile of look duration. Of note, an artifactual explanation for this relationship, whereby longer average look duration led to the appearance of a slower-changing profile of look duration, was considered and rejected on the basis that it would have led to the opposite pattern of results being observed.

INSERT FIGURE 4 HERE

Analysis 5 - do infants with higher visual sustained attention show increased arousal modulation in response to stimulus changes?

Next we wished to examine patterns of autonomic change relative to experimenter-controlled stimulus events. To do this we excerpted five moments from our testing battery, when attractive television clips (excerpts from CBeebies programs such as *Baby Jake*) were presented. Each clip lasted 25-40 seconds, and they were presented at intervals during the testing battery (see Figure S1). For consistency, the segment from 10 seconds prior to the clip to 20 seconds after the start of the clip has been analysed (see Figure 5).

INSERT FIGURE 5 HERE

Spectrograms index the change in power separately for different frequency spectra over time. Figure 5A shows the averages obtained across the entire group. It can be seen that the power across the whole spectrum <1.5Hz is relatively high before the start of the clip, and then decreases rapidly at the start of the clip. Figures 5B and 5C show the same spectrograms for the low and high visual sustained attention groups

respectively. It can be seen that Figure 5B, the low visual sustained attention group, does not show the same decrease: power in arousal remains high, even after the start of the clip. Figure 5C, the high visual sustained attention group, does however show an abrupt decrease in power. Of note, this finding is not simply the same finding as that shown in Figure 2. Figure 2 shows globally *increased* arousal power in the high sustained attention group, whereas Analysis 5 shows greater phasic *decreases* in arousal power in the high sustained attention group, relative to the appearance of attractive, attention-getting stimuli.

Of note, changes do not, however, appear to be completely consistent across the frequency spectra. Activity in the 1.5-2Hz band does not follow the same pattern as documented in other bands. This may be because frequency bands have been scaled, as described in the Methods, to correct for the lower power observed at higher frequencies, and so changes at higher frequencies show lower signal-to-noise ratios.

Analysis 6 - does training visual sustained attention lead to the same set of changes as observed correlationally?

Attention training was administered to half of the infants, with the other half forming an active control group. After training, the same pre-post assessment battery was again administered to all of the infants, in order to examine performance changes in the trained relative to the control group.

INSERT FIGURE 6 HERE

Our first analysis examined whether visual sustained attention had increased in the trained relative to the control group following training. Visual sustained attention

was indexed via look duration, calculated in an identical fashion as described above, for Parts 1-4. Before training average look duration was 21.9 (st. error 1.9) seconds in the trained group and 23.6 (st. error 2.1) secs in the control group. After training, it was 31.0 (2.2) in the trained group and 24.9 (1.8) in the control group. RM ANOVAs were conducted with Time (pre- vs post-assessment) and Group (trained vs control) as the Factors. Figure 6A shows the raw data that were entered into the ANOVA. The ANOVA revealed a significant interaction between Time and Group: $F(1,39)=5.51$, $p=.024$. Tukey HSD post hoc analysis of this interaction effect showed that the trained group increased in look duration from pre- to post-assessment ($p<.05$), but the control group did not.

Next we examined whether training led to changes in total autonomic power in the 0.1-2 Hz range in the trained relative to the control group. RM ANOVAs indicated no significant effect was observed $F(1,39)=0.4$, $p=.53$. Next we compared the relationship between the change in look duration observed as a result of training and the change in total arousal power. Both variables were non-normally distributed and so a log transform was conducted. A Pearson's product-moment correlation identified a significant bivariate relationship between the two $r(39)=.48$, $p=.004$. This suggests that individuals who showed a larger increase in total arousal power between the pre- and post-assessment also showed a larger increase in look duration. Overall these results suggest that, while global increases were not observed in arousal power as a result of training, those individuals who showed a greater change in arousal power also showed a greater increase in visual sustained attention.

