Finger pulse wave amplitude response during sleep to environmental noise

Branko ZAJAMSEK(1), Gorica MICIC(1), Kristy HANSEN(1), Peter CATCHESIDE(1)

(1) Adelaide Institute for Sleep Health, Australia, branko.zajamsek@flinders.edu.au

Abstract
Changes in finger pulse wave amplitude (FPWA) are a sensitive marker of autonomic and electro-encephalographic (EEG) activation responses evoked by relatively high level acoustic stimuli presented during sleep. FPWA responses could therefore be a particularly useful marker of physiological activation responses and sleep fragmentation caused by environmental noise during sleep. In this study we explored the FPWA response evoked by ecologically relevant environmental noise exposures at moderate sound pressure levels (SPLs) up to 48 dB(A) during sleep. Twenty-three healthy participants took part in two noise exposure nights in a sleep laboratory, separated by a recovery week. We found a significant increase in FPWA response occurrence probability after noise onset at levels down to 33 dB(A). The size of evoked FPWA responses was small and similar to the size of spontaneous responses irrespective of noise level. These data support that FPWA responses are a sensitive marker of physiological disturbances to environmental noise during sleep, although the physiological and potential clinical significance of frequent autonomic activation responses remains to be determined.

Keywords: Arousal, pulse wave amplitude, environmental noise disturbance, effects of noise

1 INTRODUCTION
Environmental noise has the potential to delay, reduce and fragment sleep via increased wake time, more frequent awakenings and micro-arousals. This can result in impaired mental and physical functioning and well-being [1]. Standard measures of sleep disturbance rely on traditional sleep scoring criteria. These use 30–second data epochs to classify sleep stages, and simple counts of full awakenings and more frequent shorter transient micro-arousal events visible in the electro-encephalogram (EEG) [2]. Brief arousals fragment sleep and degrade sleep quality, contributing to subsequent daytime sleepiness [5]. However, EEG based criteria reflect only high-level cortical activation responses in a hierarchy of autonomic sensory and physiological activation processes responsive to sensory disturbances throughout sleep. These reflect brainstem sensory and reflex processes that regulate breathing and cardiovascular activity in response to disturbances that may arise during sleep and require rapid re-engagement of high cardio-metabolic and brain activity. Amongst the most prominent of these reflexes is a powerful peripheral vasoconstriction response, which is the main element of a blood pressure surge that accompanies arousals from sleep. This response can very rapidly shunt blood to the heart, lungs, brain and activated muscles most needed for coordinated survival responses. This blood shunt can be easily detected from a transient reduction in finger photoplethysmogram pulse wave amplitude (FPWA) and be evoked by a stimuli such as noise [7]. Thus, FPWA is potentially a very useful marker of autonomic activation responses to sensory disturbances, and may be a more sensitive marker of physiological sleep disruption than traditionally scored EEG arousals. However, previous research investigating FPWA responses to acoustic stimuli used either pure tones [4] or environmental noise [6] at relatively high sound pressure levels (SPLs) with respect to World Health Organisation’s maximum recommended night-time indoor SPL of 45 dB(A) [8]. Therefore, the aim of this pilot study was to investigate FPWA responses to environmental noise at more realistic night-time levels of noise exposure during sleep.
2 METHODOLOGY

2.1 Participants and experimental conditions
Twenty-four healthy participants (11 males, mean (M) = 26.5 years, standard deviation (SD) = 16.4, age range: 18-70, 13 females, M = 21.7 years, SD = 1.2, age range: 19-23) were recruited for a two-night double-blind, randomized and counter-balanced protocol. The study was approved by the Flinders University Social and Behavioural Research Ethics Committee (SBREC) and all participants provided informed written consent. Participants were recruited from the general population via social media and posters placed on University notice boards, and were eligible for participation if they self-reported good health, and sleep of adequate quality and quantity as measured by the Insomnia Severity Index, Epworth Sleepiness Scale and Pittsburgh Sleep Quality Index.

Auditory acuity was assessed by an audiologist using a manual threshold determination test to confirm participants’ normal hearing at frequencies between 125–8000 Hz. Eligible participants were invited to attend two overnight laboratory sleep studies spaced one week apart to allow sleep recovery, and provided with a sleep diary and watch-size activity monitor to confirm normal sleeping patterns in the week prior to the overnight in-laboratory studies. Participants’ self-determined habitual lights out and wake-up times were obtained by averaging sleep diary responses across all days reported. In the morning after each laboratory study, participants also responded to self-report questions assessing the perception of their sleep in the laboratory.

