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Influences of environmental stressors on autonomic function in 12-month-old infants: understanding early common pathways to atypical emotion regulation and cognitive performance

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Abstract

Background: Previous research has suggested that children exposed to more early-life stress show worse mental health outcomes and impaired cognitive performance in later life, but the mechanisms subserving these relationships remain poorly understood.
Method: Using miniaturised microphones and physiological arousal monitors (Electro-Cardiography, Heart Rate Variability, Actigraphy), we examined for the first time infants' autonomic reactions to environmental stressors (noise) in the home environment, in a sample of 82 12-month-old infants from mixed demographic backgrounds. The same infants also attended a lab testing battery where attention- and emotion-eliciting stimuli were presented. We examined how childrens' environmental noise exposure levels at home related to their autonomic reactivity, and to their behavioural performance in the lab.
Results: Individual differences in total noise exposure were independent of other socio-economic and parenting variables. Children exposed to higher and more rapidly-fluctuating environmental noise showed more unstable autonomic arousal patterns overall in home settings. In the lab testing battery, this group showed more labile and short-lived autonomic changes in response to novel attention-eliciting stimuli, along with reduced visual sustained attention. They also showed increased arousal lability in response to an emotional stressor.
Conclusions: Our results offer new insights into the mechanisms by which environmental noise exposure may confer increased risk of adverse mental health and impaired cognitive performance during later life.

Abbreviations: ACF - Auto-Correlation Function; ANS – Autonomic Nervous System; CCF - Cross-Correlation Function; CHAOS - Confusion, Hubbub and Order Scale; ECG - Electrocardiography; GPS - Global Positioning System; HR - Heart Rate; HRV - Heart Rate Variability; PACF - Partial Auto-Correlation Function; RR interval - beat-to-beat interval (R is the peak of the QRS complex of the ECG wave); SM - Supplementary Materials

Keywords: Environmental noise, autonomic nervous system, arousal, infant, attention

Introduction

One well-replicated finding within psychology and psychiatry is that early exposure to stressful environments increases the risk of adverse long-term outcomes, including mental disorder (Businelle et al., 2013; Felitti et al., 1998) and cognitive impairment (Blair, 2010; Evans & Schamberg, 2009). Recent research has suggested that the increased mental health risk conferred by early-life stress is transdiagnostic, and not disorder-specific (Conway, Raposa, Hammen, & Brennan, 2018), offering some vital clues as to etiological pathways (Karmiloff-Smith, 1998). Early-developing impairments in brainstem-mediated arousal and regulation circuits may act as a common pathway, causing developmental impairments in domains such as socio-emotional self-regulation, inhibitory control, executive, verbal and motor functions, and cognitive processing (Geva & Feldman, 2008). Even minor alterations in responses to daily stressors may trigger a cascade of changes which cumulatively constitute a vulnerability to or risk factor for later psychopathology (Borsboom & Cramer, 2013; Charles, Piazza, Mogle, Sliwinski, & Almeida, 2013; Sonuga-Barke, Koerting, Smith, McCann, & Thompson, 2011; Trull, Lane, Koval, & Ebner-Priemer, 2015; Wichers, Wigman, & Myin-Germeys, 2015).

Stress is an umbrella term used to refer to actual life events or situations ('stressors') and to the cognitive and biological responses that such situations evoke ('stress responses') (Epel et al., 2018). Both aspects can be studied over multiple time-scales. Stressors range from life-long factors (e.g. poverty) to short-term ones (e.g. a cup of tea spilled on a laptop); stress responses diversely include both long- and slow-acting changes in diverse endocrine and nervous systems designed to help an organism maintain homeostatis and allostatis in the face of change (Cannon, 1915; McCall et al., 2015; Selye, 1951).

Within psychology and psychiatry, researchers generally measure early-life stress using questionnaire assessments that identify life-long stressors, such as parental conflict and emotional abuse (e.g. Felitti et al., 1998). Over recent years, we are increasingly becoming aware that short-term factors, such as environmental noise, also cause stress responses. Understanding these is particularly important given our current rapid urbanization as a species, with concomitant increase in noisy and cramped living environments (Evans, 2004).

Nonauditory effects of noise are known to occur at levels far below those required to damage hearing (Basner et al., 2014; Pérez-Valenzuela, Terreros, & Dagnino-Subiabre, 2018). Loud noise increases cortisol levels in several species (Kight & Swaddle, 2011), including humans (Evans, Lercher, Meis, Ising, & Kofler, 2001). In 10-year-old children, high levels of environmental noise exposure associated with elevated resting systolic blood pressure and increased heart rate reactivity in response to the presentation of a novel stressor (Evans et al., 2001). Infants exposed to high levels of noise in neonatal intensive care units show increased heart and respiratory rates and decreased oxygen saturation (Bremmer, Byers, & Kiehl, 2003) – factors also commonly reported in adults (Basner et al., 2014).

Other research has used parent report to assess household chaos using questionnaires such as the Confusion, Hubbub and Order Scale (CHAOS, Matheny, Wachs, Ludwig, & Phillips, 1995). Children who are chronically exposed to ambient noise exhibit poorer reading and language skills than matched samples (Evans, 2006; Haines, Stansfeld, Job, Berglund, & Head, 2001). Previous research has suggested that this may be because they learn to routinely screen out auditory stimuli, even those that are useful.

Virtually all previous research has, however, taken time-invariant snapshots to measure the average levels of noise to which individuals are exposed. This means that several vital questions remain unanswered. For example, we understand little about whether fluctuations in environmental noise associate with immediate changes in physiological stress, and whether individuals exposed to more rapidly fluctuating environmental noise show altered physiological stress responses. Relatedly, we understand little about how individuals exposed to more noise overall become hyper- or hypo-sensitised to noise (although see Basner, Müller, & Elmenhorst, 2011; Pearsons, Barber, Tabachnick, & Fidell, 1995). As a result of this, we understand little of the mechanisms through which noise exposure affects emotional and cognitive performance. Further, most previous research into household noise has examined children and adults – rather than infants, who potentially are highly sensitive to environmental influences during early development (e.g. Frankenhuis, Nettle, & McNamara, 2018).

We used miniaturised microphones and video cameras, along with wearable physiological stress monitors, to study infants' responsivity to real-world auditory events. The same participating infants were also brought into the lab where we measured their reactivity while administering an attention task to measure visual sustained attention, and a behavioural task (still-face protocol) to measure emotion reactivity. Early atypical performance on both of these tasks has been linked to a range of later psychopathologies (Johnson, Gliga, Jones, & Charman, 2015; Jones, Gliga, Bedford, Charman, & Johnson, 2014; Kahle, Miller, Helm, & Hastings, 2018; Santucci et al., 2008). Autonomic arousal was assessed using a combination of Electrocardiography (ECG), Heart Rate Variability (HRV) and Actigraphy (Cacioppo, Tassinary, & Berntson, 2000).

Because autonomic responsivity mediates both our cognitive responses to novel, attention-eliciting stimuli and our affective responses to unexpected or stressful events (Aston-Jones & Cohen, 2005; Geva & Feldman, 2008), we were interested to examine how environmental noise affects infants' responses both to attention- and emotion-eliciting stimuli in the lab battery. Relatively little previous research has, however, examined infants' reactivity to attention-eliciting and emotion-eliciting stimuli within a single dataset (see Wass, 2018 for review; see also Aston-Jones & Cohen, 2005; Beauchaine & Thayer, 2015). Therefore, we were agnostic as to whether noise-related atypicalities in autonomic function would most affect infants' lab-based performance in cognitive, or affective domains, or both.

Method

Participants

Participants consisted of 82 infants recruited from the London, Essex, Hertfordshire and Cambridge regions of the UK. Exclusion criteria and demographic details are given in Table S1.

Home Battery

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, accelerometer, 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 clothes were comfortable when worn and, other than a request to keep the equipment dry, participants could behave exactly as they would on a normal day. No discomfort in wearing the equipment was reported. To ensure good quality recordings, the ECG was attached using standard Ag-Cl electrodes, placed in a modified lead II position.

Details of the criteria through which sleeping and waking segments were identified are given in the Supplementary Materials (SM) (section 1.2). Details of parsing of the autonomic data, including details of the motivation for collapsing the different autonomic indices into a single composite measure, are given in the SM (section 1.3). Details of the recording and coding of the infant microphone data are given in the SM (section 1.4).

Questionnaires were also administered to assess: household income, maternal education, stressful events around birth (medical complications, preterm birth, drink or drugs while pregnant or previous miscarriage) and adverse life events since birth (serious illness, death in family, abuse/attacks/threats to family, unemployment in family, financial difficulties, committing or being victim of a crime, moving house) (Felitti et al., 1998), parental anxiety (GAD-7 - Spitzer, Kroenke, Williams, & Löwe, 2006), depression (PHQ-9 - Kroenke, Spitzer, & Williams, 2001), parental over-involvement (Hudson & Rapee, 2002) and the number of people living at home (Felitti et al., 1998). In addition, parent report of household order was assessed using the CHAOS scale (Matheny et al., 1995).