Next we repeated the analyses reported in Parts 3-5. Our dependent variable was the PACF for arousal. Based on the results of Part 3 we concentrated on the lag 1 term. A lower PACF term indicates more modulation of arousal. Figure 6C shows the change

scores observed. One outlier (shown, circled on Figure 6C) was more than 5SDs and >1.5 Inter-Quartile Ranges from the mean, and so was excluded. A RM ANOVA suggested that a significant interaction between change (pre vs post) and group $F(1,39)=5.17, p=.03$ was observed, suggesting that PACF decreased in the trained more than the control group. No significant effect of training, however, was observed for the PACF of look duration $F(1,39)=0.02, p=.88$. Comparison of the spectrograms before and after training is shown in the Supplementary Materials. In addition, we used the same analytical approach to examine how training led to changes on the HR change to the mild experimental stressor (Figure 6D). No effect was observed of attention training on HR change to stressor $F(1,39)=1.49, p=.23$.

Discussion

We presented a mixed static/dynamic viewing battery to a cohort of typical 12-month-old infants. Visual attentiveness was indexed by measuring look duration. Autonomic arousal was indexed by recording heart rate, EDA, head movement and leg movement. Our aim was to examine whether infants with increased lability in arousal showed higher, or lower, levels of visual attentiveness.

Overall, our results point to two contrasting autonomic profiles: infants with high autonomic reactivity to stressors show short attention durations, whereas infants with lower autonomic reactivity to stressors show longer attention durations. However, in addition to being *less* reactive to the experimental stressor, the more highly attentive infants showed *increased* arousal lability in a variety of other ways. They showed increased phasic (reactive) changes to the appearance of an attractive, attention-getting stimuli (baby TV clips) (Analysis 5). They also showed increased phasic changes in both arousal (Analysis 3) and look duration (Analysis 4) across the dynamically changing stimulus battery. And finally, they showed more oscillatory activity in arousal generally (Analysis 2). Results in the Supplementary Materials suggest that this finding was consistent across all four arousal measures recorded (heart rate, EDA, head movement, leg movement) (Figure S4).

Separately, we administered targeted attention training, over four visits, to a cohort of our infants. We found that attention training led to no global increases in arousal power as a result of training, but that, irrespective of training, those individuals who showed a greater change in arousal power showed a greater increase in visual sustained attention (Analysis 6). We also found that attention training led to increases in the rate of change of arousal, although not in the rate of change of look duration.

One possible explanation for our findings is that infants with greater endogenous attention control might show both longer look durations and increased look-related arousal decelerations (cf Richards, 2010; Lansink & Richards, 1997). However, analyses presented in the Supplementary Materials suggest that arousal decelerations during looks were not observed uniformly in our data (occurring in only 50% of looks). And, when arousal decelerations did occur during a look, this appeared to be strongly influenced by the infant's baseline (pre-look) arousal levels. This suggests that the observed decelerations may have been more strongly influenced by factors such as regression to the mean than by specific changes related to the start of the look. Consistent with previous evidence that changes in arousal temporally precede changes in look duration (Bacher & Robertson, 2001; de Barbaro, Clackson, & Wass, 2016a), our present findings appear inconsistent with a simple causal model in which individual differences in endogenous attention control cause both longer look duration and increased look-related arousal decelerations.

Research with animals and adults has examined how attention changes at different levels of autonomic arousal. Hyper-aroused individuals, who manifest increased SNS activity, show decreased selective attention, are more vigilant or stimulus-driven and show increased fear conditioning, memory consolidation and less flexible attentional behaviors (Arnsten, 2009). Mid-level arousal is associated with increased PNS activity, increased attentional flexibility and superior 'top-down' attention control. Hypo-arousal is associated with general inattentiveness (Aston-Jones & Cohen, 2005).

One possible interpretation for our findings is that infants who show increased HR changes to a mild unexpected stressor show a behavioral profile more consistent with a high-SNS phenotype: shorter look durations, increased memory consolidation

and more rigid, inflexible attentional behaviors. Conversely, infants who show increased general oscillatory activity in arousal show a behavioral profile more consistent with a high-PNS phenotype: longer look durations, together with more flexible attentional behaviors. Of note, though, no relationships were observed between either of these measures and tonic arousal (averaged across the entire session).