2.2 Sleep and FPWA measurement
During each study night, participants were set-up with polysomnography (PSG) electrodes to record electroencephalograms (EEG; F3, F4, C3, C4, Cz, O1 and O2), electro-oculograms (EOG; E1 and E2), chin electromyogram (EMG), leg movements, the electrocardiogram (ECG), respiratory signals (nasal cannula pressure and thermistor, and chest and abdominal motion) and pulse-oximetry recordings. These signals were recorded using Compumedics GRAEL v2 (Abbotsford, Vic, Australia) data acquisition system at a sampling rate between 256 Hz (pulse-oximetry) and 512 Hz (EEG, EOG, EMG, ECG). These data were subsequently used for sleep staging and arousal scoring. To synchronise sleep and acoustic systems, a trigger signal for noise delivery indication was recorded using National Instruments 9234 module at a sampling rate of 8192 Hz on the acoustic system and the maximum DC input channel recording rate of 64 Hz on the Grael system.

2.3 Noise intervention
A battery of block-randomised noise stimuli were presented at least 5 minutes into established stage 2 sleep at the start of the protocol and after at least 1 minute of stage 2 sleep on any subsequent return to sleep after an awakening (>15 sec arousal). One night consisted of 20 second noise stimuli (N20) and the other used 180 second stimuli (N180). During both nights there was a 20 second pause between consecutive noise deliveries. The N20 noise battery was played at overall SPLs of 33–48 dB(A) in 3 dB increments giving 6 distinct levels and included wind farm noise with amplitude modulation (WFN AM), wind farm noise without amplitude modulation (WFN NoAM), wind farm noise with amplitude modulation and mid- to high-frequency content (Swish), traffic noise recorded next to a road (TN short-range) and traffic noise recorded inside a suburban house in a room with an open window (TN long-range). The N180 noise battery contained 33, 38 and 43 dB(A) levels of TFN short-range and WFN AM. Both nights also contained a background noise only condition at 23 dB(A) as a baseline control exposure.

2.4 FPWA response detection algorithm
An algorithm was developed in the MATLAB programming language to detect and characterise FPWA responses. The FPWA response is characterised by a distinguishable rapid drop, over a few seconds, from the preceding baseline followed by a more gradual return back to baseline over 10–30 seconds. The main response feature calculated was the area under the curve (AUC) from baseline in arbitrary units (au; given that the photo-
plethysmogram provides an un-calibrated light absorbance signal) in order to quantify both response magnitude and duration within a single summary measure. Any FPWA response curve associated with a characteristic rapid drop followed by a more gradual return to baseline and an AUC exceeding 200 au before the return to baseline was classified as a vasoconstriction response. This is an arbitrary cut-off.

2.5 Statistical analysis
Cumulative event rate curves for each SPL were estimated using the Kaplan–Meier product-limit method. The overall cumulative risk was compared between noise samples at the various SPLs and the control using a two-sided log-rank test. The hazard ratios and confidence intervals for SPLs, relative to the control group, were estimated with the use of a Cox proportional hazards model. Cumulative event rates at fixed time points (landmark points) and log-transformed 95% confidence interval were derived from the Kaplan–Meier estimates. The landmark point at 5 seconds (LM₅) was chosen based on visual inspection of the cumulative event curves which showed a clear rate change at that time. The analysis was performed over 40 and 200 seconds-long time windows for N₂₀ and N₁₈₀, respectively, which is in accordance with the length of noise samples and pause between the noise deliveries on each night. FPWA response events were censored if they occurred after 40 or 200 seconds from the onset and if the FPWA response size was less than 200 au. Linear Mixed Model analysis was used to examine whether chronological night and noise duration (20-sec vs. 3-min) had an overall effect on sleep efficiency (i.e., total sleep time/total time in bed, expressed as percentage) and subjective sleep quality. The data are presented as mean ± SEM and 95% confidence limits. A value of P < 0.05 was considered statistically significant.