Lab Battery

The lab battery was conducted within median (*st err*) 17.5 (3.5) days of the home battery. Details of participant drop-out for different individual tasks in the lab battery are given in the SM (section 1.5).

For Tests 1 and 2, ECG was recorded using the same devices as for the home battery. For Test 3, ECG was recorded using Bionomadix BN-ECG2 and BM-ACCL3 units, along with an MP160 amp, from Biopac. For all ECG recordings, standard Ag-Cl electrodes placed in a modified lead II position were used.

Test 1: Still face protocol. Parent and child were seated across an 80cm-wide table, and instructed to play naturally with four toys positioned on the table. After four minutes, on an instruction from the experimenter, the parent was instructed not to respond to the infant and to hold a neutral face for two minutes. On a further instruction from the experimenter, the play resumed for a further two minutes. If the infant become distressed during the still face period, as judged using the standard guidelines (Weinberg & Tronick, 1996), the experiment was curtailed.

Test 2: Repetitive, static audio-visual stimuli were presented to elicit a baseline; these were followed immediately by attention-eliciting videos, lasting c. 30 seconds each. The baseline stimuli were short auditory sounds and static pictures of animals; the attention-eliciting video were videos of the BBC children's presenter Mr Tumble singing nursery rhymes. 4 blocks were presented, and averaged. Infants' visual attention towards the stimulus presentation area was recorded and coded *post hoc*, and their heart rate (RR intervals) was recorded.

Test 3: In addition, a secondary test of visual sustained attention was also administered. For reasons of space, the method for this is given in the SM (section 1.6).

Results

The results section is in five parts. In part 1 we present descriptive analyses of the home data. In part 2 we examine infants' autonomic reactions to naturally occurring environmental noise in the home data. In part 3 we present analyses examining sustained attention and autonomic responsivity to attention-eliciting stimuli in the lab battery. In part 4 we present analyses examining negative affect and autonomic lability in the home data. In part 5 we examine infants' stress reactivity and arousal lability to an emotional stressor in the lab battery.

Kolmogorov-Smirnov results indicated that not all test results observed for all variables were parametrically distributed. Because of this, more conservative non-parametric statistical analyses have been used throughout, for consistency.

Part 1 - Descriptive analyses

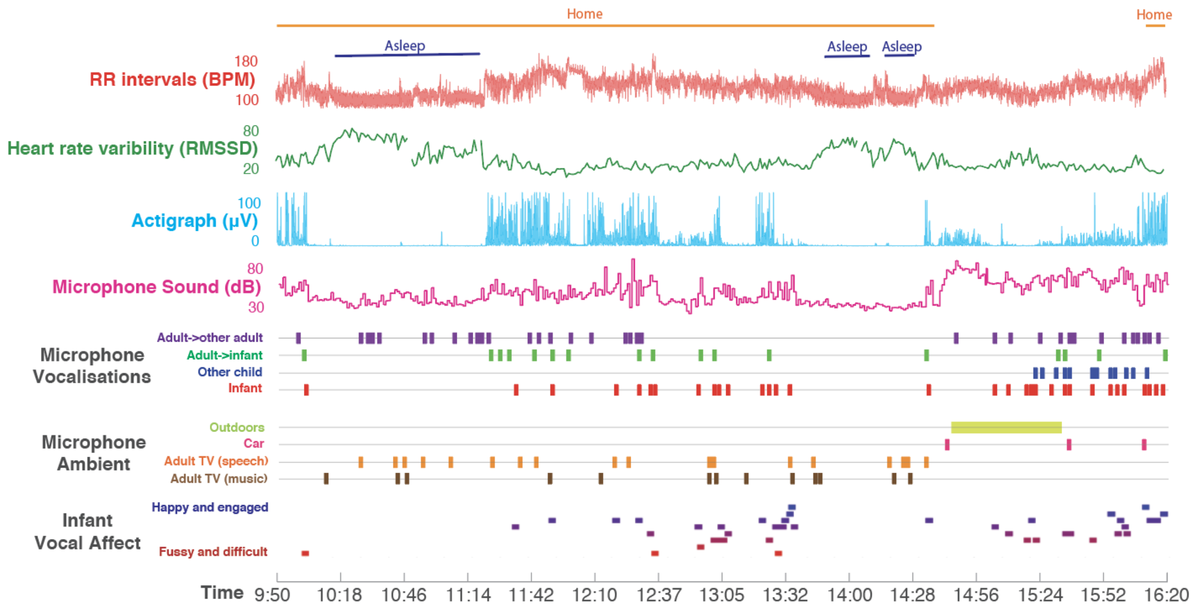

Figure 1: Data sample illustrating the raw data collected from a single participant. Six and a half hours' data is presented (see time axis at the bottom). From top to bottom: the RR (inter-beat) intervals derived from the electro-cardiography recording, indexed as Beats Per Minute (BPM); the heart rate variability (indexed as the Root Mean Square of Successive Differences (RMSSD); actigraphy (indexed as micro-Volts); the sound levels on the infant microphone (indexed as decibels (dB)); the results of the coding for Microphone Vocalisations, Microphone Ambient and Infant Vocal Affect (see SM section 1.4). For Microphone Ambient, only those categories that were present in the data sample are shown.

Figure 2 shows the results of the descriptive statistical analyses of the home data. Figure 2a illustrates how the average noise levels varied across different individual data samples recorded. For the five participants who were lowest overall on noise, the average levels of waking noise are lower, and there is also a clear differentiation between the Asleep and Awake samples. For the participants who scored higher overall on noise, this is not the case. See SM Figure S3 for the same plot showing all data, and see here[1] for a list showing average decibel levels across different categories of real-world noise.

[1] http://www.industrialnoisecontrol.com/comparative-noise-examples.htm

For subsequent analyses, participants were split into ‘Low noise’ and ‘High noise’ using a median split, based on the average decibel levels observed in the microphone data recorded while infants were sleep. In the SM section 2.3 we also include identical analyses based on quartile splits. We used sleeping data because we judged that this was likely to be more free of possible self-generated microphone artifacts, and thus to be an accurate measure of background noise. Sleeping noise also showed positive bivariate associations with waking microphone noise r_s=.33, p=.005 and with the CHAOS questionnaire r_s=.29, p=.02.

We also examined bivariate associations between noise and other socio-economic variables. Full results are given in the SM (section 1.7). In brief, sleeping microphone noise showed bivariate associations with the number of other people living at home (p=.02), but did not associate with maternal education, household income, birth stressors, adverse life events, parent anxiety or depression and parental over-involvement. There was no relationship between noise and the proportion of the recording spent sleeping.

In addition to total noise levels we also examined the change in noise across time, by calculating Poincaré plots (see Figure 2b) (see further details in SM section 1.8). Analyses presented in the SM indicate that the high-noise group showed significantly more sudden changes in noise between consecutive 60-second epochs (Wilcoxon p=.01), when differences in mean noise are controlled for.

Figure 2c shows the average noise levels by category of vocal/ambient noise (see SM section 1.4), and Figure 2d shows the proportion of audio samples in each category. The high-noise group shows consistent trends towards higher decibel levels across different vocal/ambient categories. Between-group differences are larger for the sleeping relative to the waking sections, which is expected given that groups were defined by sleeping noise. Other differences can also be seen: for example, infants in the high-noise group were exposed to significantly less speech where the adult was talking directly to the infant, and more speech where the adult was talking to another adult.