Our findings are consistent with previous research into RSA and attention. RSA, indexed as oscillatory activity in the c. 0.5 Hz range, is known to associate positively with sustained attention in infants (Richards, 1985). Infants with higher RSA also show increased phasic reactivity to novel stimulus events (Richards & Casey, 1991), suggesting increased behavioral flexibility. Consistent with this we observed a peak at c. 0.5 Hz in our HR data (Figure S4E). Of note, though, we also found that increased visual attention associated with increased oscillatory activity in head movement, foot movement and electrodermal activity (see Figure S4F, S4G, S4H). This is despite the fact that, to our knowledge, no previous research has directly linked cyclical oscillatory activity at these frequencies to RSA.

This finding may reflect the important role that stochastic and oscillatory activity plays in regulating physiological and behavioral systems (Hebb, 1949; Feldman & Mayes, 1999). They are considered essential in maintaining balance between mechanisms that raise the level of systematic activity and those that control the inhibition of activity. Consistent with this, Feldman and Mayes found that infants whose attention was regulated in cyclic oscillations showed a more mature behavioral profile on a habituation task (Feldman & Mayes, 1999; see also De Graaf et al., 2013; Landau & Fries, 2012). And Surwillo and Quilter observed, in adults, associations between spontaneous changes in EDA and performance on a vigilance task (Surwillo & Quilter, 1965).

Our results also suggested that increased visual attention, as well as being associated with increased general oscillatory activity in arousal, was also associated with a more labile (faster-changing) profile of attentional behaviors. This may suggest that, in addition to showing increased general oscillatory activity in arousal, more attentive individuals show a superior ability to modulate their autonomic and attentional behaviors contingent on context (Aston-Jones & Cohen, 2005; Wass, Jones, et al., 2015; Wass & Smith, 2014). Whereas inattentive individuals show a more inflexible, rigid orienting style, more attentive individuals are better able to modulate their response behaviours in response to attention-eliciting events in the external environment (cf de Barbaro et al., 2011; Feldman & Mayes, 1999).

Consistent with this, we also found that infants who showed a greater increase in look duration between pre- and post-test in the training intervention showed a greater increase in arousal power (Figure 6B), along with a faster rate of change of arousal (Figure 6C), following training. Again, this is consistent with the hypothesis that increasing visual attention led to increased ability to modulate behaviors contingent on context. (Although the results of the spectrogram analyses examining this were inconclusive (Figure S5).)

Of note, we found that training led to no changes in HR reactivity to a stressor (Figure 6D). This may be because the training led to two contrasting effects: first, of increasing infants' sensitivity, but second, of increasing self-regulatory behaviors such as gaze suppression, that would minimize negative arousal changes following presentation of a stressor (Aksan & Kochanska, 2004; Rothbart, Ellis, Rueda, & Posner, 2003; Sheese, Rothbart, Posner, White, & Fraundorf, 2008). Of note, we also reported separately that the same attention training regime led to reductions in infants' levels of resting salivary cortisol (Wass et al., in press).

In sum, our present results suggest that infants with high reactivity to mild stressors show short look durations and reduced general ability to modulate arousal patterns contingent on context. Infants with lower reactivity to mild stressors showed the opposite pattern: longer look durations, increased lability in arousal, and poorer recognition memory.

One challenge, however, is to integrate our present findings with Differential Susceptibility Theory (Obradovic, 2016). Previous research has suggested that infants with higher RSA show increased reactivity both to negative stimulus events, such as a heel stick procedure for drawing blood (Gunnar, Porter, Wolf, Rigatuso, & Larson, 1995) and to sought-for stimulus events, such as during sustained attention (Richards & Casey, 1991). Thus, RSA reflects the capacity to engage in both a positive and a negative manner (Beauchaine, 2001). Consistent with this, high-RSA infants show the best outcomes in optimal settings and the worst outcomes in non-optimal settings (Obradovic, Bush, Stamperdahl, Adler, & Boyce, 2010; Skowron, Cipriano-Essel, Gatzke-Kopp, Teti, & Ammerman, 2014). These findings currently appear inconsistent with our present findings, which suggest that infants who show *less* reactivity to stressors show *more* reactivity to interesting, attractive stimulus events.

