International Journal of Psychophysiology xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Reliability of measurements for sub-painful and painful perception on artificial electrical stimulations

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ARTICLE INFO

Keywords:
Pain
Tactile sensation
Numerical Rating Scale
Reliability
Electrical stimulation

ABSTRACT

Artificial electrical stimulation is a common type of stimulus to induce sub-painful and painful sensation in clinical or neuroscience experiments. The Numerical Rating Scale (NRS) is often used to evaluate subjective perception due to external stimulations. Yet the relationship between the intensity levels of electrical stimulations and self-perception has seldom been examined. The aim of the study was to obtain evidence on the reliability and accuracy of sub-painful and painful perceptions of healthy participants using the NRS under different levels of electrical stimulus. A total of 72 pain-free healthy volunteers (female = 44) were recruited. In the first experiment, each participant was given different levels of a non-nociceptive or nociceptive electrical stimulus and then asked to give a perception rating based on an 11-point NRS. In the second experiment, each participant was asked to memorize 5 levels of sub-nociceptive or nociceptive stimuli and to recognize the level of stimulus given each time. For the NRS rating task, intraclass coefficients (ICCs) reached satisfactory level for sub-nociceptive ($0.85 < ICC < 0.93$) and nociceptive stimulation ($0.90 < ICC < 0.96$). The ICCs were the highest for the weakest sub-nociceptive and nociceptive stimuli. For the stimulus recognition task, accuracy was also found to be highest for the weakest sub-nociceptive stimulus ($\kappa = 0.67$) and lowest for the strongest nociceptive stimulus ($\kappa = 0.34$). The results suggest that, with adequate training, NRS can be a reliable measurement tool for both sub-painful and painful rating due to electrical stimulation.

1. Introduction

Electrical stimulation, such as transcutaneous electrical nerve stimulation (TENS), acupressure-TENS, is one of the most applied physical modalities in the rehabilitation field for pain control in patients with pain conditions (Rodríguez-Fernández et al., 2011; Seo et al., 2013), those with motor paresis, such as stroke (Au-Yeung and Hui-Chan, 2014; Rosewilliam et al., 2012) and spinal cord injury (Carty et al., 2012). The bottom-up nociceptive signals travel from the nociceptors to the somatosensory cortex via secondary and tertiary neurons. The signals are then perceived by the associated cortex leading to a subjective painful experience. Thus, the variability of top-down interpretation of a bottom-up signal with the same intensity may vary across different individuals. In order to quantify perceptions of pain, different sensory scales have been established and validated to measure perceptions of both acute and chronic pain, such as the visual analogue scale (VAS), the verbal rating scale (VRS) and the numeric rating scale (NRS) (Hjermstad et al., 2011; Williamson and Hoggart, 2005). The NRS is regarded as having better sensitivity to changes and requires less training time when compared to VAS, which is more cognitively demanding (Hjermstad et al., 2011; Williamson and Hoggart, 2005). Yet how the NRS scale can be applied to sub-painful (tactile) or painful perception induced by sub-nociceptive or nociceptive electrical stimulation has not been well examined.

Repetitive stimulation at the same location of skin could affect the stability of somatosensory perception due to the accumulated signals at the second-order sensory neurons and the higher cortical levels (Mouraux et al., 2011). This is a phenomenon called temporal summation of stimulation, and it can lower the stability of bottom-up signal and top-down perception of the upcoming sensation, compromising the reliability of the sensory scale, such as NRS (Granot et al., 2006; Graven-Nielsen et al., 2015). Increasing temporal summation with higher stimulation intensity could lead to sensitization of neurons due to a lowering of the membrane threshold (Granot et al., 2006). This leads to stronger intensity of bottom-up signals from nociceptors to the higher cortical regions and stronger salient signals at the top-down level (Price et al., 2002; Staud et al., 2003). Previous studies used different means to induce perceptions of pain, such as contact heat (Jutzeler et al., 2016), mechanical stimuli (Bulls et al., 2017; Manafi-Khanian et al., 2017) and electrical stimuli (Dowman, 2007a; De Pascalis et al.,

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https://doi.org/10.1016/j.ijpsycho.2017.11.012
Received 28 June 2017; Received in revised form 15 November 2017; Accepted 17 November 2017

2008). It has been assumed that the relationships between the stimulation intensity and the perception of the related sensation, either sub-painful or painful, would be more or less in linear relationship. Those studies, in which painful sensation was induced by different levels of electrical stimulations, did not examine whether painful perception is stable across different levels of electrical stimulations (Herr et al., 2004; Kenny et al., 2006). It is not known whether different levels of electrical stimulation, with various levels of temporal summation, would influence the subjective rating in pain-free individuals. The results obtained from this reliability study could provide insights into the extent of temporal summation due to different levels of electrical intensity that would affect the top-down perceptual process of the painful and sub-painful sensations. This would also shed light on whether separate rating scales would be used for artificial or clinical pain.