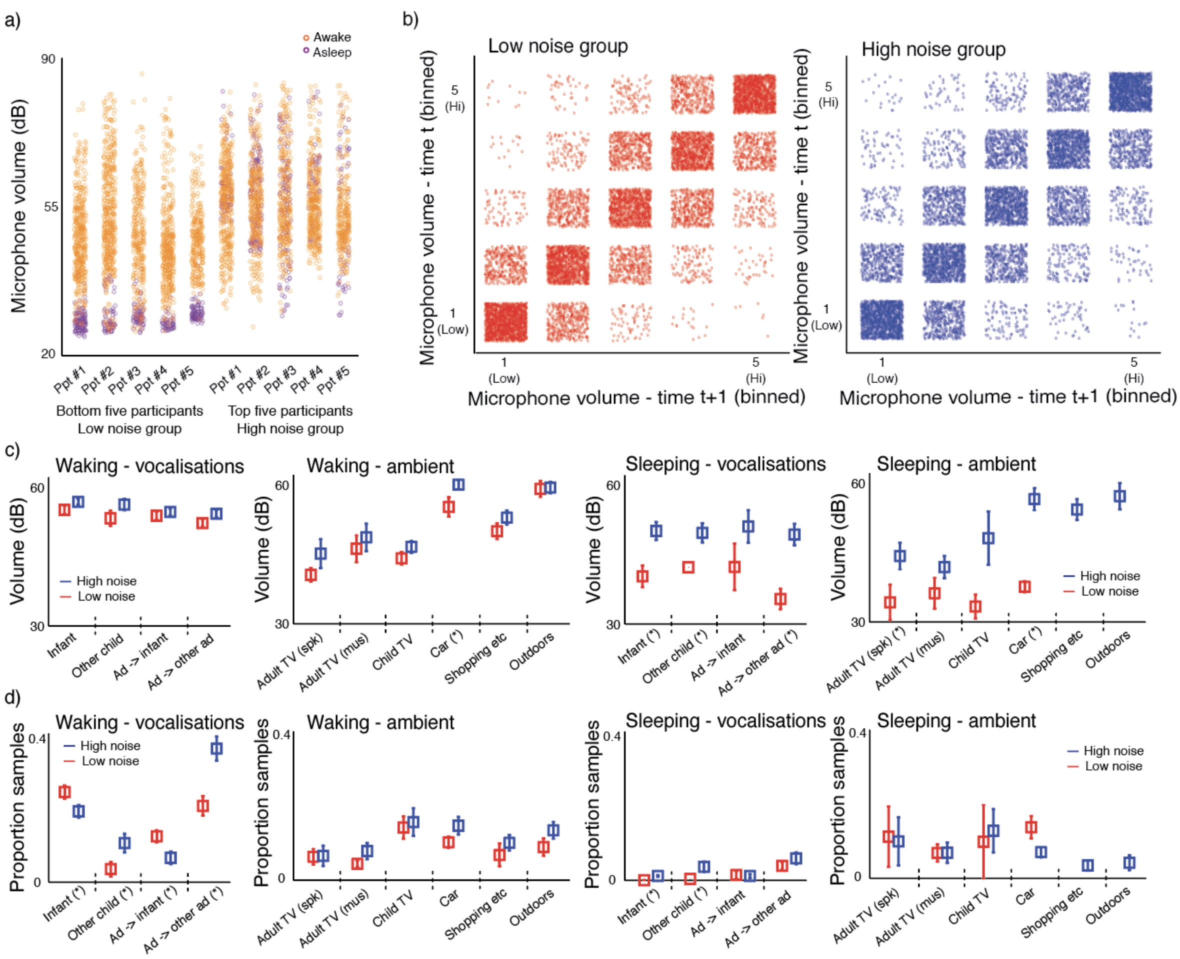

Figure 2: a) Illustrative data samples. Each column shows the microphone data recorded from an individual participant. Within each column, each dot shows the average noise level for an individual sample (recorded once per minute). The five participants who scored lowest on overall noise levels are shown on the left; those who scored highest are shown on the right. Samples recorded while the infant was sleeping are shown in orange; those while the infant was awake, in purple. Full data are shown in the SM Figure S3. b) Poincaré plots, calculated as described in SM section 1.8. Noise levels were averaged into 60-second epochs and sorted into equal-sized bins on a per-participant basis to control for inter-individual differences in mean noise level. Noise at time t is shown on the y-axis and time t+1 on the x-axis. Data more tightly clustered on the identity line show greater consistency across time. It can be seen that the high noise group show more abrupt changes in noise (e.g. from bin 1 at time t to bin 5 at time t+1). Statistical analyses described in the SM (section 1.8) confirm this as a significant pattern in the data. c) Mean volumes (in dB) recorded from the high noise group (blue) and low noise group (red), sorted by vocalisation/ambient category and sleeping/waking (see SM section 1.4 for more details). Error bars show the standard error of the means. d) The proportion of total samples that each vocalisation/ambient category was present for. For c) and d), independent samples t-tests were conducted to examine the significance of group differences between the high and low-noise groups. Where significant, these have been indicated with (*) in the legends on the x-axis.

Part 2 - Autonomic sensitivity to environmental noise in home data

To examine how external noise in the home data related to autonomic changes in the child, we calculated the Cross-Correlation Function (CCF) between auditory noise and autonomic arousal (see SM section 1.9). Prior to conducting calculations, all epochs in which the infant was vocalising were excluded, to ensure that only external noise sources were considered. Analyses only included segments in which infants were at home, because in these segments infants were generally free-roaming (i.e. not strapped in a buggy or car seat), allowing more accurate estimation of autonomic arousal. Subsequent analyses found that outdoor segments showed similar relationships. At Time lag=0 (i.e. examining the concurrent co-fluctuation of autonomic arousal and external noise across the day), Wilcoxon tests indicated that both groups were significantly above the chance value of 0: low noise group: Z=6.2, p<.001, high noise group: Z=6.1, p<.001. Zero-lag correlations were also higher in the low-noise group than the high-noise group Z=3.2, p=.004. This indicates that for both groups, autonomic arousal was increased at times when external noise was higher; but that the association between external noise and autonomic arousal was lower in the group exposed to higher average levels of noise.

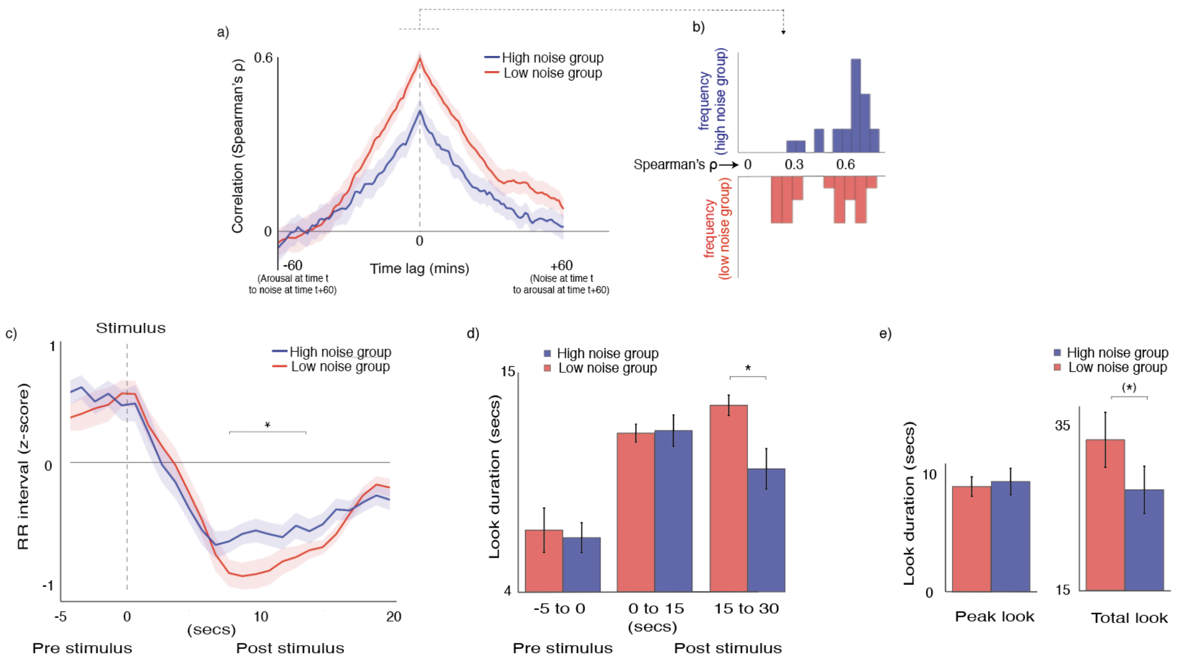

*Figure 3: a) Cross-correlation plot showing the relationship between auditory noise and autonomic arousal in the home data. For all plots, red shows the low-noise group and blue the high-noise group. Shaded areas show the standard error of the means. b) histograms showing the cross-correlation values for time lag=0 only from Figure 3a. c) RR interval changes to a novel attention-eliciting event in the lab battery. Shaded areas show the S.E. Star indicates the area of significant difference identified by the permutation test * - p<.05. d) Look durations during the period -5 to 0, 0 to 15 and 15 to 30 seconds relative to stimulus change. Stars indicate areas of significant difference - * - p<.05; (*) – p<.10. e) Look durations during the secondary sustained attention task (described SM section 1.6).*

Part 3 - Visual sustained attention in lab battery

To examine infants' responses to attention-eliciting stimuli in the lab battery, infants were habituated to repetitive, static stimuli before an attractive, novel stimulus was presented. Figure 3c shows infants' autonomic responsiveness (indexed as RR interval change) to the novel stimuli. Data were z-scored to control for individual differences, and RR interval changes relative to the appearance of the novel stimulus were assessed. The permutation-based clustering analyses (SM section 1.10) indicated that infants in the high-noise group showed significantly more short-lived decreases in arousal (p=.004) relative to the appearance of the novel stimulus.

Next, we examined the change in infants' visual attention. Both groups showed an increase in visual attention in response to the novel stimulus (Figure 3d). Immediately following the stimulus, Wilcoxon tests indicated no group differences in attention (p=.38); but at later time intervals a significant difference emerges (p=.024). In addition, we also administered a separate test of visual sustained attention (see Figure 3e and SM section 1.6) which showed results consistent with this. Overall, these results suggest that infants from the high-noise group showed reduced visual sustained attention, along with more short-lived autonomic changes following the appearance of novel attention-eliciting stimuli.