Future research should address this question. It should also address a further prediction arising from our present research, which is that similar patterns of results should be observed within- as between-participants. Future research should also explicitly address the generalizability of our findings to populations other than the wealthy, largely Caucasian and university-affiliated families tested here. Finally, future research should investigate the role of context, such as social context, on arousal modulation. Recent research has identified autonomic phase-locking – the entrainment of heart rate patterns between infants and parents during free play (Feldman, Magori-

Cohen, Galili, Singer, & Louzoun, 2011) – a phenomenon that can be compared to neural phase-locking during the perception, for example, of natural speech (Giraud & Poeppel, 2012; Hämäläinen, Rupp, Soltész, Szücs, & Goswami, 2012). Previous research has identified autonomic changes during free play in naturalistic contexts (Lansink, Mintz, & Richards, 2000), but it would be interesting to investigate the wider role that autonomic *entrainment* in social and non-social contexts plays during learning (Feldman, Greenbaum, & Yirmiya, 1999).

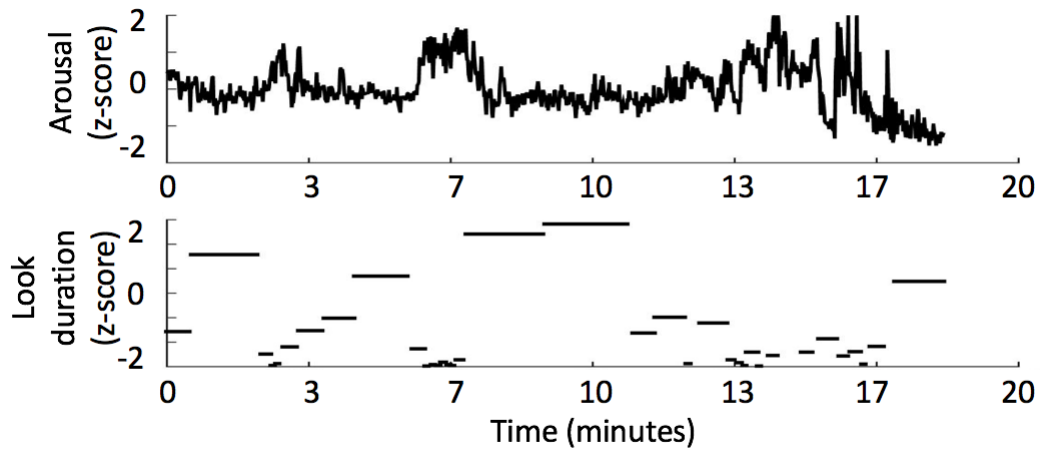
Figures

Figure 1: Sample illustration of data collected from a single infant. The top plot shows infants' changing arousal levels (calculated as a composite of the four measures reported in the main text). The bottom plot shows the duration of infant's individual looks to and away from the screen.