This first aim of the study thus was to investigate the test-retest reliability of the commonly used sensory rating scale, NRS, for sub-painful and painful perception of pain-free participants for different levels of sub-nociceptive and nociceptive electrical stimulation at levels. The stimuli were the different levels of electrical intensity produced by an electrical stimulator, while the ratings represented the painful intensity perceived by the participants. The second aim was to examine the effect of repetitive sub-nociceptive and nociceptive electrical stimulations of different levels of intensity on the accuracy of discriminating sub-painful and painful sensations. For the first aim, it was hypothesized that the reliability of NRS rating for higher intensity of sub-nociceptive and nociceptive stimuli would be lower compared to that of the lower intensity of counterparts. This could be due to the fact that the stronger intensity stimulations would have a longer offset time to lead to more conspicuous effect of temporal summation. For the second aim, it is hypothesized that conspicuous temporal summation could impede the accuracy of stronger nociceptive stimulations. On the other hand, the accuracy could also be lowered for weaker sub-nociceptive stimulation due to the lower saliency of the sub-nociceptive stimuli requiring more attention The knowledge obtained in healthy individuals could shed light on appropriate ways to obtain reliable sensory ratings and sensory discrimination data when using electrical stimulations repetitively with patients in clinical contexts or participants in experiments. It also serves as a foundation for understanding pain ratings based on artificial sub-nociceptive and nociceptive stimuli from patients with chronic pain.

2. Methods

2.1. Study design

In order to obtain the reliability of the painful and sub-painful NRS rating, each volunteering participant repeatedly received nociceptive and sub-nociceptive electrical stimulations with different (five) levels of intensity. He or she was then required to give an NRS painful or sub-painful rating for each electrical stimulation. The same design was also applied to obtain the accuracy of pain rating. After each level of nociceptive and sub-nociceptive electrical stimulations, each participant was asked to determine which level of n nociceptive or sub-nociceptive electrical stimulation was felt.

2.2. Participants

A total of 72 participants were recruited to the study via convenience sampling. Forty-four (61.11%) were female, and all but two were right-handed. The mean age was 39.91 years (standard deviation (SD) = 15.96 years). They were free of neurological conditions that could affect their somatosensory functions. The purpose of the study was explained to each recruited participant and he or she was informed that all personal information and data obtained from the study were to be kept strictly confidential. Ethics approval was obtained from the Ethics Committee of the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, and the study design complied with the Declaration of Helsinki.

2.3. Electrical stimuli

The electrical stimulations were generated by the *S88K Dual Output Square Pulse Stimulator*[1] (Grass Technologies, Grass-telefactor, West Warwick, RI). The apparatus is a dual-channel, general purpose stimulator for nerve and muscle stimulation. The stimulator emits electrical impulses in varied intensity and patterns which can elicit responses from a single nerve cell to an entire muscle. The two output channels can be operated in an independent or synchronized manner to meet requirements in complex paradigms. The equipment consists of four-parameter control of two different outputs. In addition to single, repetitive, twin pulses, pairs of unlike pulse, train of pulses and mid- and post-train pulses, continuous or trains of pulses are available at one output with continuous and discontinuous operation at the other output. The Constant Current Unit connected in series with the pulse stimulator controls a constant current emission. The meter panel gives a reading in milliamperes (mA) (Dowman, 2007a, 2007b). For this study, one electrical output of a stimulator[1] was used in the procedure. The positive and negative Ag/AgCl electrodes (8 mm in diameter) were filled with electro-conductive hypocollagen gel to minimize the skin impedance. The positive electrode was securely positioned at the volar side of the index finger tip of the dominant hand (C6 dermatome) of the participant. Current specification was referenced to specifications reported by Katayama et al.'s study (Katayama et al., 1985). A 25-pulse train pulse with train duration of 50 ms was set (pulse duration: 0.5 ms; frequency: 500 Hz). The outputs emitted from the stimulator are non-isolated constant voltage positive pulses.

2.4. Sensory threshold determination

Since each participant was given individual-specific levels of sub-nociceptive and nociceptive electrical stimulations, each of them was asked to go through a standardized sensory threshold procedure referenced in the methods described by De Pascalis et al. (2008). The minimal detectable threshold, which is defined as the minimum level of electrical intensity that could be felt by a participant, was first obtained by ascending and descending procedures. Each participant was given a series of single pulse trains. The intensity of the electrical stimulus started from 0.0 mA and increased with increments of 1.0 mA until the participant detected a minimal detectible sensation which was reported to the investigator (called first minimal detectible sensation). The procedure was then repeated in a descending manner. It started from 1.0 mA above the first minimal detectible sensation and decreasing with steps of 1.0 mA. The second threshold for minimal detectible sensation was the weakest electrical stimulation which could be perceived by the participant. The two thresholds obtained from the ascending and descending procedures were then averaged to determine the participant's average sub-painful threshold. Subsequently, the intensity of the electrical stimulus for producing sub-nociceptive sensation was increased with steps of 1.0 mA. Each time a sub-nociceptive stimulus was presented to the participant, the participant was required to perceive the sub-nociceptive sensation and rate its intensity based on the 11-point Numerical Rating Scale (NRS) (Williamson and Hoggart, 2005). The maximum sub-nociceptive level was 1 mA below the painful threshold, which was determined in the next step.

The next step was to determine the painful threshold of the participant. The minimal painful threshold is defined as the minimum level of electrical intensity at which the participant starts to perceive a pin-prick sensation. The minimal painful threshold was determined by

[1] Supplier: Natus Neurology Incorporated - Grass Products, 200 Metro Center Blvd, Unit 8, Warwick, RI 02886, U.S.A.