

Allodynography: Reliability of a New Procedure for Objective Clinical Examination of Static Mechanical Allodynia

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Abstract

Objective. There is a need for reliable and valid clinical assessment tools for quantifying allodynia in neuropathic pain. Allodynography has been proposed as a useful standardized procedure for clinical assessment of mechanical allodynia. This study (www.clinicaltrials.gov NCT02070367) undertook preliminary investigation of the measurement properties of allodynography, a new standardized clinical examination procedure for mapping the area of cutaneous allodynia. **Methods.** Persons with pain in one upper extremity after complex regional pain syndrome, a peripheral nerve injury, or who had recently experienced a hand fracture were recruited for assessment of static mechanical allodynia (based on perception of a 15g force stimulus delivered by Semmes-Weinstein monofilament #5.18 as painful) by two raters at baseline; the assessment was repeated one week later. **Results.** Single-measures estimates suggested inter-rater reliability for allodynography was excellent at an intraclass correlation coefficient (ICC) of 0.97 (N = 12); test–retest reliability was also excellent at ICC = 0.89 (N = 10) for allodynography ($P < 0.001$ for both). Confidence intervals' lower bounds confirm inter-rater reliability as excellent (0.90) but were less definitive for test–retest (0.59). **Conclusions.** This preliminary study supports the inter-rater and test–retest reliability of allodynography. Studies on larger samples in multiple contexts and reporting other measurement properties are warranted.

Key Words: Neuropathic Pain; Allodynia; Mapping; Evaluation; Reliability; Somatosensory Rehabilitation

Introduction

Allodynia is commonly referred to as hypersensitivity but is more precisely defined as “pain due to a stimulus which does not normally provoke pain” [1]. It is frequently associated with neuropathic pain and/or the resultant peripheral and central sensitization [2–4]. Allodynia adds to the clinical challenge of effective management for a spectrum of conditions, including burns, peripheral nerve and plexus injuries, post-herpetic neuralgia, and complex regional pain syndrome (CRPS)

[5–8]. For research purposes, mechanical allodynia (MA) is often measured dynamically by stroking the tender area of the skin with a brush; however, both the tools and techniques used are difficult to standardize in the clinical setting because of variability in application force, distance, and speed [9]. Furthermore, it is generally used for diagnostic purposes, and the responsiveness to change remains to be established [10]. A need exists for clinically useful but accurate evaluations for the identification and quantification of allodynia and monitoring of changing allodynia over time.

The Somatosensory Rehabilitation Method (SRM) has been proposed as a nonpharmacological treatment for neuropathic pain, including allodynia [11]. It uses the principles of somatosensory re-education through targeted comfortable sensory stimulation (e.g., mindful perception of the different textures and temperatures of materials, and the dynamics and intensity of the application of the stimulus) based on contemporary understandings of the function and dysfunction of the somatosensory system [12]. To tailor the intervention, it relies on first precisely defining the topographical territory demonstrating static mechanical allodynia (SMA) using a standardized procedure of testing with a calibrated monofilament, known as allodyngography [12, 13]. This strategic consideration of the peripheral nerve branches residing in the painful territory is used to form a neuroanatomic hypothesis [14] to inform the application of comfortable tactile or vibratory “counterstimulation” to a distant zone of a neuroanatomically related cutaneous nerve branch [12].

For an objective clinical examination procedure to have utility as a diagnostic indicator, it requires three psychometric properties: validity, reliability, and responsiveness to change [15]. The validity of allodyngography to diagnose A β axonal lesions has already received some preliminary examination [13, 16]. From these findings, it can be postulated that patients report symptoms of neuropathic pain because of lesions of the A β fibers of a cutaneous nerve branch [17, 18]. However, the reliability and responsiveness to change of allodyngography have not been formally evaluated in the literature.

Purpose of the Study

The purpose of this study was to evaluate persons with allodynia to estimate the reliability of a new clinical examination to map the allodynic territory. Therefore, our primary research question was as follows: Is allodyngography a reliable assessment tool for describing the allodynic territory? The secondary question as follows: What is the inter-rater agreement for the formation of a clinical neuroanatomic hypothesis?