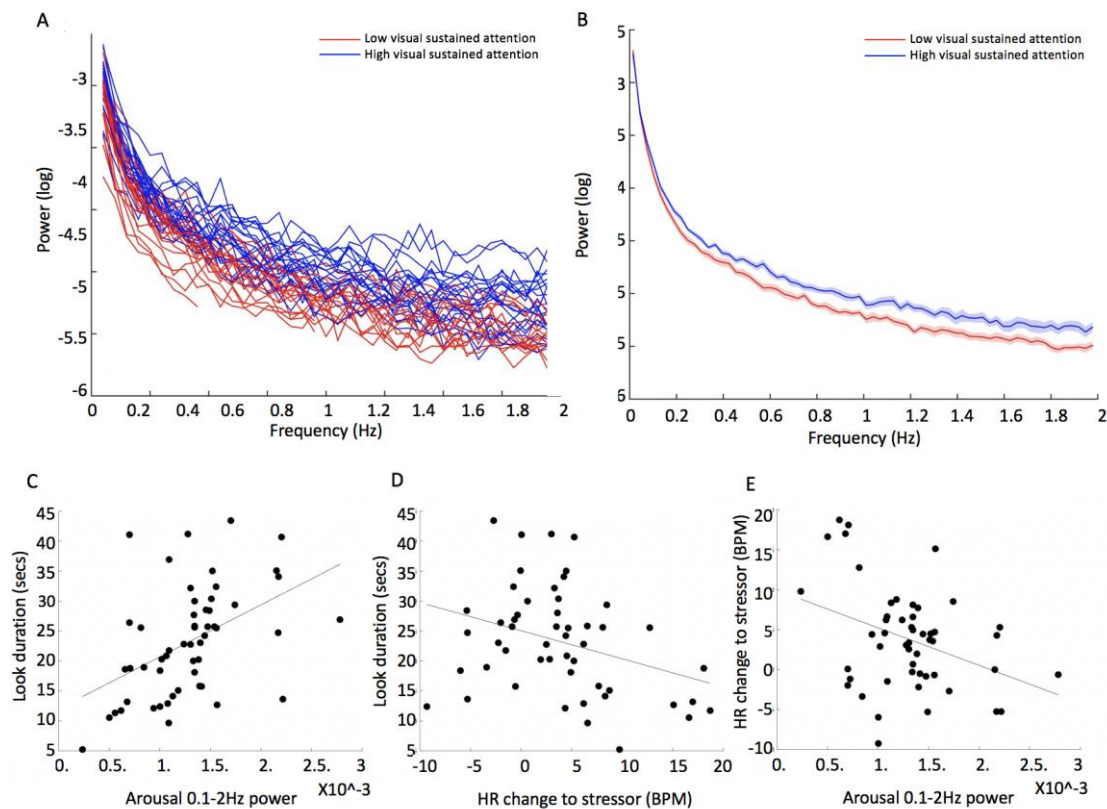


Figure 2. Fourier-derived power spectra for changes in arousal, split using a median split into low and high visual sustained attention groups. A – individual data. B – same as A, but averaged into high and low sustained attention groups. C scatterplot showing the relationship between arousal power and look duration. D scatterplot showing the relationship between HR change to stressor and look duration. E. scatterplot showing the relationship between HR change to stressor and arousal power. On each scatterplot, linear best-fit lines illustrate the significant bivariate relationships observed between the variables.