Part 4 – Arousal lability in home data

Next we examined whether the rate of change of autonomic arousal differed between the high-noise and low-noise groups in the home data, by calculating the auto-correlation function (ACF) and partial auto-correlation function (PACF) of arousal (see Figure 4a). The ACF indexes the relationship between a variable and itself, considered at varied time intervals. Cases where the ACF shows a faster fall-off indicate that the relationship between a variable at time t and the same variable at time t+x is lower – i.e. that the rate of change of that variable overall is higher. The partial auto-correlation function (PACF) indexes the autocorrelation of a measure, but at each lag it controls for the effect of previous autocorrelations at smaller lags (Chatfield, 2004). PACFs presented in the main text are calculated based on 10-minute bins (see Figure 4b); in the SM section 2.2 we present the results of identical analyses using different epoch sizes. The first- and second-lag terms were both strongly significant (~=0) in both groups, indicating a second-order autoregressive model; the first term was highly positive, but the second term was negative (arousal levels at time t were negatively associated with arousal levels c.15 minutes after time t). Wilcoxon tests were conducted to assess how the PACF terms differed between the high- and low-noise groups, controlling for multiple comparisons using the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995). The first-order term was greater in the low-noise group Z=3.1, p=.002, but no significant difference was observed for the second-order term. In the SM section 2.2 we present analyses suggesting that the same pattern is consistently observed at epoch sizes greater than 10 minutes, but not at smaller epoch sizes. Overall, these results indicate a faster rate of change between consecutive epochs of 10 minutes (and upwards) in the high-noise group.

Figure 4c shows infants' autonomic responsivity to naturally occurring negative affect in the home data. We identified (see SM section 1.4) moments where infants showed peak negative affect in their vocalisations (<=3 on a scale from 1 (most negative affect) to 9 (most positive)). A mean *(S.E.)* of 13.6 *(1.2)* such instances were identified per infant. Infants' arousal was z-scored (to control for between-participant differences in average arousal) and averaged during the period from +/- 10 minutes relative to each instance (see Figure 4c). Although the arousal increase at the time of the negative affect vocalisations is equivalent, the high-noise group show faster decreases in autonomic arousal in the period c.1-5 minutes after the vocalisation, as indicated by a significant difference on the permutation-based temporal clustering analyses (p=.042) (see SM section 1.10). This suggests that the high-noise group showed faster physiological recovery following moments of naturally occurring negative affect.

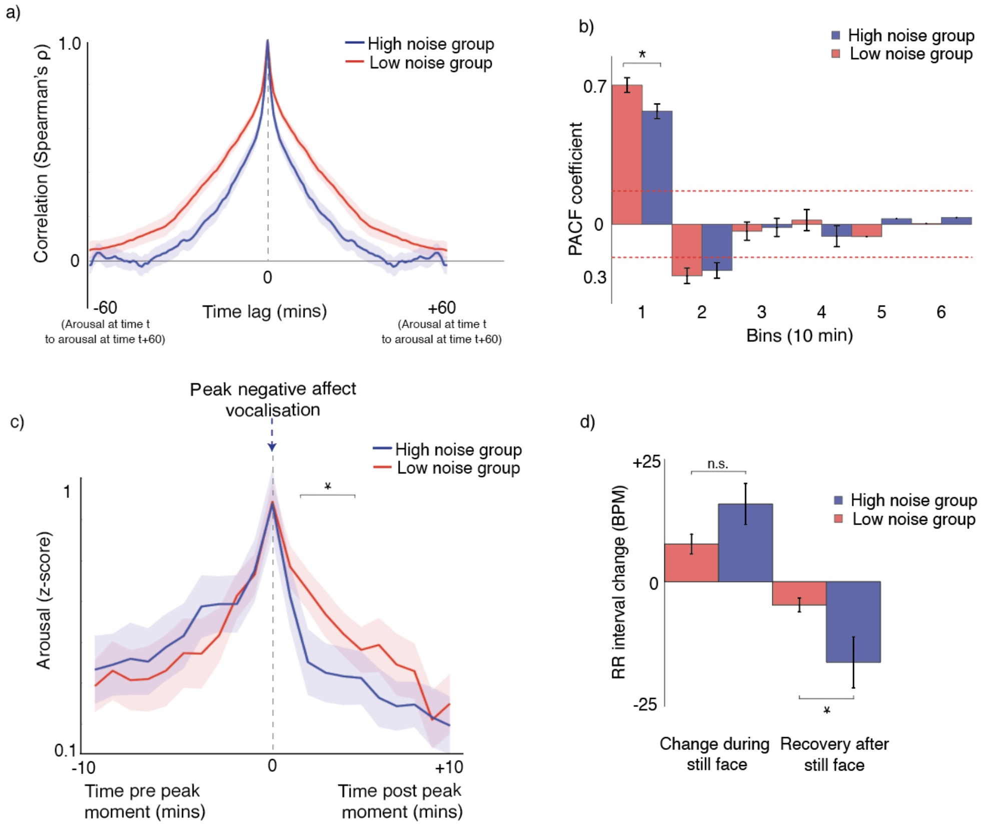

*Figure 4: a) Auto-Correlation Function (ACF) for arousal in the home data. Red shows the low-noise group; blue the high-noise group. b) Partial Auto-Correlation Function (PACF) for arousal in the home data. Dashed red line indicates cut-off for significant PACF coefficients. Star indicates significant results of Wilcoxon test to examine between-group differences. * - p<.05. c) Arousal changes to moments of naturally occurring negative affect in the home data. Shaded areas show the S.E. Red shows the low-noise group; blue, the high-noise group. Star indicates the area of significant difference identified by the permutation-based temporal clustering analyses. * - p<.05 d) RR interval change during the still face procedure, and recovery afterwards in the lab battery. Red shows the low-noise group; blue, the high-noise group. * - p<.05.*

Part 5 –Arousal lability to emotional stressor in lab battery

We also examined infants' autonomic responsiveness to experimentally induced negative affect, using a still face procedure (Weinberg & Tronick, 1996) (see Figure 4d). Data were windowed in 30-second windows. Change during the still face was calculated as the final window during the still face minus the initial window of free play; recovery was calculated as the final window of resumed free play minus the final window during the still face. A non-significant bivariate correlation was observed between home noise and HR increase during the still face r_s=.49, p=.15; a significant bivariate correlation was observed between home noise and HR recovery following the still face r_s =-.65, p=.049. This indicates that, in the lab battery, children with noisier home backgrounds showed both (non-significantly) greater HR increase during the still face, and greater recovery after.

Discussion

We measured infants' exposure to environmental noise and autonomic reactivity in a cohort of 12-month-old infants from diverse socio-economic backgrounds. Our noise recordings indicated consistent individual differences in mean levels of noise exposure across our sleeping and waking samples; microphone noise data also associated with parent report via questionnaire (the CHAOS scale - Matheny et al., 1995). Noise associated with the number of people living in the home, but did not associate with other socio-economic variables such as maternal education and household income, parenting, or life-long stressors such as adverse childhood experiences. Mean levels of noise exposure also associated with variability in noise, such that children exposed to higher average levels of noise also experienced a faster-changing noise profile (Figure 2b).

Our results pointed to a strong phasic association between environmental noise and arousal: at times during the day when environmental noise was higher, infants' autonomic arousal was elevated (Figure 3a). To our knowledge this is the first time that such a relationship has been documented. Our analyses examined externally generated noise, excluding sections in which the infants were themselves vocalising. The same pattern was observed in samples recorded at home, and outdoors.

We also found that, in infants who experienced higher levels of noise at home, their autonomic responsiveness to noise was lower. This is consistent with previous research suggesting that adults exposed to more noise at home are less likely to show noise-induced arousal-based awakenings (Pearsons et al., 1995), and a previous study in which adults were exposed to noise across eight successive nights in a sleep lab (Basner et al., 2011).

When we examined the same infants in controlled experimental settings we found that infants exposed to noisier home environments showed similar autonomic and behavioural responses to the 'low-noise' group immediately following the appearance of an attention-eliciting stimulus, but that these changes were more short-lived (Figure 3c-e, and Figure S5). Visual sustained attention was also lower in the 'high-noise' group. The close correspondence we observed between our autonomic and behavioural findings on this measure is expected, given extensive previous research that has identified strong associations between attention-elicited autonomic changes and sustained attention in infants (de Barbaro, Clackson, & Wass, 2016; Richards, 1985, 2010; Winterer & Weinberger, 2004).

