# Enhanced sensory recovery after median nerve repair using cortical audio-tactile interaction. A randomised multicentre study.

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# Enhanced sensory recovery aftermedian nerve repair using cortical audio-tactile interaction.

A randomised multicentre study.

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ABSTRACT

The "Sensor Glove System" offers an alternate afferent inflow from the hand early after nerve repair in the forearm, mediated through the hearing sense, implying that deprivation of one sense can be compensated by another sense. This "sensory by-pass" was used early after repair of the median nerve with the intention of improving recovery of functional sensibility by maintaining an active sensory map of the hand in the somatosensory cortex during the deafferentation period. In a prospective multicentre clinical study one group (n=14) started early after surgery with sensory re-education using the Sensor Glove System and the control group (n=12) received conventional sensory re-education starting three months postoperatively. The patients were checked regularly during a one-year period with focus on recovery of tactile gnosis. After 12 months, tactile gnosis was significantly better in the Sensor Glove System group. This highlights the timing for introduction of training after nerve repair, focusing on the importance of immediate sensory re-learning.

## INTRODUCTION

Recent advances in neuroscience and cognitive science have opened new possibilities for the future to improve sensory recovery after nerve repair, especially with respect to functional sensibility and, specifically, the capacity for identification and discrimination of touch (Lundborg, 1994; Rosén et al., 2003).

In classical sensory re-education, nothing is done to the denervated hand and the de-afferented brain during the first months after nerve repair. Sensory re-education programmes are started when some perception of touch can be demonstrated in the distal palm, i e about three months after nerve repair at the wrist level (Dellon et al., 1974; Wynn-Parry and Salter, 1976). The insensate hand and the changes in the corresponding cerebral cortical areas which occur after injury are left unattended, from the sensory relearning point of view, for a time period of several months.

Within minutes after a deafferentation injury, such as amputation of an arm or major nerve injury, there is a cortical response with an immediate and long-standing reorganisation of the sensory brain cortex. The silent area, no longer receiving any sensory input, triggers an expansion and invasion from adjacent cortical areas (Kaas et al., 1983; Merzenich and Jenkins, 1993; Wall et al., 2002). This is the initiation of a dynamic interplay in the cortical neural networks, which is influenced by several biological and psychological events during regeneration and re-innervation.

The outcome of nerve division then repair, in terms of recovered tactile gnosis, in adults is often disappointing (Allan, 2000; Jaquet et al., 2001; Jerosch-Herold, 1993; Kallio and Vastamäki, 1993; Lundborg et al., 2004). We think that one reason for this is the long initial period of absent sensibility, which allows major functional cortical reorganisation changes to take place as a result of lost sensory input initially and misdirected axonal outgrowth later : the "cortical hand map" is completely changed. The timing for onset of sensory re-education may be of critical importance. We should differentiate between ‘Phase 1’(before any reinnervation has occurred in the hand) and ‘Phase 2’ (when some reinnervation of the hand has occurred). There are good reasons to use strategies to enhance the recovery during both of these two phases and to initiate sensory re-education  very early, ie.in Phase 1, during the first postoperative days.

The brain is organised holistically, with an extensive capacity for cross-and multimodality and there is an ongoing, activity-dependent competition for “brain space” between different sensory inputs. The use of vision to guide the re-training of sensation is the base for classical sensory re-education, but there is a continuous interplay between all of the senses. This multi- and cross modal activity of the brain is based on multisensory neurons that receive more than one type of sensory signals and it has been demonstrated that we are able to extract information from one sensory modality and use it in another by using polymodal association centres (Bavelier and Neville, 2002; Pascual-Leone and Hamilton, 2001; Tanabe et al., 2005). This holistic concept, with functional interdependence of activity between the different areas of the brain, makes a re-evaluation of the traditional territorial concept of the brain necessary. It also opens up new possibilities to use the plastic potential of the brain at a very much earlier stage in rehabilitation after nerve repair.

Cortical audiotactile interaction has been reported in animal and human studies (Gobbele et al., 2003; Lutkenhoner et al., 2002) and we have presented a model for alternative sensibility, based on sense substitution, using hearing as a substitute for sensibility (Lundborg et al., 1999). Miniature microphones are mounted in the fingertips of a glove or attached dorsally with a silicone ring directly onto the finger ( