Mechanical Noise Improves the Vibration Perception Threshold of the Foot in People With Diabetic Neuropathy

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Abstract

Background: Mechanical noise may improve somatosensation at the dorsal side of the foot, but the effect at the plantar side of the foot, the side most at risk for foot ulceration, is unknown. Moreover, techniques used in research so far have several problems that limit applicability in daily practice. Piezoelectric actuators may provide mechanical noise with better clinical applicability. We assessed the effects of piezoelectric actuators generating mechanical noise on the vibration perception threshold (VPT) at the plantar side of the foot in people with diabetic neuropathy.

Methods: Double-blind within-subjects design in a controlled laboratory setting including participants with diabetic neuropathy (N = 40; 18 male; mean age 69.6 years; mean duration of diabetes 14.1 years; mean BMI 30.5). VPT was measured at three plantar foot locations with and without mechanical noise applied via piezoelectric actuators.

Results: Mechanical noise improved VPT at metatarsophalangeal joint (MTP) 1 (left 39.3V vs 43.5V; right 39.0 vs 42.6 V), MTP5 (left 37.5V vs 41.7V; right 34.5V vs 40.8V) and the heel (left 40.0V vs 44.0V; right 39.3V vs 41.0V), all P < .001.

Conclusions: Mechanical noise improves VPT at the plantar side of the foot in people with diabetic neuropathy. This is an important step for further development of insoles using mechanical noise that may have the potential to improve VPT and decrease the risk of foot ulceration.

Keywords
diabetic neuropathy, foot ulcer, mechanical noise, random vibration, vibrating insoles, vibration perception threshold

Diabetic neuropathy is one of the most common complications of diabetes mellitus, affecting up to 50% of the people with diabetes.1 Diabetic neuropathy causes reduced somatosensation, which is the greatest risk factor for diabetic foot ulceration.2 The vibration perception threshold (VPT), measured at the plantar side of the foot, is an effective indicator for identifying patients with diabetes at increased risk of foot ulceration. A recent systematic review showed that a VPT >25V was the greatest risk factor for recurrent foot ulceration.3 Patients with a VPT higher than 25V have a seven- to twelvefold increased risk of foot ulceration in comparison with patients with a VPT lower than 15V.3,5 For each 1-unit increase in VPT, the risk of first foot ulceration increases with 5.6%.6 Improving the VPT of people with diabetic neuropathy may be of great value for the prevention of foot (re)ulceration.

Although there is presently no widely recognized curative treatment for diabetic neuropathy, previous research has indicated somatosensation may be improved with the use of external stimuli. One option is the application of mechanical noise to the feet, administered as random vibrations from specific elements.7,9 Mechanical noise induces stochastic resonance, to increase previously unfelt subthreshold stimuli into superthreshold stimuli that do produce action potentials.8,10,11 Mechanical noise has been used in previous studies to improve standing balance,12-16 gait,17 movement sensation,18

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and tactile sensation. Two pilot studies have indicated that mechanical noise may improve VPT in people with diabetes when mechanical noise is applied at the plantar side, while the VPT is measured at the dorsal side. However, it is not clear if VPT at the dorsal side is predictive of diabetic foot ulceration. Both studies did not report outcomes on plantar VPT. A further limitation is that they included only a small group of patients (N = 20), of which Khaodhia expressed only patients with low VPT scores who are unlikely to ulcerate. It is therefore not clear if these positive early findings apply in larger groups of patients and, most important, to VPT at the plantar side of the foot, the site where VPT is predictive of foot ulceration.

Another limitation of previous studies was the equipment used. Mechanical noise was applied using equipment that is unsuitable for daily life due to several disadvantages such as vibrating elements that generate heat during usage or need heavy battery to function. This might explain the lack of interest from industry in creating ulcer prevention insoles based on mechanical noise. Other options to apply mechanical noise are available, without the limitations of the equipment used in previous studies, such as cheap and small piezoelectric actuators. The effect of mechanical noise generated by these piezoelectric actuators on VPT has not been determined yet. If such equipment shows an improvement in VPT of people with diabetic neuropathy, there is potential for the further development of foot ulcer prevention insoles that can actually be used in daily life. The aim of this study was to determine the effects of mechanical noise generated by piezoelectric actuators on VPT at the plantar side of the foot in people with diabetic neuropathy.

**Methods**

**Participants**

Forty participants with diabetes and peripheral neuropathy were included in this study with a double-blind cross-over within-subjects design in a controlled laboratory setting. To detect a difference of 5 volts in a population with an expected mean (standard deviation) VPT of 40 (11) volts, with 80% power and alpha 0.05, a minimum of 38 participants were needed. Exclusion criteria were severe visual problems that could not be solved by wearing glasses or lenses, current foot ulcer(s), a history of two or more ulcers on the same location, amputation of more than two lesser toes or the hallux at one foot, and problems with the somatosensory or motor system affecting balance or plantar sensation not related to diabetes mellitus. Participants were recruited by podiatrists at the multidisciplinary diabetic foot outpatient clinic of Ziekenhuisgroep Twente (Hospital Group Twente), Almelo and Hengelo, the Netherlands. Successive patients with diabetes and peripheral neuropathy attending the outpatient clinic were subsequently asked to participate until 40 participants were included. In all, 23 participants refused a screening and one person was excluded due to balance problems. All participants gave written informed consent prior to the start of the study. The study protocol was approved by the medical ethics committee of the University Medical Center Groningen, registration number NL48517.042.14. All study measurements were consistent with the principles of the Declaration of Helsinki.

**Clinical Examination**

Participation started with a clinical examination, including medical history evaluation (age, sex, type and duration of diabetes, weight, height, BMI and history of ulceration) and screening for diabetic neuropathy. Diabetic neuropathy was assessed using the Michigan Neuropathy Screening Instrument (MNSI). The MNSI includes two separate assessments that consist of a 15-item questionnaire (MNSI-A) and a lower extremity examination (MNSI-B). Participants who scored abnormal on at least one of the two separate assessments were included in the study. In addition, VPT was measured at three locations of the plantar side of each foot (first metatarsophalangeal joint [MTP1], fifth metatarsophalangeal joint [MTP5], and the heel), using a biothesiometer (Biomedical Instruments, Newbury, OH, USA). The stimulation level of the biothesiometer was increased and decreased until the participant audibly indicated that they did feel and did not feel the stimulation, respectively; the average of these two recordings was the outcome of one measurement. VPT (in volts) was measured three times at each location and averaged.

**Experimental Setup**

The experimental setup comprised an actuator, a battery, a transformer, a piezo driver, and a mobile phone (specifications in the appendix). The actuator was a 0.2 mm thick piezoelectrode with a surface of 17.55 cm² (4.5 x 3.9 cm), weighing 5.7 grams (Face International Corporation, THUNDER TH-6R, Norfolk, Virginia, USA). The actuator was adapted to allow for VPT measurements by a 10 mm circular hole in the middle. The output from the battery was converted by a transformer and stepped-up between 50V and 100V by a piezo driver. The mechanical noise signal (white noise low-pass filtered at 100 Hz) was generated using the white noise function in Audacity (Version 2.0.4, http://wiki.audacityteam.org/wiki/Audacity_Wiki_Home_Page) and transmitted via Bluetooth. The setup was designed to resemble an actuator that can be included in an ulcer prevention insole.

**Measurements**

Participants lay in a prone position with the adapted actuator directly placed against the foot, placing was ensured by a bandage shoe with holes in the sole of it (Figure 1). The bandage shoe would be put on the foot of patients for measurements, and the biothesiometer placed exactly in the hole of...
the actuator for VPT assessment. First, the sensation threshold for the actuator (ie, the minimum level of mechanical noise that the participant was aware of) was determined for each location separately. The output of the actuator was slowly increased until the participant indicated they did feel the noise and subsequently decreased from maximum output until the participant indicated they did not feel the noise anymore; the maximum output was the average of these two measurements. The stimulation level of the adapted actuator was set at 90% of this averaged threshold, to ensure the mechanical noise applied was subthreshold. If the maximum stimulation level was not felt, that level was used. VPT was measured three times at each location (MTP1, MTP5, and the heel) during two conditions (mechanical noise on or off). For each participant, the order of measurement conditions was determined by generating a random number (at http://www.random.org), and following the sequence of conditions as marked by the generated number in a list with all possible sequences. Both the participant and investigator were blinded to the stimulation condition. The assistant-investigator applied the conditions in the determined sequence, while the investigator remained blinded and measured VPT. The average voltage of these measurements per location and per condition was calculated and used for further analyses.

**Statistical Analysis**

All outcomes were continuous data. Data were not normally distributed, therefore nonparametric tests were used. To investigate differences in baseline VPT between the left and right foot a Mann-Whitney $U$ test was performed. A Friedman test was conducted to investigate differences between locations within one foot. To determine the effect of mechanical noise, differences in VPT at each location during both conditions (mechanical noise on or off) were analyzed using a Wilcoxon signed rank test. Effect sizes are based on the Wilcoxon signed rank test score ($Z$) and calculated with the formula $r=Z/\sqrt{N}$. Subsequently, a Kruskal-Wallis test was conducted to investigate differences in the effect of the vibrating insoles between locations within one foot. Statistical analyses were performed using SPSS for windows (IBM SPSS Statistics version 22, Armonk, NY, USA). All tests were performed with alpha .05.