We also examined infants' reactivity to lab-based experimental stressors, by administering a still-face procedure (Figure 4d) (Weinberg & Tronick, 1996). We observed non-significantly greater increases in arousal in response to the still-face, and significantly greater recovery after the still-face (Figure 4d). Here, our results were not exactly as predicted, based on previous research. Evans and colleagues found that children exposed to more environmental noise showed increased reactivity to an experimental stressor (Evans et al., 2001), and our present findings were directionally consistent with that. However, whereas most previous research has found increased reactivity to be associated with slower recovery (e.g. Beauchaine & Thayer, 2015), we observed *both* increased reactivity *and* faster recovery in the high-noise group. This may be because we used a more fine-grained temporal measure than in previous studies, that allows reactivity and regulation to be differentiated (cf Obradović & Finch, 2016; see also Fox, 1989; Gottman & Katz, 2002 for consistent results). Our finding that the high-noise group showed a generally more labile profile of change in autonomic arousal was also observed in the home data, where we also observed faster recovery from moments of naturally occurring negative affect (Fig 4c), and greater variability (more change in autonomic arousal) over longer time-scales (see further discussion below and Fig 4a, 4b). Thus, we found that children exposed to higher and more variable levels of noise at home showed autonomic responses that were more labile across both the lab and the home battery and, within the lab battery, in both cognitive and affective domains.

Brainstem-mediated autonomic reactivity is involved in maintaining allostasis and homeostasis in the face of external environmental change (Cacioppo et al., 2000). It also mediates cognitive responses such as reactions to a novel, unexpected external stimulus (e.g. Sechenov, 1965), and affective processes such as reactions to an experimental stressor (Aston-Jones & Cohen, 2005; Geva & Feldman, 2008; McCall et al., 2015; Wass, 2018). Early research identified the orienting response (Pavlov, 1927; Sechenov, 1965; Sokolov, 1963), which is elicited by stimuli that are novel, complex, or incongruous, and which is now thought to be mediated largely by the *parasympathetic* branch of the Autonomic Nervous System (ANS) (Sokolov, 1963). This was differentiated from the Defensive Reaction (Pavlov, 1927), which is elicited by stimuli that are intense or unexpected (Sechenov, 1965), and which is thought to be mediated largely by the *sympathetic* branch of the ANS (Cacioppo et al., 2000; although see e.g. Porges & Furman, 2011).

Extensive previous research has suggested that children raised in noisy and unpredictable home environments show atypical responses within both subdivisions of the ANS (e.g. Evans & Wachs, 2010; Bremmer et al., 2003; Basner et al., 2014). Our finding that these relationships can be identified earlier in development than had previously been appreciated is novel, but unsurprising: extensive evidence suggests that early development is highly sensitive to environmental influence (Frankenhuis et al., 2018). Similarly novel, but theoretically predicted (Wass, 2018), is our finding that environmental influences on autonomic function affect performance in both cognitive, and affective, domains. Consistent with this, other research has shown that brainstem integrity even shortly after birth can influence both cognitive and social developmental outcomes over longer time-frames (Geva, Schreiber, Segal-Caspi, & Markys-Shiffman, 2013; Geva & Feldman, 2008).

Neural control over the ANS is governed by a range of brain areas centred on the locus coeruleus (LC) and reticular pathways in the brainstem, communicating via thalamic and cortical projections (e.g. Amaral & Sinnamon, 1977; Arnsten & Goldman-Rakic, 1984); partially discrete neural substrates control the parasympathetic and sympathetic subdivisions (Samuels & Szabadi, 2008). Recent research has argued that these different subdivisions cannot, however, reliably be differentiated in humans by comparing change in peripheral ANS indicators such as heart rate over different time-scales (Billman, 2013), as others had previously claimed. Here, we report that infants who show more long-term autonomic fluctuations on a >10 minute scale (but not on shorter time-scales – see Wass, de Barbaro, Clackson, & Leong, 2018 and SM section 2.2) show superior sustained attention, and that these differences associated with more labile response patterns over shorter time-frames in our lab testing battery. Tentatively, these findings might be attributed more to the sympathetic subdivision of the ANS (see Wass, de Barbaro, Clackson, & Leong, 2018). This is plausible, given extensive previous research suggesting that both parasympathetic and sympathetic subdivisions influence cognitive functions such as sustained attention in infants (Wass, 2018). However, future research should investigate this in more detail.

Our findings may, therefore, give insight into how noisy home environments can adversely affect long-term affective and cognitive outcomes. However, further work remains to elucidate the mechanisms underlying this relationship. For example, we found that average autonomic arousal did not differ between our high- and low-noise groups, but that the rate of change of arousal did. This begs the question of whether the differences we observed were due to repeated stimulation of the sympathetic nervous system (excessive long-term levels of chronic noise), or due to unpredictability in noise levels (excessive short-term phasic variability in noise). Both types of difference were present in our data (Figure 2a, 2b).

In order further to investigate how autonomic lability during early development may, for example, disrupt the development of inter-personal emotion regulatory mechanisms, longitudinal studies would also be useful (Beatty & Lucero-Wagoner, 2000; Cacioppo et al., 2000; Feldman, 2006; Geva, Sopher, et al., 2013). Animal research has also suggested that early-life stress can act as a risk factor in sub-optimal home environments, but an opportunity factor in supportive home environments (Hartman, Freeman, Bales, & Belsky, 2018). One possibility is that increased arousal lability may be a physiological mechanism subserving these bivalent effects (Boyce & Ellis, 2005; Feldman, 2006; Weinberg & Tronick, 1996; Obradovic, 2016).

Causative pathways are hard to untangle, and it may also be that the relationships we observed are mediated by other, unobserved factors. For example, in our high-noise group, parents spent less time talking to the infant, and more time talking to other adults (Figure 2d), and it is possible that factors such as parental engagement may influence the relationships observed. Another potential factor is the duration or quality of infant sleep (Brink, 2012; Pearsons et al., 1995), although we found no association between noise and time sleeping. Intervention studies, that examine how minimising environmental noise affects infants' autonomic reactivity, may further improve our understanding of these pathways of causation.

Key Points:

- Early-life stress is known to confer increased transdiagnostic risk of adverse mental health outcomes.
- For the first time we examined how fluctuations in external environmental noise affect the developing autonomic nervous system.
- We found that children exposed to more noisy environments showed reduced autonomic responsiveness to novel stimuli and more fast-changing profiles of autonomic arousal.
- Our results suggest new mechanisms through which high exposure to environmental noise stressors can confer increased risk of transdiagnostic impairment during later life.

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Supplementary Materials for:

Influences of environmental stressors on autonomic function in 12-month-old infants: understanding early common pathways to atypical emotion regulation and cognitive performance

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

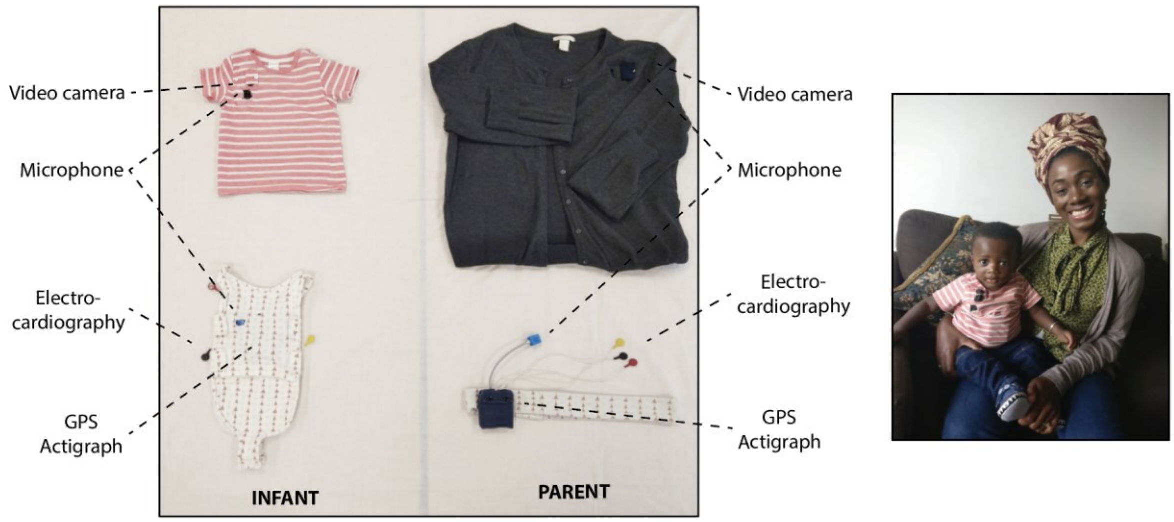

Figure S1: a) equipment used. b) child and parent wearing the equipment

1.2 Home/Awake coding

Coding of when participants were at home was performed using the GPS monitors that were 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). 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 Supplementary Materials Figure S1), 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.

1.3 Autonomic data parsing and calculation of the autonomic composite measure

Analysis of the inter-beat intervals was calculated using custom-built Matlab scripts, using an adaption of a standard threshold procedure (Wass, de Barbaro, & Clackson, 2015), and verified *post hoc* via visual inspection. Heart rate variability was calculated using the PhysioNet Cardiovascular Signal Toolbox (Vest et al., 2018). 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. To parse the actigraphy data we first manually inspected the data, then corrected artifacts specific to the recording device used, and then applied a Butterworth low-pass filter with a cut-off of 0.1 Hz to remove high-frequency noise.