Methods

Design and Setting

This study was conducted at the outpatient hand rehabilitation clinic at a regional trauma center and teaching hospital in Hamilton, Ontario, as part of a prospective pilot study examining the somatosensory rehabilitation method (the SARA study: www.clinicaltrials.gov NCT02070367). Data were collected between September 2014 and January 2017. Baseline evaluations were conducted by the first author (an occupational therapist and Certified Somatosensory Therapist for Pain [CSTP]) [19] and one of two other independent evaluators (one physiotherapist, one occupational therapist) who had basic

training (about six hours) in the allodyngography procedure. All participants gave written informed consent, and the study was approved by the local ethics committee (Hamilton Integrated Research Ethics Board).

Subjects

Participants were recruited from local hand therapy facilities and pain programs. Inclusion criteria were 1) a diagnosis of CRPS meeting the Budapest criteria [20] in a single upper limb, 2) a unilateral peripheral nerve injury (PNI) in the upper limb verified intra-operatively, or 3) a recent hand fracture (clinically stable but still requiring rehabilitation). Inclusion criteria were confirmed by medical record to ensure eligibility. Exclusion criteria were the presence of open wounds, other forms of nerve compression or dysfunction (i.e., radiculopathy, diabetic peripheral neuropathy) or inability to complete the study questionnaires in English. The screening process for allodynia is described below. The target sample size for the explorations of reliability was set at N=35 using Donner’s estimates to achieve substantial reliability at 80% power over two test occasions [21].

Evaluations

All participants were screened for SMA using standardized procedures: 1) they were asked to point (without touching) to indicate their most painful area, 2) participants rated (using a four-point always/often/sometimes/never scale) if the pain became worse with movement or touch and/or if it occurred spontaneously, and 3) a single stimulus of two seconds’ duration with a 15g monofilament applied (after demonstration on their nonpainful limb), and the person was asked if it produced pain (yes or no). If they answered yes, then the examiner proceeded with the allodyngography procedure.

Allodyngography

Allodyngography is a standardized clinical examination procedure for mapping the borders of the cutaneous territory where application of a 15g force stimulus (Semmes-Weinstein monofilament #5.18) on the skin generates a painful response (defined as 30 mm on a 100-mm visual analog scale [VAS] or pain at rest + 10 mm on a 100-mm VAS) [13]. With the client in a comfortable position, with the limb supported and the painful area of skin exposed, the stimulus was applied for two seconds, starting proximally to the pain. Subsequent stimuli were applied in 1-cm increments proceeding distally down the central axis of the limb, with an interstimulus interval of 10 seconds. The client was asked to say “STOP” when they experienced pain (as defined above = 30 mm on a VAS). After “STOP” was indicated, the tester moved back 1 cm, and then advanced in 1-mm increments until “STOP” was indicated again: this point was recorded with a dot of water-soluble ink. This procedure was repeated, starting distally on the same limb axis, and



Figure 1. Allodyngraphy testing. Note the limb is stabilized on a cushion, while the filament is carefully applied with sufficient pressure until slight bowing is observed. This photograph illustrates the second step of evaluation, working from proximal to distal down the central limb axis on the volar surface towards the area of allodynia (in distal forearm for this participant).

moving proximally, until again the client indicated “STOP” (see Figure 1 for an illustrative photograph). A transverse axis roughly bisecting the painful area was similarly evaluated. The territory of the allodyngraphy was measured using anatomical landmarks (recording the distance from the landmark to the final “STOP” point on each axis) and recorded visually on graph paper (see Spicher et al. [12] for a detailed description of the procedure). For precision in our study, we asked the participant to identify when the qualities of the stimulus perception started to change. At that point, we would tap the monofilament on a water-based ink pad before subsequent application of every stimulus and switch to 1-mm increments, thus creating an accurate measurement point to record the “STOP” point when the subject indicated a painful response, without the need to reverse. Four “STOP” points were identified and measured with a flexible clear plastic ruler held approximately 2 cm above the skin. These were recorded visually on a standardized diagram (front and back of right and left hands) with the measurement indicators (Figure 2). To pragmatically account for the nonrectangular shape of the allodynic territory, we calculated the area of allodynia as length (most proximal and distal points identified) * width (most lateral points identified) * 0.66 (Figure 2).