**Results**

A total of 40 participants were included in the study (Table 1). All participants were already diagnosed with diabetic peripheral neuropathy by the medical specialist in the diabetic foot team, which was confirmed by the MNSI scores during clinical examination at the start of the study. VPT at the six locations, measured without mechanical noise, ranged from 40.8 to 44.0 volts (Table 2); no significant differences were found between the same locations of the left and right foot ($P$ values range .42-.60), and within the left and right foot ($P$ values range .31-.82). The sensation threshold for the actuator was reached in 2 patients. For those patients, the stimulation level of the actuator was set at 90%; for the remaining patients this was kept at the maximum stimulation level. Mechanical noise applied to the plantar side of the foot resulted in a statistically significant decrease (ie, a clinical improvement) of VPT at all locations, with a median of 3 volts (Table 2). VPT at the six locations when measured with mechanical noise ranged from 34.5 to 40 volts (Table 2); no significant differences in improvement were found between the same locations of the left and right foot and within the left and right foot ($P$ values range .16-.95).

**Discussion**

Mechanical noise generated by piezoelectric actuators decreases VPT of the plantar side of the foot in people with
diabetic neuropathy, in the setup in this study this reduction was a median of 3 volts. This decrease in VPT was consistent for the left and right foot and for different locations at the plantar side of both feet. With an increase in risk for foot ulceration of 5.6% for each 1 Volt increase in VPT,6 these findings provide a basis for further development of foot ulcer prevention insoles based on the application of mechanical noise.

With the increasing burden of diabetic foot ulcers, prevention is of paramount importance.27-29 Various strategies have been described, among others based on integration of preventative care, improvement of offloading and detection of inflammation.27-29 However, none of these strategies targets the greatest risk factor for foot ulceration of all, which is the loss of protective sensation.2,27-29 This is the first study to show significant improvement using an intervention targeting this loss of protective sensation at the plantar side of the foot with equipment that can be used for application in daily life. The piezoelectric actuators used in this study are cheap, small, thin and do not require a heavy battery to function. They can be easily integrated at individually determined locations in foot ulcer prevention insoles for people with diabetic neuropathy. Such design may also pose risks such as increase in peak plantar pressure as a result of the actuator, however, it is expected that these can be dealt with in subsequent design phases.

This study was based on previous pilot studies showing similar improvements in VPT after the application of mechanical noise, however, with VPT measured on the dorsal side of the foot and in small groups of patients only.20,21 In contrast to the previous studies, not all participants in the current study were able to feel the maximum level of mechanical noise. Hence, it is unknown if the mechanical noise was set at 90% in these patients, which was shown to be the most effective subthreshold level.7,9,20,21 It may be expected that improvements in VPT could be larger than currently found, especially when a piezoelectrode setup capable of generating a higher level of mechanical noise would be used. Such equipment was not available at the start of the study, but is now. Another difference was the creation of a hole in the piezoelectric actuators, which was imperative for the VPT measurements. The total surface was kept similar to a piezoelectric actuator without a hole, and if anything, we expect this difference created a reduced effectiveness from the mechanical noise in the current study.

It is unknown if effects from subthreshold stimulation may persist, even when stimulation stops. Our hypothesis is that mechanical noise increases previously unfelt subthreshold stimuli into stimuli that do produce action potentials. As such, these action potentials may create changes in both the central and peripheral neural systems. Encouraging in this sense are findings from other studies using mechanical noise stimulation that could be felt by patients (ie, suprathreshold, in contrast to the subthreshold used in our study), where it was found these benefits persisted after stimulation.30,31 Future studies are required to assess the poststimulation effects of mechanical noise on VPT in patients with diabetic neuropathy, especially when the stimulation is subthreshold. A limitation of VPT measurements is that participants need to lie in a prone, none weight-bearing, position. It is not possible to measure VPT during standing or dynamic activities like walking, when the skin is more stressed due to pressure. It is unknown if mechanical noise also reduces VPT during such activities. However, the VPT thresholds for classifying neuropathy and predicting foot ulceration risk are also determined for a nonloaded position.2,6 A limitation of the piezoelectric actuator is that it has not been investigated in prolonged application scenarios, and it is therefore not yet known how the actuator will behave when used for days or weeks. This needs to be investigated as a next step in research, as part of future insole developments.

