**A couple of people sitting at a table

Description automatically generated**

This demonstration protocol describes the concept of alloknesis, a brief overview of the mechanism behind it and the assessment technique applied to quantify it. As a demonstration protocol it is not intended to be a protocol for an actual experiment. Instead, it is intended as a demonstration of one specific experimental procedure that can be used as a building block in more comprehensive protocols.

alloknesis

**Silvia Lo Vecchio**

Logo

Description automatically generated

# Introduction

The term alloknesis, first coined by LaMotte et al. in 19881–4, represents one of the mechanical itch dysesthesias, that describe dysfunctional sensory states, in which itch is evoked by light tactile stimuli (e.g. from clothing or touch), or by stimuli which normally would only induce mild itching 1,5–8. Alloknesis (“allo”, and “knesis”, an ancient Greek word for itching) is described as a pruriceptive sensation or a scratching behavior evoked by a stimulus that is normally non itchy, such as light stroking of the skin with a cotton swab or a brush (Figure 1) 1,9.

A diagram of strength and strength

Description automatically generated

Figure 1: Graphical representation of the alloknesis phenomenon. The curve represents the stimulus-response curve, that is the association between the intensity of the applied stimulus (x-axis) and the itch response (Y-axis) under normal condi­tions and when dysesthesias are present. Created with BioRender.com and adapted from Andersen et al. 1with inspiration from Sandkühler J 13.

This concept reflects a similar dysfunctional state evoked by pain and termed allodynia, in which pain is cause by a stimulus that normally does not provoke pain 10,11. Often, alloknesis represents a symptom in acute itch, chronic itch conditions such as neuropathic itch and atopic dermatitis but could also be induced experimentally in healthy volunteers 1,10,11. The primary cause of alloknesis is the sensitization of itch signaling pathways inducing amplified response to pruritogens and increased reactivity to other types of stimuli1,11–13. Moreover, also the dysregulation of the inhibitory systems in the spinal cord seems to contribute to alloknesis11. In humans, the intensity of alloknesis is often assessed by using brush strokes 1,14, as illustrated below under the section “protocol”.

Alloknesis can be assessed by applying brush strokes to the skin of a subject and asking them to rate the evoked itch on a rating scale. This demonstration protocol provides two alternative experimental procedures for assessing alloknesis; one where the evoked itch is rated on a numerical rating scale (NRS), and one where it is rated on a visual analog scale (VAS). In an actual experiment, only one of these procedures should be used. This demonstration protocol can be used to evaluate which experimental procedure (NRS or VAS) is appropriate for your experiment. Once a decision is made the chosen experimental procedure can be copied from this demonstration protocol into the protocol for your experiment.

# Experimental Setup

The experimental setup is designed to record the itch ratings of the subject automatically without the need for manual actions taken by the investigator, and to display instructions to the investigator and subject throughout the experiment.

The experimental setup consists of a computer running LabBench with two screens attached. The primary screen is used for displaying LabBench to the investigator and the secondary screen is used to display instructions to the subject prior to running an experimental procedure and to display either the NRS or VAS scale on which the subject rates their sensation (see Figure 2).

A blue box with a blue box and a red box with black text

Description automatically generated

Figure 2: Illustration of the experimental setup that consists of a computer running LabBench to which two screens are attached. One screen is used to display LabBench to the operator, and one is used to display rating scales and instructions to the subject. A LabBench SCALE is used by the subject to perform the rating on either NRS or VAS scales, which is connected to LabBench with a LabBench I/O device.

Typically, laptops for experimental setups, and in that case the screen of the laptop should be configured to be the primary display. Connect the external screen to an HDMI port on the laptop and configure this screen as a secondary display. Connect the LabBench I/O with the USB cable to the computer and to power with its accompanying power supply. Connect the LabBench SCALE to Response Port 1 on the LabBench I/O.

Somedic SENSELab Brush no. 5 is used to determinate the intensity of alloknesis.

# Protocol

Alloknesis will be measured using a standardized sensory brush (SENSELab Brush-05, Somedic AB, Hörby, Sweden) exerting a force of in the range of 200 +/- 100 mN. The investigator should perform 3 stimulations, in different directions, along the diagonals of the area of interest (AOI).

Each stimulation consists of a set of 3 brush strokes (2-3 cm in length) in short succession (approximately 1 s in between) over the treated/control areas. The strokes are applied by keeping the brush perpendicular to the skin at a speed of 3-6 cm/sec.

A person painting a person's arm

Description automatically generated

Fig 3: Application of brush strokes perpendicular to the skin while the subject rates the sensation of itch on a Numerical Rating Scale.