3 RESULTS

3.1 Sleep architecture
No significant interaction effects of chronological night and noise sample duration (F(1, 42) = 0.23, P = 0.633), and no significant main effects of chronological night or noise duration (F(1, 42) = 2.48, P = 0.123 and F(1,42) = 1.05, P = 0.311), were observed. Young adults aged 20 – 30 years (i.e., analogous to the present study’s sample) in the general population have a sleep efficiency of 85 – 95%, suggesting that sleep in the present study was comparatively normal, albeit on the lower end of the range. Subjective sleep quality ratings reflected “fair” sleep, which was “a little worse than usual”. These results suggest that participants who were specifically selected as good sleepers for this study, exhibited generally good sleep quality that was perhaps somewhat reduced in the laboratory and noise exposure context.

3.2 Number of noise presentations
Tables 1 and 2 show the number of delivered noise samples during stage 2 sleep for N₂₀ and N₁₈₀, respectively. The distribution of noise types at various levels is fairly even for nights with overall more noise samples being delivered during N₂₀ due to the shorter noise samples.

<table>
<thead>
<tr>
<th>SPL, dBA</th>
<th>23</th>
<th>33</th>
<th>38</th>
<th>43</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background noise (Control)</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TN short-range</td>
<td>62</td>
<td>68</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>WFN AM</td>
<td>64</td>
<td>63</td>
<td>65</td>
<td></td>
</tr>
</tbody>
</table>
Table 1. Number of noise and control deliveries for N20.

<table>
<thead>
<tr>
<th>SPL, dBA</th>
<th>23</th>
<th>33</th>
<th>36</th>
<th>39</th>
<th>42</th>
<th>45</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background noise (Control)</td>
<td>110</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swish</td>
<td>102</td>
<td>110</td>
<td>107</td>
<td>122</td>
<td>118</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>TN short-range</td>
<td>113</td>
<td>103</td>
<td>103</td>
<td>107</td>
<td>102</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>TN long-range</td>
<td>120</td>
<td>121</td>
<td>106</td>
<td>113</td>
<td>107</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>WFN AM</td>
<td>115</td>
<td>121</td>
<td>104</td>
<td>107</td>
<td>110</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>WFN noAM</td>
<td>107</td>
<td>118</td>
<td>108</td>
<td>119</td>
<td>117</td>
<td>120</td>
<td></td>
</tr>
</tbody>
</table>

3.3 FPWA response probability

These results are presented using a Kaplan-Meier cumulative incidence curves which show the cumulative probability of FPWA response occurrence as a function of time. A vertical increase in these curves indicates event occurrence and furthermore the curves can never decrease as the cumulative number of occurred events can only remain stable or increase over time. The vertical tick lines on the curves indicate censored events which in this case are FPWA responses smaller than 200 au. At time zero, the cumulative incidence is zero as no event has occurred yet. Cumulative incidence curves are accompanied by risk tables with the information about the number of events at risk at selected time points. Number of events at risk decreases with increasing time and eventually reaches 0 (at which point the cumulative incidence curve would then reach 1) if the time window is sufficiently long.

Figure 1 shows the cumulative incidence of FPWA responses for SPLs and control over N180. The control curve shows a steady near constant rate of rise likely reflecting quite frequent spontaneous FPWA response occurrence in the absence of noise. For the FPWA responses evoked by noise, the incidence rate increased rapidly in the first 5 seconds from noise onset and then abruptly returned to the spontaneous rate. This strongly supports that evoked FPWA responses occur shortly after the noise onset, and is consistent with previous observations [4]. At LM5, the evoked FPWA responses were 2–3 times, and statistically significantly, more likely to occur as in the control group for 33, 38 and 43 dB(A), respectively.

Similar trends were also observed for N20 and are shown in Figure 2. However, for N20 only the 48 dB(A) level was different from the control condition, although there was a strong trend for a difference with 45 dB(A).

To investigate for potential habituation of repeated brief noise exposures or time of night effects on N20, the FPWA responses were divided in half by the median of their time occurrences across the night as measured from the first noise delivery. Figure 3 shows cumulative incidence curves for two halves of all FPWA response occurrences across the night. In the first half of all response occurrences shown in Figure 3A, all SPLs above 40 dB(A) were significantly different from the control condition. However, in the second half of all noise exposures across the night only the loudest noise evoked a FPWA response above the spontaneous rate (Figure 3).

Figure 4 shows group-averaged FPWA responses for N20 and N180 in sub-figures A and B, respectively. Averaging was done over all responses that occurred within 5 seconds from the noise onset to capture evoked responses. The responses were aligned along their onsets as identified by the algorithm. The maximum drops or the size of the responses are similar among different levels and control.