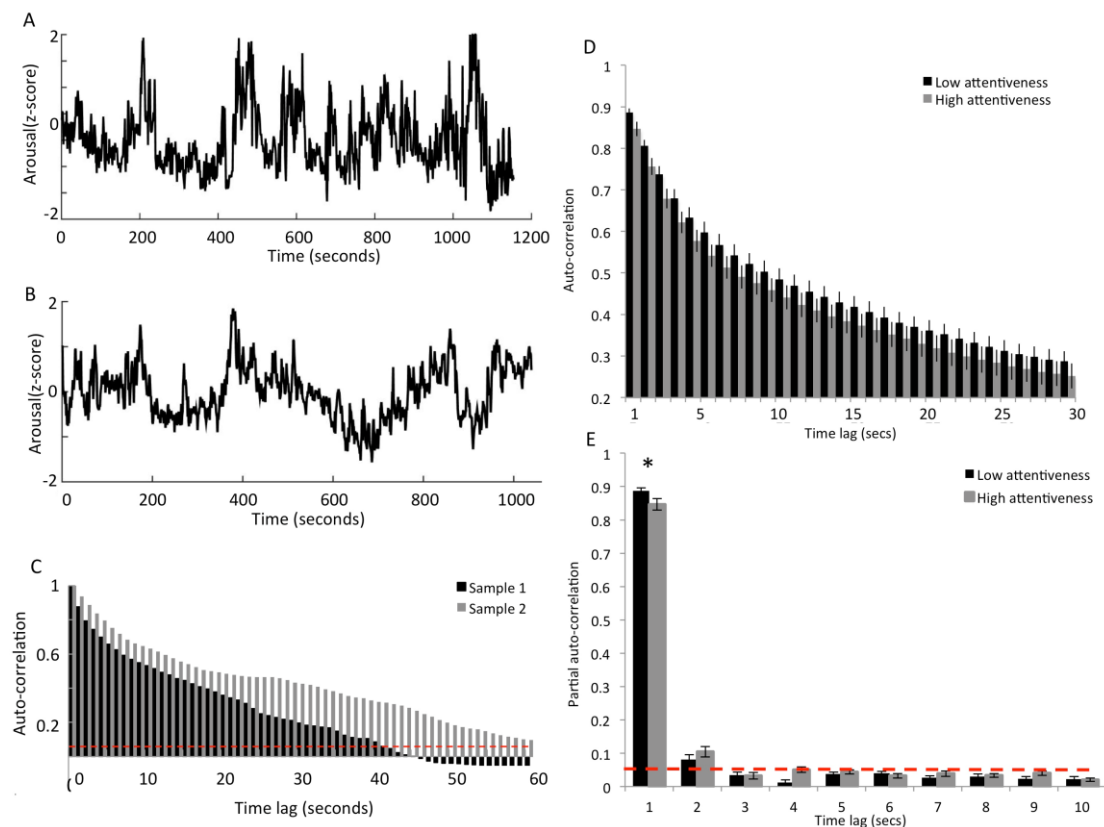


Figure 3: Demonstration of the auto-correlation analyses for arousal. a) and b) show samples of arousal data from two infants. It can be seen that sample 1 shows rapid change (e.g. a sudden increase followed by a sudden decrease between look 0 and 600 seconds), whereas changes in sample 2 tend to be more continuous (e.g. a gradual decrease between 400 and 700 seconds). c) shows the ACF functions for the two samples. For sample 1, the faster-changing measure, the ACF function falls off more rapidly. d) shows ACF comparisons, split by high/low visual sustained attention. e) shows the PACF comparisons, split by high/low visual sustained attention. The dashed red line shows the 95% confidence intervals. Any correlations above this threshold are significantly greater than zero. For e), stars above the lines show the significance of the group comparisons, that were conducted as described in the text. * - significant at $p < .05$.