The second step of allodyngraphy is the formation of a clinical neuroanatomic hypothesis proposing which cutaneous nerve branch might be implicated as the site of the painful nerve lesion [14, 18, 22]. This hypothesis is derived from the known innervation territory situated within the allodynia map that has been generated from the monofilament testing: Within the SRM, it is critical for subsequent development of the treatment plan. For the purposes of our study, a single allodyngraphy map was developed for

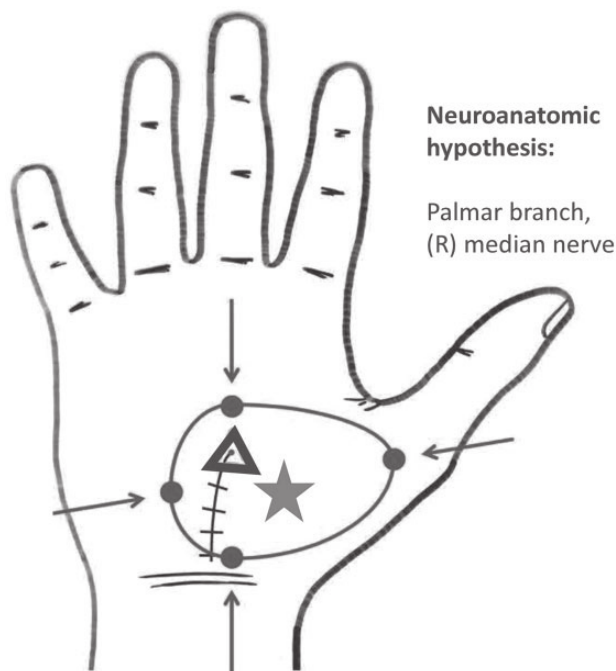


Figure 2. Sample allodynia map. a) Neuroanatomic hypothesis designates the cutaneous nerve branch related to the mapped territory. b) Arrows indicate the direction of testing, while the dot indicates where the subject indicated ‘STOP’. c) Triangle indicates invariant measurement reference point (an anatomical landmark). d) Star indicates the point where the rainbow pain scale rating was tested [12].

the territory identified by the participant as the most painful area. Raters were provided with the most recent version of a clinical atlas of the cutaneous nerve origins [22] to use as a reference when generating these hypotheses.

McGill Pain Questionnaire

The other established outcome measure used in the SRM is the McGill Pain Questionnaire (MPQ) [23]. The original English version of the MPQ is comprised of 78 pain descriptors: words are further arranged in 20 construct clusters (e.g., temporal, spatial, thermal) [24]. The person is instructed to first choose all words describing their current pain (yielding a total number of words/78). From these chosen words, the “best” word from each cluster is rated using a 0–5 scale with qualifiers (0 = absent, 1 = mild, 2 = discomforting, 3 = distressing, 4 = horrible, 5 = excruciating) to indicate the intensity of the pain quality at the present time. We then summed these ratings and converted to percent scores for ease of interpretation, yielding a total score of tMPQ/100, a sensory pain score of (sMPQ)/65, and an affective pain score of (aMPQ)/35, following the SRM recommendations [12].

Statistical Analysis

After data screening, demographics and clinical variables were described with means \pm SDs for continuous

Table 1. Participant demographics and baseline characteristics (N = 38)