In previous research we have shown strong 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 analyses 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 S1a 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 S1c shows how these zero-lagged correlations vary on a per-participant basis. S1b 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 S1c), albeit that the variability in heart rate and movement is lower. Figure S1 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.

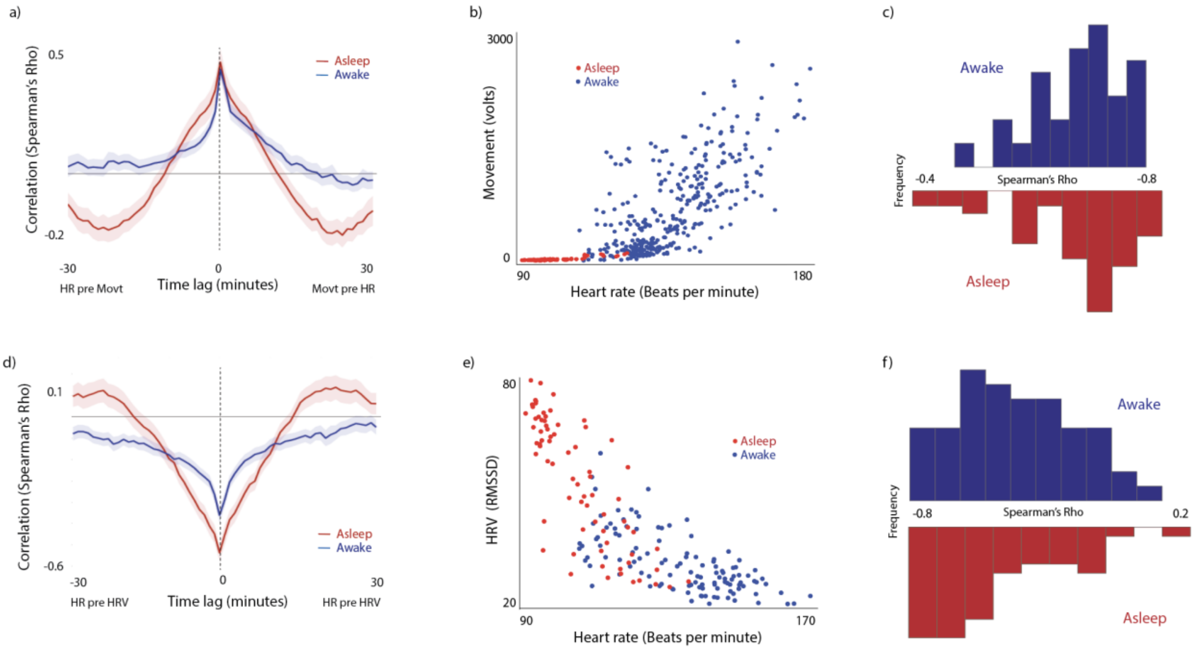

Figure S1: Illustrating the relationship between the individual physiological measures included in the composite measure. a) Cross-correlation of the relationship between HR and Movement. b) Scatterplot from a sample participant. Each datapoint represents and individual 60-second epoch of data. c) Histograms 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.

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

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 indubitably true, these findings should be seen as rendering incorrect our treatment 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).

Due to technical problems with the ECG recording leads (N=10) and to problems with the placement of the ECG recording electrodes (N=2), the arousal composite data was unavailable for 12 of the participants tested.

1.4 Microphone data coding

Microphone data were recorded at 11.56 kHz, and converted to decibel values using the mag2db function in MATLAB. For reasons of recording bandwidth, the microphone did not record continuously, but recorded a 5-second snapshot of the auditory environment every 60 seconds throughout the day. *Post hoc*, trained coders listened to all audio samples recorded to classify the recording samples. Three types of categorisation were applied:

First, coders identified whether a vocalisation was present in that sample. Four categories of vocalisation were identified: 'Infant' (samples in which the infant was vocalising); 'Other child' (samples in which another child was vocalising, as recorded on the infant's microphone); 'Ad->Infant' (samples in which an adult was talking, and the speech was directed to the infant); 'Ad->other ad' (samples in which an adult was talking, and the speech was directed no to the infant but to another adult, or infant). Categories were non-exclusive – so, for example, a segment could be classified as containing both an infant and an ad->infant vocalisation. The relative proportions with which each of these categories were coded in the data is given in Figure 2d in the main text.

Second, coders identified the ambient noises present in the microphone sample. This coding was performed by identifying those categories that could be reliably identified in the recordings. The following categories were identified: 'Adult TV (speaking)' (samples in which non-infant-directed TV or radio was audible, and the content was mainly speaking); 'Adult TV (music)' (samples in which non-infant-directed TV or radio was audible, and the content was mainly music); 'Child TV' (samples in which infant-directed TV or radio was audible); 'Car' (samples in which the background noise of driving was audible); 'Shopping etc' (samples containing background interior noise, such as that of a shopping centre or other large public space); 'Outdoor' (samples containing outdoor noise).

Third, coders examined just those samples in which the infant was vocalising. Each vocalisation was then coded for vocal affect on a scale from 1 ('fussy and difficult' – most negative affect) to 9 ('happy and engaged' – most positive affect). Due to its labour-intensive nature, this coding was conducted for 46 participants in total. In addition, 24% of the sample was double coded to assess inter-rater reliability; Cohen's kappa was found to be 0.60, which is considered acceptable (McHugh, 2012). All coders were blinded to group outcome and to all intended analyses, and so the risk of Type I errors arising as a result of inconsistent data coding is low.

In section 1.11 below (Figure S2) we examine how hand-coding of vocal affect varied as a function of the infants' autonomic arousal at the time of the vocalisation.

1.5 Participant drop-out for individual tasks in lab battery

Of the infants who participated in the home testing battery, 57 also attended the lab battery. Full demographic details for this population are given below:

Table S2: Demographic details for the sample (lab battery only)

Infant age (days) – mean		351.7
- *SE*		*7.7*
Gender (% male)		43.9
Infant Ethnicity (%)	White British	26.6
	Other white	10.1
	Afro-Caribbean	8.9
	Asian, Indian & Pakistani	7.6
	Mixed - White/Afro-Caribbean	3.8
	Mixed - White/Asian	6.3
	Other mixed	3.8
Household Income (%)	Under £16k	22.8
	£16-£25k	11.4
	£26-£35k	10.1
	£36-£50k	6.3
	£51-£80k	8.7
	>£80k	5.1
Maternal education (%)	Postgraduate	13.9
	Undergraduate	36.7
	FE qualification	2.5
	A-level	1.2
	GCSE	6.3
	No formal qualifications	2.5
	Other	2.5

Participant drop-out for lab tasks:

Test 1 (Figure 4d): Due to technical problems (a faulty ECG cable (N=21); inaccurate synching (N=13) with the recording equipment for this procedure, physiology data was available for 23 infants.

Test 2: Autonomic data (Figure 3c) were available from this task from all participants who attended the lab testing session (N=57). Due to its labour-intensive nature, coding of the looking behaviour for this task (Figure 3d) was only completed for a subset (N=32) of participants.

Test 3 (Figure 3e): Due to non-compliance during testing, data from this task were unavailable from N=7 participants. N=50 were included in the test sample.

1.6 Supplementary experiment to measure visual sustained attention.

In addition to the test described in the main text (Test 2), for which the results are shown in Figure 3c and 3d), a supplementary experiment was also administered to measure visual sustained attention (results shown Figure 3e). The method for this experiment is given below:

Test 3: Visual sustained attention was assessed using an established procedure (Wass, Porayska-Pomsta, & Johnson, 2011). A static image of a child's face was presented on-screen. An experimenter, watching a video feed, coded infant's looking behaviour towards the screen using a key press. When the child looked away from the screen, the picture disappeared and the same image was re-presented. Stimuli were re-presented until: i) the last two successive looks were less than 50% of the longest unbroken look, ii) eight successive looks had occurred without reaching criterion, or iii) the total presentation length exceeded 120 seconds. Three blocks were presented, each using different images.

The results obtained for this experiment were analysed using the same procedures as described in the main text. For peak look duration, Wilcoxon tests indicated no group difference ($p=.92$); however, when examining total look duration across multiple looks towards a particular stimulus, a marginally non-significant group difference emerged ($p=.09$). These results are consistent with the significant results presented in the main text, indicating that, across two entirely separate experiments, reduced visual sustained attention was observed in the high-noise group.

1.7 Relationships of microphone noise to other socio-economic variables

Bivariate correlations were conducted to assess the relationship between sleeping microphone noise and other socio-economic variables. Following the procedure used throughout the paper, these were calculated using the more conservative non-parametric statistics (Spearman's Rho) as not all variables were normally distributed.