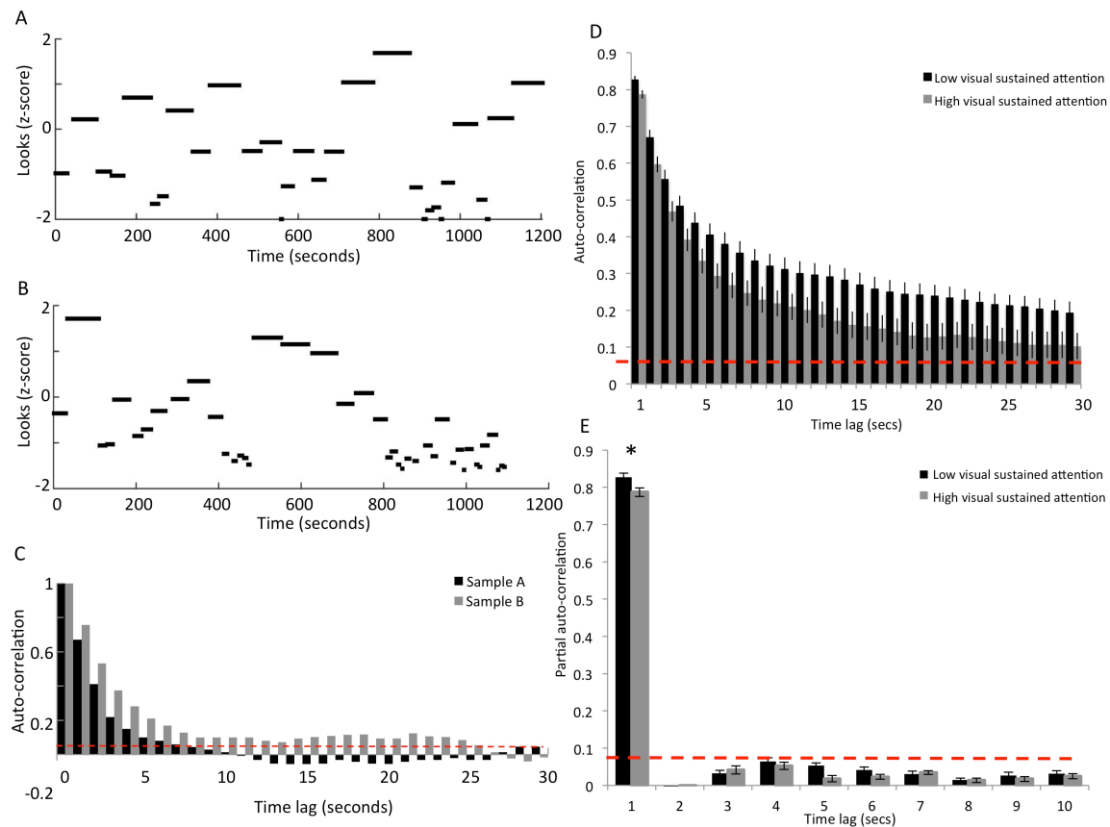


Figure 4: Demonstration of the cross-correlation analyses for look duration. A and B show examples of look duration data collected from two infants. It can be seen that sample A shifts rapidly between long, and short looks (see for example the section between 800 and 1000 seconds). In sample B, changes occur less rapidly. A period of continuously long looks (e.g. 500-700 seconds) is followed by a period of continuously short looks (e.g. 800-1100 seconds). C shows the ACF functions for the two samples. The black line (sample A) falls off more sharply, as the similarity between observations declines more rapidly as a function of an increasing time-lag. The dashed red line shows the 95% confidence intervals. All correlations above this line are significant. D – group ACF data calculated identically to C, but split by visual sustained attention. E

*– PACF data, based on the same group split as D. Red lines show the 95%CI threshold. Any correlations above this threshold are significantly greater than zero. For E, the star shows the significance of the group comparisons, that were conducted as described in the text. * - significant at $p < .05$.*

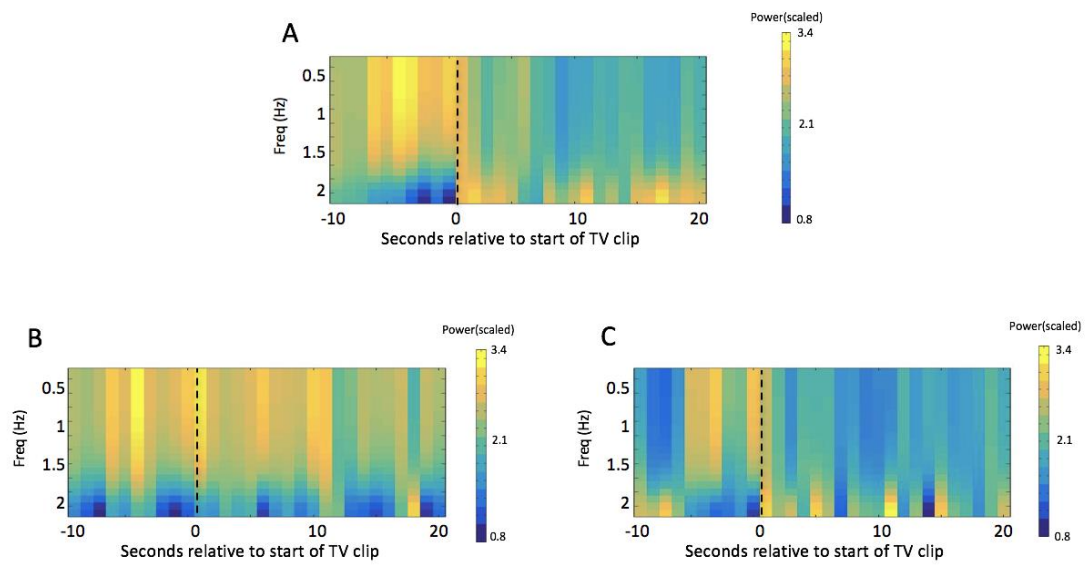


Figure 5: A - Spectrogram of changes in arousal power relative to the start of TV clips across all participating infants. B – Same as A, but just showing individuals from the low visual sustained attention group. C – Same as A, but just showing individuals from the high visual sustained attention group.