Characteristic	Mean	SD	Range
Age	45.9	14.4	15–76
Duration of injury or pain, mo	17.9	38.5	1–168
Shoulder flexion (% of unaffected side)	88.8	20.3	0–100
Wrist extension, % of unaffected side	74.5	23.6	0–100
Forearm supination, % of unaffected side	84.8	13.3	38.9–100
Grip strength, kg	R = 24.4 L = 26.6	19.2 16.6	0–63.3 0–54.7
% of normal grip in affected hand	39.1	29.7	0–90.1
Total No. of words from MPQ	24.7	16.3	0–64
Total MPQ score (tMPQ/100)	38.3	26.4	0–93
Allodyngraphy (N = 16 persons, rater 1), area in cm ²	136.5	117.2	12.3–349.4
Characteristic	Frequency	Percentage	
Gender	M = 19 F = 19	M = 50 F = 50	
Diagnosis	CRPS = 20 PNI = 10 Fracture = 8	52.6 26.3 21.1	
Dominance	R = 32 L = 6	R = 84 L = 15.8	
Side of injury	R = 24 L = 14	R = 63.2 L = 36.8	
Patient-reported pain with movement or touch (N = 35)	None = 4 Sometimes = 7 Often = 7 Always = 17	None = 11.4 Sometimes = 20 Often = 20 Always = 48.6	
Patient-reported spontaneous pain (N = 35)	None = 7 Sometimes = 10 Often = 9 Always = 8	None = 20 Sometimes = 28.6 Often = 25.7 Always = 22.9	
Allodynia present (reports pain with 15g filament applied)	Yes = 17 No = 18 Declined = 3	Yes = 44.7 No = 47.4 Declined = 7.9	

CRPS = complex regional pain syndrome; PNI = peripheral nerve injury; tMPQ = McGill Pain Questionnaire total score.

variables and frequencies and percentages for categorical variables. A contingency table was generated to examine the proportion of persons from each diagnostic group who were identified as having allodynia, and the Fisher exact test was used to calculate the significance. To calculate inter-rater and test–retest reliability for allodyngraphy, intraclass correlation coefficients (ICCs) for individual measures were used. Agreement for clinical neuroanatomic hypothesis formation was estimated using Spearman’s *rho* (*r*) statistic; each nerve branch in the upper extremity was given a numerical “dummy” code. All analyses were performed with STATA 13, with statistical significance set at $P=0.05$ unless otherwise noted.

Results

Although 38 persons were recruited to this study, not all data sets are complete, as a result of some participants declining to complete portions of the evaluations; we have therefore reported the sample size separately for each analysis. Table 1 contains a description of

participant demographic and clinical characteristics. The frequency at which SMA was identified across diagnostic groups is documented in Table 2; the Fisher exact test was significant at 0.045.

For examining the inter-rater reliability of allodyngraphy, we had 12 cases with repeated measures at baseline representing those participants who 1) had allodynia according to our definition of pain with a static touch of 15g and therefore were eligible for mapping and 2) consented to the procedure with both raters. In those persons, we found an excellent intraclass correlation

Table 2. Frequency of positive screening results for static mechanical allodynia by diagnostic group (N = 35)

Diagnostic Group	No Allodynia	Allodynia	Total
CRPS	6	12	18
PNI	5	4	9
Fracture	7	1	8
Totals	18	17	35

CRPS = complex regional pain syndrome; PNI = peripheral nerve injury.
Fisher exact $P = 0.045$.

coefficient (ICC) of 0.97 (95% confidence interval [CI] = 0.90–0.99) for single measures and 0.99 (95% CI = 0.95–0.99) for average measures ($P < 0.001$ for both).

Test–retest reliability of allodyngraphy, based on ratings of the same persons ($N = 10$) by a single rater one week apart, was estimated at $ICC_{2,1} = 0.89$ (95% CI = 0.59–0.97, $P < 0.001$) for single measures and $ICC_{2,1} = 0.94$ (95% CI = 0.74–0.99) for average measures ($P < 0.001$).

The final rating of agreement we explored in this study was the clinical neuroanatomic hypothesis formed by each rater independently after completing the allodyngraphy. Inter-rater agreement across the 12 cases was excellent [25], at Spearman's $r = 0.91$ ($P < 0.001$).