Sleeping microphone noise showed bivariate associations with the number of other people living in the infant's home $r_s=.28$, $p=.02$, but did not associate with maternal education $r_s=.07$, $p=.59$, household income $r_s=.14$, $p=.23$, pre-, peri- and post-natal stressors $r_s=-.04$, $p=.75$, adverse life events $r_s=-.04$, $p=.72$, parental anxiety $r_s=-.14$, $p=.26$, depression $r_s=.01$, $p=.94$, or parental overinvolvement $r_s=.14$, $p=.27$. There was no relationship between noise and the proportion of the recording spent sleeping $r_s=-.12$, $p=.30$.

1.8 Poincaré analysis

In order to examine intra-individual variability in noise whilst controlling for the inter-individual differences in average noise, data were averaged into 60-second epochs and grouped on a per-participant basis into 5 equal-sized bins. The noise levels at time t were plotted on *y* axis and time t+1 on the *x* axis. Data that are more tightly clustered around the identity line show greater stability between consecutive epochs. From visual inspection, it appears that the high noise group are less tightly clustered around this line. To assess the significance of this difference, the standard deviation (SD) of points perpendicular to the identity line was calculated (Mirescu & Harden, 2012) on a per-participant basis. A Wilcoxon test indicated that the SDs in the high noise group were significantly higher than those in the low noise group Z=2.56, p=.01. This suggests that the high-noise group show more sudden changes in noise, even when differences in mean and variance are controlled for.

1.9 Cross-correlation analysis

In a cross-correlation, the Time lag=0 moment shows the correlation across all epochs between the two variables considered simultaneously. The Time lag=60 moment indicates the correlation between noise at time t and arousal at time t+60 (i.e. 60 minutes after that moment). Analyses were conducted using custom-built MATLAB scripts described in further detail in a previous paper (de Barbaro, Clackson, & Wass, 2016), but verified using built-in MATLAB functions (crosscorr.m).

One challenge to interpreting the significance of cross-correlations is that each variable is itself auto-correlated (i.e. shows a profile of change that is either slower, or faster changing (Chatfield, 2004; Thiebaux & Zwiers, 1984; Thorson, West, & Mendes, 2018). Thus in calculating a cross-correlation to index the relationship between two variables at a given time-lag, it is first necessary to estimate how each variable relates to *itself* at that time lag (which is described by the auto-correlation). A variety of techniques are available to do this, including Autoregressive Integrated Moving Average models (e.g. (Feldman, Magori-Cohen, Galili, Singer, & Louzoun, 2011)) or the Actor-Partner Interdependence Model (Thorson et al., 2018). We opted to correct for auto-correlation by calculating the Effective Sample Size (Clifford, Richardson, & Hemon, 1989; Thiebaux & Zwiers, 1984). At each time interval, the cross-correlation (i.e. the relationship between the two variables) was first calculated, and then the auto-correlation value for each variable (i.e. the relationship of that variable to itself, at that time-lag) was then calculated. The higher of these two values was used to calculate the Effective Sample Size, using the standard formula: $N^* = \frac{N(1-r)}{(1+r)}$, where N^* is the Effective Sample Size, N is the actual sample size and r is the higher of the two auto-correlation values obtained at that time interval for each of the two measures independently (Thiebaux & Zwiers, 1984). The significance level of the cross-correlation obtained was then adjusted based on the Effective Sample Size. In this way, we calculated the significance level of the relationship between two variables at a particular time-lag, *independent of the relationship of each variable to itself* at that time-lag.

In order to assess the significance of the asymmetry noted for Figure 3a in the cross-correlation function of the low-noise group, the following procedure was used. The ϱ values of the cross-correlation were calculated separately for each participant from y+1 to y+60 and from y-1 to y-60, where y is the time=0 bin and the integers represent the time lag in minutes between the two variables included in the cross-correlation. A series of separate t-tests were then conducted to directly compare the ϱ values between y+t and y-t, for each value of t from 1 to 60 seconds. Multiple comparisons were then corrected for using the permutation-based temporal clustering analysis described below (section 1.10). Results suggested that a significant asymmetry was present in the cross-correlation function shown in Figure 3a for the high-noise group (p<.001) but not the low-noise group (p=n.s.). This suggests that, in the low-noise group only, external noise levels forwards-predict subsequent arousal levels.

1.10 Permutation-based temporal clustering analyses

To estimate the significance of the time-series relationships in the results, a permutation-based temporal clustering approach was used. This procedure, which is adapted from approaches widely used in neuroimaging analyses (Maris, 2012; Maris & Oostenveld, 2007), allows us to estimate the probability of temporally contiguous relationships being observed in our results, a fact that standard approaches to correcting for multiple comparisons fail to account for (Maris & Oostenveld, 2007). See also (Oakes, Baumgartner, Barrett, Messenger, & Luck, 2013) for a similar approach. The analysis used was designed to identify temporally contiguous patterns of change in instances where the centre-point of the expected response window is unknown (Maris & Oostenveld, 2007).

In each case, the test statistic (generally paired/unpaired t-test) was calculated independently for each time window. Series of significant effects across contiguous time windows were identified using an alpha level of .05. 1000 random datasets were then generated with the same dimensions as the test data, the same sequence of analyses was repeated, and the longest series of significant effects across contiguous time windows was identified. The results obtained from the random datasets were used to generate a histogram, and the likelihood of observed results have been obtained by chance was calculated by comparing the observed values with the randomly generated values using a standard bootstrapping procedure. Thus, a p value of <.01 indicates that an equivalent pattern of temporally contiguous group differences was observed in 10 or fewer of the 1000 simulated datasets created.

<u>1.11 Relationship of vocal affect to autonomic arousal</u>

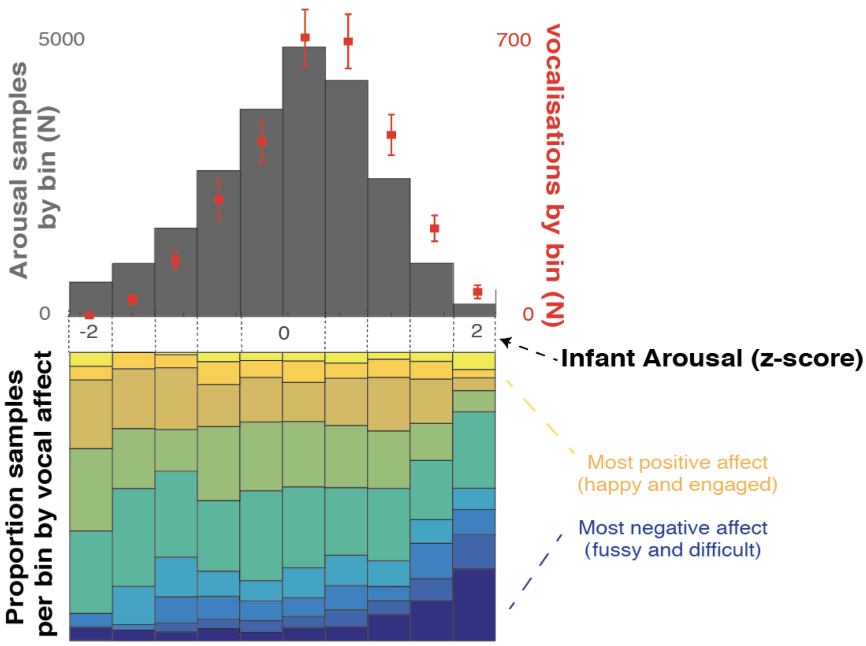

Figure S2: grey bars show a histogram of the distribution of arousal data across the entire sample. Red line shows a histogram of vocalisations by arousal bin. Bottom: stacked bar-chart illustrating the proportion of samples by vocal affect, sorted per arousal bin using the same bins as the histograms in the plot above. Yellow colours indicate positive affect vocalisations, and blue colours indicate negative affect vocalisations.

Figure S2 shows the distribution of infant arousal samples (grey bars). Overall, this shows a mild negative skew with a mode>0, replicating a pattern we have noted and discussed previously (Wass, Clackson, & Leong, 2018). The red line, showing vocalisations by autonomic arousal bin, indicates that infant vocalisations were more commonly observed at higher autonomic arousal states. The bottom section of Figure S2 shows the distribution of hand-coded vocal affect by autonomic arousal. Intense negative affect was more commonly observed at high arousal, but intense positive states were equally common throughout.

Of note, this figure has already appeared in another publication (Wass. et al., under review), and is only included in the Supplementary Materials here for convenience.

2 Supplementary Results

2.1 Supplementary Figure – raw microphone data from individual participants – entire sample.

At the request of a reviewer we also include, for all participants, the same illustrative plots of the raw microphone data that Figure 2a shows for a subset of individual participants. These data have been processed and treated in exactly the same way as the data included in Figure 2a.