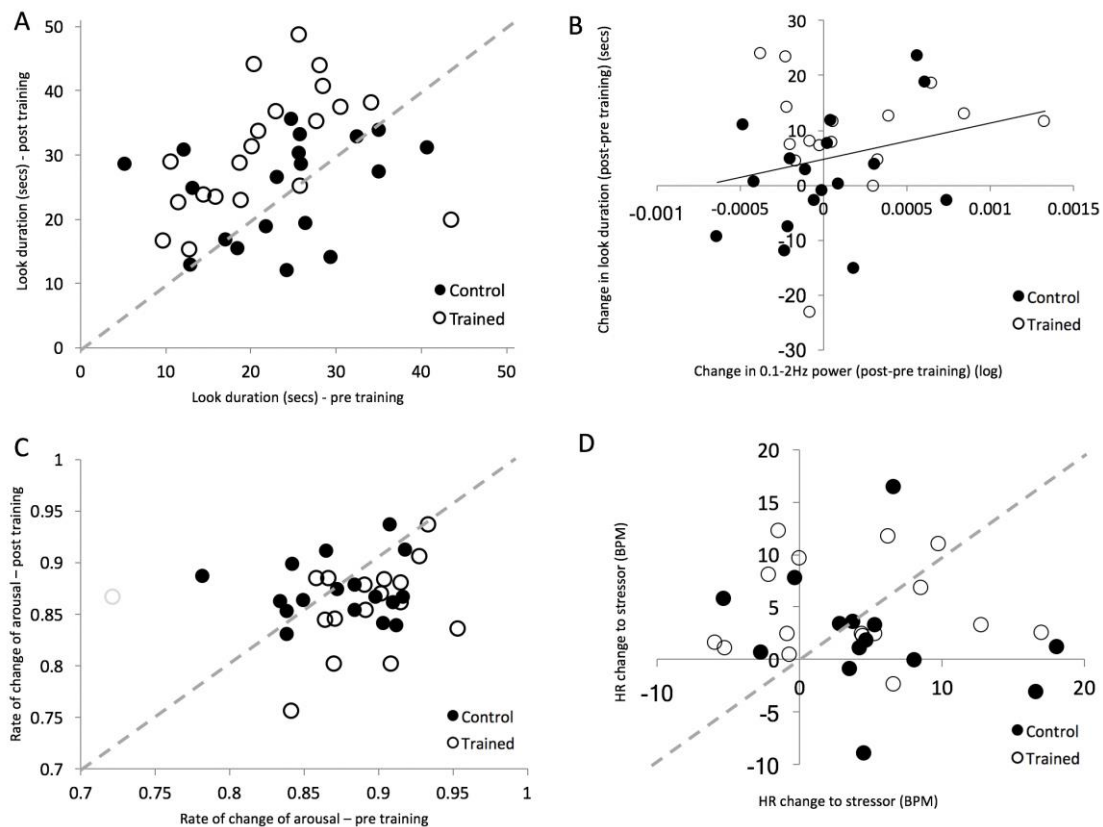


Figure 6. A – scatterplot showing look duration at visit 1 (x-axis) and visit 5 (y-axis). Training and control participants are plotted separately. The 1:1 line is also drawn. A position above the 1:1 line indicates that look durations for that individual were longer at visit 5 (after training) than at visit 1 (before training). B – scatterplot showing the change in total arousal power between pre- and post-test (post-pre, x-axis) and the change in look duration between post- and pre-test (post-pre, y-axis). The best-fit line indicates the significant bivariate relationship observed between these two measures, described in the main text. C – scatterplot showing the PACF function for arousal at visit 1 (x-axis) and visit 5 (y-axis) (same analysis as Part 2). Just lag 1 scores are shown. Training and control participants are shown in different colours. The 1:1 line has been drawn for ease of comparison. A position below the 1:1 line indicates that lower scores were observed at visit 5 (after training) than at visit 1 (before training).

Overall the trained group showed lower PACF values, indicating a faster rate of change of arousal, after training. D – identical scatterplot to C, but showing the HR change to stressor (Analysis 1). For this measure no significant changes were observed following training.

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