On a clinical level, this study confirms the potential for further development of foot ulcer prevention insoles using mechanical noise generated by piezoelectric actuators. Such prevention insoles may have the potential to improve VPT with a minimum of 3 volts. Such an improvement can be expected to reduce ulcer risk,6 however, the preventative effects of VPT reductions need to be investigated further in future research.

When ulcer prevention insoles are designed, the piezoelectric actuators could be integrated with other sensors, measuring for example temperature or pressure.29,32 That

### Table 2. VPT of Three Plantar Locations During Both Conditions.

| Location     | VPT (actuator off) | VPT (actuator on) | Differencea | P value | r  |
|--------------|--------------------|-------------------|-------------|---------|----|
| L- MTP1      | 43.5 [36.8-47.5]   | 39.3 [31.2-44.3]  | 3.0 [1.3-4.3] | <.001 | .12 | -0.43 |
| L- MTP5      | 41.7 [33.8-47.0]   | 37.5 [30.0-42.4]  | 2.7 [1.3-5.4] | <.001 | .19 | -0.57 |
| L- Heel      | 44.0 [32.0-47.1]   | 40.0 [32.5-44.8]  | 2.0 [1.0-3.0] | <.001 | .08 | -0.44 |
| R- MTP1      | 42.6 [32.7-47.0]   | 39.0 [30.6-46.0]  | 2.5 [1.4-4.9] | <.001 | .15 | -0.48 |
| R- MTP5      | 40.8 [29.0-45.0]   | 34.5 [28.7-40.0]  | 4.0 [1.9-7.1] | <.001 | .22 | -0.53 |
| R- Heel      | 41.0 [30.6-47.0]   | 39.3 [26.3-45.6]  | 2.3 [1.0-6.2] | <.001 | .17 | -0.51 |

Values are median [IQR]. L, left foot; R, right foot.

aDifference is the median value of all differences between the conditions at the plantar location.
b r is the rank correlation coefficient.
may create foot ulcer prevention insoles based on early warning signals, while at the same time reversing the loss of protective sensation. Adherence will be an important factor in potential clinical efficacy of such insoles. A suggested reason for nonadherence is that patients with diabetic neuropathy do not feel discomfort and therefore do not realize that they are at risk of foot ulcers. From this point of view, it may be expected that insoles that will generate peripheral sensations might have higher adherence compared to insoles that do not result in patients feeling anything of the potential benefits of the device. Clinical testing to prove their (long-term) effectiveness would still be needed, but such insoles could provide unique possibilities of reducing the burden of diabetic foot disease.

Conclusion

Mechanical noise improves the vibration perception threshold at the plantar side of the foot in patients with diabetic neuropathy. Mechanical noise, generated by piezoelectric actuators, may be helpful in reversing the loss of protective sensation and preventing foot ulceration in patients with diabetic neuropathy. This is an important step for further development of insoles using mechanical noise that may have the potential to improve VPT and decrease the risk of foot ulceration.

Appendix

Specifications of the Components in the Experimental Setup

| Component | Specifications |
|-----------|----------------|
| Battery (to provide power for the actuator) | • BBM Batteries  
• Custom lithium-ion battery  
• Provides 3.7 V/600 mAh  
• Dimensions: 50 mm × 27 mm × 5.0 mm |
| Transformer (to convert the output signal from the battery) | • Chipworld, nonisolated, DC/DC  
step-up voltage regulator  
• Converts 3.7V to 5.0V  
• Input voltage: 2.5V-6V  
• Output voltage: 4V-12V  
• Output current: 1000 mA  
• Dimensions: 28 × 19 × 3 mm |
| Piezodriver (to change the input voltage of the actuator) | • Texas Instruments, Piezo Haptic Driver  
• With integrated boost converter, model number DRV8662  
• 5V output stepped up to between 50 and 100V |
| Bluetooth (to transmit the mechanical noise signal from the mobile phone to the actuator) | • Parts Express, Bluetooth module BT-1  
• Class 2 range of up to 15 meters  
• 16-bit A2DP support  
• Bluetooth v1.2 compliant |

Abbreviations

MNSI, Michigan Neuropathy Screening Instrument; MTP, metatarsophalangeal joint; MTP1, first metatarsophalangeal joint; MTP5, fifth metatarsophalangeal joint; VPT, vibration perception threshold.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Face International Corporation, Virginia, USA, provided the equipment for this study free of charge, without any involvement in measurements and interpretation of data.

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