After each set of 3 brush strokes, the participant rates the sensation induced by the brush on a:

1. NRS Test: NRS scale from 0 to 10 (0 = “No Itch”; 10 = “Worst Imaginable Itch”).
2. VAS Test: VAS scale of 10cm in length, with a lower anchor of “No Itch” and upper anchor of “Worst Imaginable Itch”.

# Using the protocol

The protocol can be installed from the (labbench.io) repository, which is available by default when LabBench is installed.

Before the protocol can be installed a LabBench I/O device must first be added to the LabBench installation (see Figure X). First start the LabBench Designer, to check that a LabBench I/O device is present or to add such a device if it is not, and then: 1) Select the Protocols Page, 2) Select the LabBench I/O device, 3) check that a LabBench I/O device is installed and available.

If a LabBench I/O device is not installed, then install one by first ensuring that the device is connected to the computer and then clicking on the (+) add device button.

A screenshot of a computer

Description automatically generated

Figure 4: Illustration of how to check if a LabBench I/O has been added to the LabBench system.

To install the protocol; 1) Select the Protocols page, 2) Select the labbench.io repository, 3) Select the Alloknesis protocol, and 4) click the (+) add protocol button.

A screenshot of a computer

Description automatically generated

Figure 5: Procedure for how to install the protocol.

# Results

Data is saved automatically by LabBench during the experiment as three NRS values between 0 (no itch) and 10 (maximal itch) or three VAS values between 0cm and 10cm; one for each measurement that is performed in the experimental procedure.

# Discussion

# License

Alloknesis Demonstration Protocol (alloknesisDemo@labbench.io) © 2024 by Inventors’ Way ApS is licensed under Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International.

A close up of words

Description automatically generated

For a full explanation for the conditions of its use and the full license text, please refer to: https://creativecommons.org/licenses/by-nc-sa/4.0/

# References

1 Andersen HH, Akiyama T, Nattkemper LA, *et al.* Alloknesis and hyperknesis—mechanisms, assessment methodology, and clinical implications of itch sensitization. *Pain* 2018; **159**:1185–97.

2 Bickford RGL. Experiments relating to the itch sensation, it’s peripheral mechanism, and central pathays. *Clin Sci* 1938; **3**:377–86.

3 LaMotte RH. Subpopulations of “nocifensor neurons” contributing to pain and allodynia, itch and alloknesis. *APS Journal* 1992; **1**:115–26.

4 LaMotte RH. Psychophysical and neurophysiological studies of chemically induced cutaneous pain and itch: the case of the missing nociceptor. In: *Progress in brain research*. , Elsevier, 1988; 331–5.

5 Andersen HH, Elberling J, Sølvsten H, *et al.* Nonhistaminergic and mechanical itch sensitization in atopic dermatitis. *Pain* 2017; **158**:1780–91.

6 G. Atanassoff P, Brull SJ, Zhang J, *et al.* Enhancement of experimental pruritus and mechanically evoked dysesthesiae with local anesthesia. *Somatosens Mot Res* 1999; **16**:291–8.

7 Ikoma A, Fartasch M, Heyer G, *et al.* Painful stimuli evoke itch in patients with chronic pruritus: central sensitization for itch. *AAN Enterprises*URL https://n.neurology.org/content/62/2/212.short [accessed on 22 November 2021].

8 Schmelz M. Itch and pain differences and commonalities. In: *Pain Control*. , Springer, 2015; 285–301.

9 LaMotte RH. Allodynia and Alloknesis. In: *Encyclopedia of Pain*. Berlin, Heidelberg, Springer Berlin Heidelberg; 52–5.

10 Jensen TS, Finnerup NB. Allodynia and hyperalgesia in neuropathic pain: clinical manifestations and mechanisms. *Lancet Neurol* 2014; **13**:924–35.

11 Tsagareli Merab. Hyperalgesia and Allodynia: A Closer Look. Symptoms, Mechanisms and Treatment. , Nova Science Publishers, 2019.

12 LaMotte RH, Dong X, Ringkamp M. Sensory neurons and circuits mediating itch. *Nat Rev Neurosci* 2014; **15**:19–31.

13 Sandkuhler J. Models and mechanisms of hyperalgesia and allodynia. *Physiol Rev* 2009; **89**:707–58.

14 Weisshaar E, Dunker N, Gollnick H. Topical capsaicin therapy in humans with hemodialysis-related pruritus. *Neurosci Lett* 2003; **345**:192–4.