Discussion

Reliability

This clinical measurement study of allodyngraphy has generated preliminary support for the reliability of this objective clinical examination procedure. Our single-measures estimate suggested that the reliability for allodyngraphy was excellent at $ICC = 0.97$ (95% CI = 0.90–0.99). However, Donner's estimates for the minimum number of subjects required to achieve 0.80 power for inter-rater reliability based on single ratings by two raters [21] suggest 12 subjects as adequate to demonstrate only slight reliability. Despite the potential underpowering, this estimate was statistically significant with a relatively small confidence interval. Our test–retest reliability estimates for allodyngraphy were from only 10 subjects. The decrease in sample size at follow-up is reflected in both the lower ICC estimate ($ICC = 0.89$) and larger confidence interval (95% CI = 0.59–0.97) when compared with the inter-rater reliability estimates. The difference illustrates greater variability between test occasions than between two raters on the same occasion. This suggests that there may be some instability of the map from day to day, posing a potential threat to responsiveness. In clinical application, this symptom variability underpins Spicher's recommendations for 1) frequency of re-evaluation (monthly) [12] and 2) repeated testing one week later after a negative allodyngraphy (that is, no territory of painful skin is identified related to stimulation with a 15g monofilament) before progressing somatosensory treatment from distant counterstimulation to decrease allodynia to somatosensory re-education for underlying hypoesthesia [19]. It is also important to note SMA was identified in all diagnostic groups, albeit at different rates (Fisher exact test $P = 0.045$). Further, the high level of agreement between raters for the resultant neuroanatomic hypothesis positing which specific cutaneous nerve branch was involved reinforces the reliability of the examination procedure. From a clinical standpoint, our identification of a person with mechanical allodynia postfracture may also have relevance; the

detailed diagnostic code for this individual revealed that they had had a fracture with percutaneous pinning. The allodynia seen may represent nerve irritation related to fracture management.

Allodyngraphy uses a standardized stimulus (15g #5.18 monofilament) and defines pain (the targeted perception) as 30 mm on a VAS or pain at rest + 10 mm on a VAS. This standard was derived from earlier attempts to categorize VAS scores, where 85% of persons reporting moderate pain also gave a VAS rating of at least 30 mm [26]. Although more recent work suggests a cut-point of 34 mm for mild pain [27], our experience is that the 30-mm standard is clinically useful and easily understood by the persons being tested. On the basis of a standardized stimulus combined with a rated perceptual response, allodyngraphy should be considered a form of psychophysical clinical examination [28].

Utility Considerations

A positive allodyngraphy, combined with the formation of clinical neuroanatomic hypothesis, meets the diagnostic standards for a probable diagnosis of neuropathic pain [14]. In the SRM, the ability to identify underlying somatosensory tactile hypoesthesia (termed a positive secondary aesthesiography) [13, 19] after reduction and total resolution of the mapped allodynia provides a form of criterion validation: the pathognomonic hypoesthesia of a nerve lesion is only unmasked by resolution of the allodynia [13, 16, 29]. The reliability of this standardized clinical examination procedure adds to previous validation work [13, 16] and creates a foundation for further explorations of validity, such as comparison with other forms of screening for neuropathic pain [30].

Allodyngraphy provides a clinical sign for static mechanical allodynia that cannot be quantified by standard electrophysiological testing [28, 31]. As the monofilament tests receptor field after receptor field as it moves down the limb axis, allodyngraphy is objectively signaling the presence of A β axonal lesions—not C-fiber lesions, as would be induced by hyperalgesia to pin prick [32]. Allodyngraphy makes use of inexpensive somatosensory evaluation equipment and is aligned with calls to increase the use of standardized evaluations for both neuropathic and chronic musculoskeletal pain [30, 33, 34]. Further, the results are useful to inform treatment planning by giving precise guidance regarding which areas should not be flooded with sensory stimuli to limit evocation of abnormal pain signaling, and where instead to focus on sensory retraining to address sensory loss on adjacent areas. In rehabilitation, such non-pharmacological interventions may include providing advice on activity modification, use of orthoses or adaptive equipment, and tailoring of exercise programs to minimize repetitive motions evoking pain [11, 19].

Allodyngraphy, the clinical examination procedure described here for mapping a territory of painful somatosensory abnormality [34], differs from other descriptions

in the literature. LaMotte et al. [29] described use of a von Frey-type nylon monofilament of 225 mN (22.9g) of force, applied in 5-mm increments along at least eight linear pathways radiating from the painful site, with a duration of 0.5 to one second, and a delay between stimuli of approximately three seconds. Stop points were marked on the skin with felt pen and then traced onto an acetate sheet for subsequent computerized analysis of the area [29]. Wallace et al. refined LaMotte's eight-pathway technique using a 12.9g monofilament advanced in 1-cm increments [35]. They recorded this static form of mechanical sensory testing in combination with brush-stroking to map dynamic allodynia and reported the results as an end point showing statistically significant change in several randomized controlled trials of neuropathic pain agents [35, 36]. They also used acetates and technology to generate the area calculations, but noted at times that the allodynic territory was larger than a single sheet of acetate, necessitating other forms of recording [35]. Walk et al. included mapping in their recommended clinical protocol for the evaluation of neuropathic pain [34] but did not provide "how to" guidance beyond referencing earlier papers [29, 35, 36]. Other authors evaluating neuropathic and musculoskeletal pain have used a matrix method of evaluating a grid of predetermined anatomical points and recorded the pressure pain threshold at each site [37, 38].