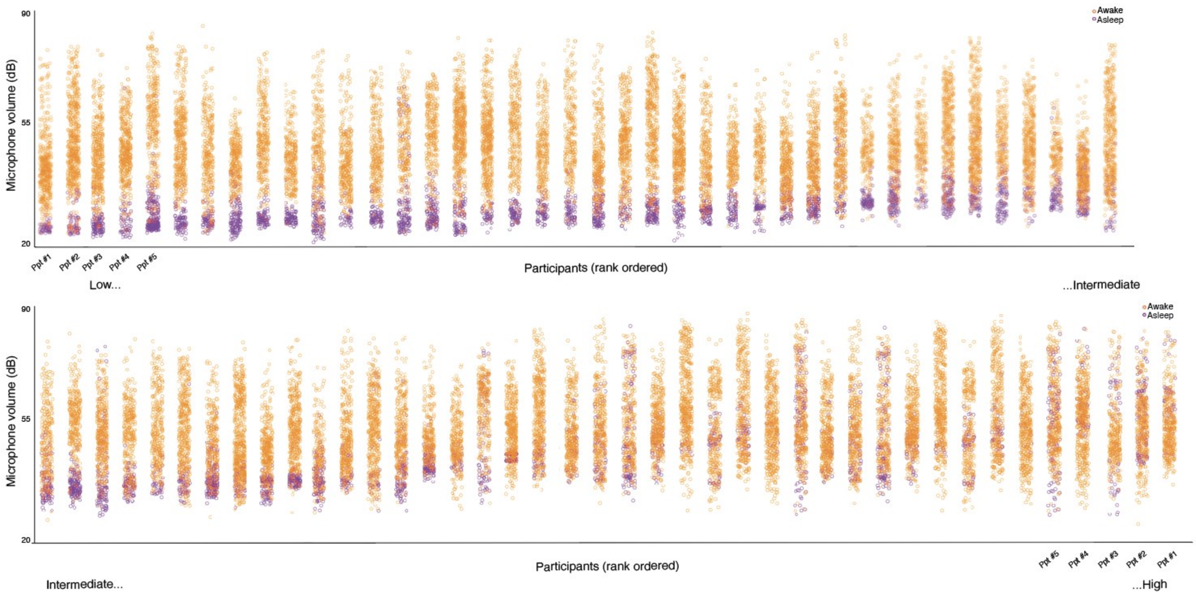

Figure S3: Illustrative plots of raw microphone data for all participants. These data have been processed in exactly the same way as the same plots, shown for a subset of participants, in Figure 2a in the main text.

2.2 Supplementary Figure – PACF analyses with variable-sized time bins

Figure 4b in the main text shows the PACF coefficients at different time lags, based on data epoched into 10-minute bins. Results presented in the main text indicate that the lag 1 term was significantly higher in the low noise group, indicating a lower rate of change between consecutive 10-minute epochs in the low noise group. In order to investigate the degree to which this finding was specific to the epoch size used in the analysis, the analysis was repeated using variable epoch durations. Figure S4 shows the results of this analysis. Only the lag 1 terms are shown. In addition, significant negative lag 2 terms were also observed for all epoch sizes greater than 10 minutes, but these are not illustrated.

The lag 1 PACF term decreases with increasing epoch sizes, which is as expected given the autocorrelation present in autonomic data (Wass et al., 2016; Wass et al., 2015). The same group comparison was conducted as described in the main text to investigate how far this finding was specific to the epoch size used in the analysis. At shorter epoch durations (1 second/10 second), no group differences were observed. The group differences reported in the main text (low noise group>high noise group) were consistently significant for epoch durations longer than 10 minutes. These were non-significant at the longest epoch durations (60 minutes), but we cannot preclude the possibility that the quantity of data included in this analysis (average 7.3 hours per participant) rendered findings of analyses with very long epoch durations unreliable.

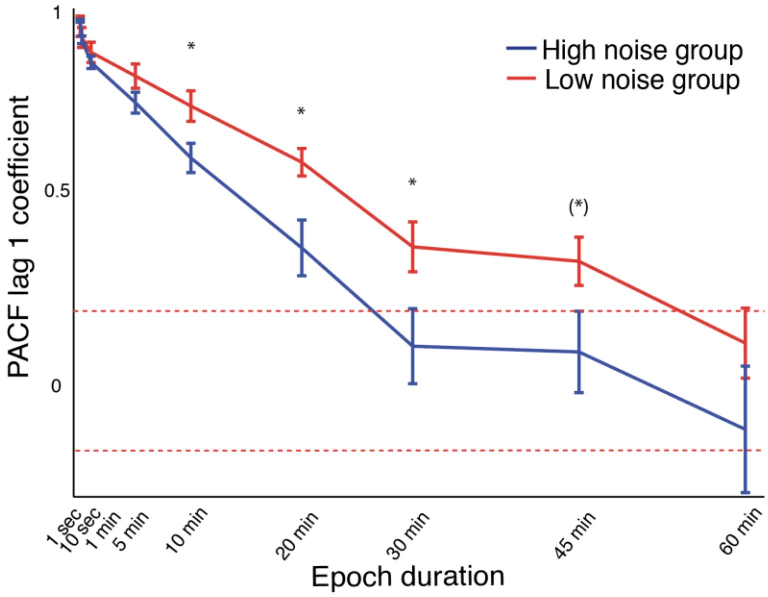

*Figure S4: Partial Auto-Correlation Function (PACF) for arousal in the home data, calculated at variable epoch durations. In each case, only the lag 1 PACF term is shown. Dashed red line indicates cut-off for significant PACF coefficients. Star indicates significant results of Wilcoxon test to examine between-group differences. * - p<.05, (*) – p<.10.*

<u>2.3 Supplementary Figure – Main analyses subdivided using a quartile split rather than median split</u>

At the request of a reviewer we also include the same primary analyses featured in the main text, but subdivided using a quartile split, rather than a median split.

The results observed are consistent with the findings based on median split analyses. The exception is the analysis shown in Figure S5f. The reason for this is likely to be the relatively higher rate of participant drop-out on this measure, due to equipment failure (see SM section 1.5), rendering this analysis based on smaller group sizes less reliable.

One further pattern of note is that group 4, representing the children exposed to highest levels of noise, show markedly more extreme variability across all measures presented. This suggests the possibility of a non-linear exposure-response relationship – i.e., that the patterns we have documented in the main text may be particularly extreme for infants exposed to the highest levels of noise. In future research, we hope to investigate this issue in more detail.

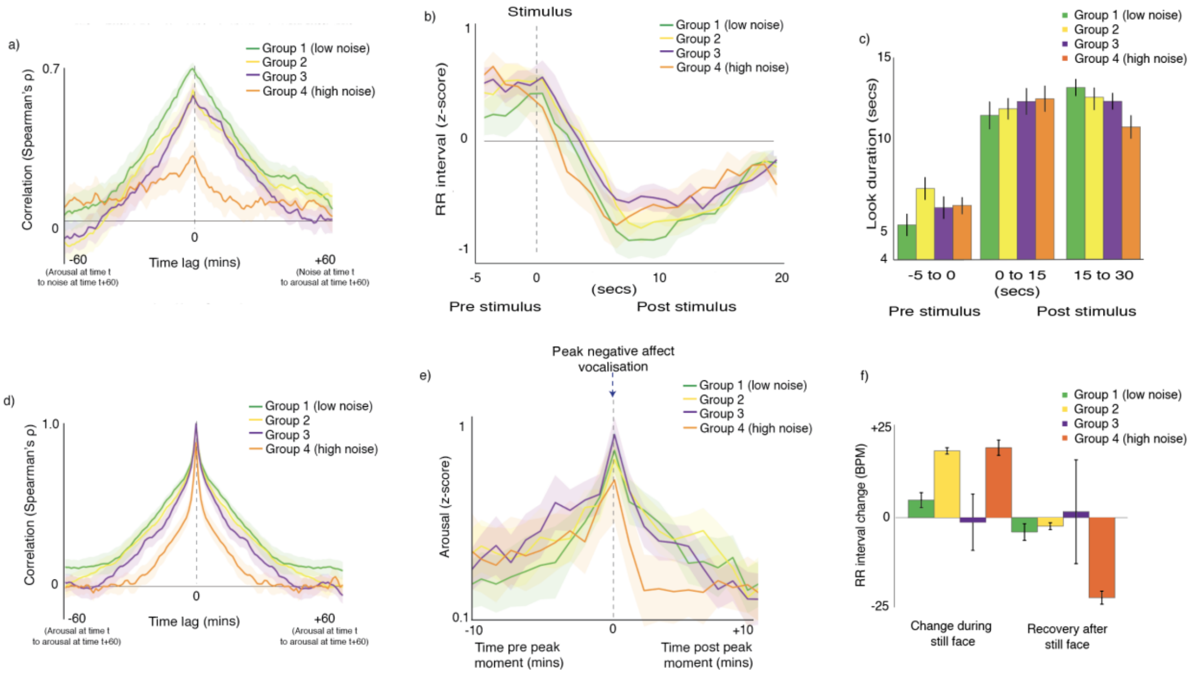

Figure S5: Main analyses subdivided using a quartile split, rather than a median split. a) equivalent to Fig 3a in main text; b) equivalent to Fig 3c; c) equivalent to Fig 4d; d) equivalent to Fig 4a; e) equivalent to Fig 4c; f) equivalent to Fig 4d.

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