4 DISCUSSION AND CONCLUSIONS

This paper reports an exploratory analysis of FPWA responses evoked by realistic levels of environmental noise during sleep. This response was observed at all sound pressure levels at variable rates of occurrence, depending on the SPL and duration. During protocols with shorter 20-sec noise exposures only 45 and 48 dB(A) SPLs
Figure 1. Cumulative event incidence rate curves for FPWA during N180 with the landmark point (LM5) at 5 seconds during stage 2 sleep and 95% CI denoted by shaded areas. The hazard ratio (HR) is evaluated with respect to the control.

Consistently exceeded the spontaneous rate of FPWA response occurrence. Despite fewer presentations with longer 180-sec noise exposures all SPLs examined, including 33 dB(A), exceeded the spontaneous rate. Given strong evidence for reduced incidence rate in the second compared to the first half of all exposures on the N20 night these effects are strongly suggestive of important habituation or perhaps sensory fatigue effects with repeated short noise exposures.

Noise duration had no effect on either the time of occurrence or response magnitude of the FPWA response. A sharp rise was evident in cumulative incidence curves shortly after noise onset irrespective of noise duration. These findings strongly suggest that FPWA responses are governed by noise onset effects (i.e., sudden change in SPL) rather than exposure length, and elicit a probabilistic “all-or-none” reflex response largely independent of SPL above background in the 33–48 dB(A) range examined in this study. Noise frequency content had no significant effect on FPWA responses (results not shown) somewhat contrary to previous findings [6]. However, SPL variations within noise samples (such as amplitude modulation (AM) in wind farm noise) in our study were <12 dB while previous studies [6] used noise with up to 40 dB in SPL variations.
Figure 2. Cumulative incidence rate curves for FPWA during N20 with the landmark point at 5 seconds (LM5) during stage 2 sleep and 95% CI denoted by shaded areas. The hazard ratio (HR) is evaluated with respect to the control. Statistics are shown only for levels showing statistically significant differences or a strong trend for a difference.

The lack of FPWA responses at lower SPLs observed during N20 may reflect habituation of peripheral vasoconstriction system responses to brief noise exposures. Thus, it is plausible that habituation effects were reduced during N180 at 33 dB(A) since the total number of responses is approximately 3–4 times less than during N20 (see risk tables in Figures 1 and 2). Apart from habituation, sleep architecture and different SPLs between N20 and N180 and carry-over effects could also contribute towards observed differences. Sleep architecture varies across the night such that deep sleep is predominant in the first half of the night where cortical arousal responses are much less likely suggesting that brainstem sensory information transmission to higher cortical levels in the brain is more strongly gated to protect sleep in deep sleep. Given that deep sleep reduces and REM sleep increases during the course of the night changing sensory gating effects might have contributed to time-of-night effects. Whilst we controlled for sleep stage effects by only examining noise presentations within stage 2 sleep, this does not rule out time-dependent sensory processing changes not captured by traditional sleep scoring. Further studies would be useful to examine stage and potential habituation or sensory fatigue effects in
Figure 3. Cumulative incidence rate curves for FPWA response during N20 with the landmark point at 5 seconds (LM5) for all FPWA responses divided in half by the median of their occurrence time across the night. A) shows responses occurring from the first noise onset up until the median and B) shows responses occurring from the median onwards until the last noise onset of the night. Hazard ratios (HR) evaluated with respect to the control are only shown for where there were significant effects. Shaded areas indicate 95% CI.

more detail.

The absence of any differences in FPWA response magnitude with different SPLs and duration is consistent with a remarkably sensitive all-or-none cardiovascular reflex response to small noise disturbances. The overall drop in FPWA was approx. 20% from the baseline, consistent with previous observations [4]. This response is relatively small in comparison to a response proceeding an awakening or a response to a loud tone (>80 dB(A)), which can cause up to a 60% reduction in FPWA magnitude [4]. Thus, although we found no difference in response magnitude between noise types (results not shown) the strength of peripheral vasoconstriction responses does may only be important when stimulus intensity is sufficiently high (>48 dB(A)). Given these observations, the effects of other noise features on FPWA response magnitude in the higher range of sound pressure levels relevant to environmental noise exposures also warrants further investigation. The physiological and clinical significance of frequent cardiovascular activation responses is yet to be determined and clearly warrants further research.

REFERENCES
Figure 4. Group averaged FPWA responses for A) N_{20} and B) N_{180} with 20 seconds pre-response baseline level during stage 2 sleep. Shaded areas indicate 95% CI.