Standardization

Our procedure for allodyngraphy, where application of a 15g force on the skin generates a painful response (defined as 30 mm on a VAS or pain at rest + 10 mm on a VAS), uses a commonly available Semmes-Weinstein sensory evaluation kit stimulus (#5.18). In this study, we added precision to the notation by using the monofilament itself and a water-based ink pad to mark the borders of the territory. Spicher advocates measurement of four points on standard a x/y-axis relative to a fixed anatomic reference point [18]; for the purposes of calculating reliability in this study, we used these measurements as the basis for our calculations of area but applied a standard adjustment ($\times 0.66$) to account for the nonlinear shape. In clinical practice, we have found that the linear measurements without the calculation of area are sufficient to monitor change and are easy to execute using an inexpensive flexible clear plastic ruler. Additionally, when measuring over the contours of the hand, we have also found it useful to include additional measurement points for monitoring of change.

The allodyngraphy procedure is in contrast to the repeated stimuli applied using the method of limits by Keizer et al. [39], who used von Frey monofilaments to establish a minimum threshold of allodynia in persons with allodynia in a single limb. They asked the subjects to indicate the most painful area of the skin, and this was compared bilaterally by testing with progressively larger

monofilaments. Once the person perceived two of three stimuli to be painful (most commonly at #4.56 pressure), they were also asked to rate the intensity of the pain evoked: reporting a mean evoked pain of 6.8/10 on a numeric rating scale (range = 4–9). However, they reported that none of their subjects found any size of monofilament to be painful on the nonaffected limb, including an additional five healthy volunteers tested [39]. This is concordant with our findings of only 12 persons of the 38 tested meeting our criterion for allodynia (i.e., perceiving pressure from a #5.18 monofilament as evoking pain of at least 3/10 on a VAS). It is also worth noting the make-up of our sample: while we also tested persons with recent fractures and peripheral nerve injuries, 50% of the sample met the Budapest criteria for CRPS. The unique features of this syndrome may reflect a severity bias in our sampling, and the measurement properties reported here may not generalize to more heterogeneous samples.

Limitations and Recommendations for Future Research

It is important to note some participants declined repeated testing, or declined evaluation with monofilaments altogether. We cannot know if this group would represent important data that would influence the values and relationships reported here, although our general observation is that this may reflect persons with chronic symptoms and high levels of catastrophizing. All of our participants had a history of upper limb injury, and the measurement estimates were on the basis of evaluations of the hand and upper limb. More research on the measurement properties of these evaluations should be conducted in larger samples including other cutaneous areas in the body and other forms of neuropathic pain.

Conclusions

This initial investigation of the measurement properties of allodyngraphy supports at least fair inter-rater and test-retest reliability of the method in persons with CRPS, peripheral nerve injuries, or pain after hand fracture when conducted by trained therapists and good agreement for the formation of a neuroanatomic hypothesis. However, more study in larger and diverse samples is needed to generate estimates of criterion and construct validity and responsiveness to change if the method is to be used in research and clinical practice. The results presented here can inform the rigor and scope of those investigations. We leave the reader with a quote from a paper published by the Neuropathic Pain Research Consortium [34]:

Novel clinical observations emerge from novel methods of observation and measurement. Therefore, the advancement of our understanding of neuropathic pain is dependent upon the development of tools to observe the phenomenon of neuropathic pain. As neuropathic pain is a

fundamentally clinical physiologic phenomenon rather than a histologic, electrophysiologic, or laboratory phenomenon, the fundamental tools for the study of neuropathic pain must be clinical. (p. 639)

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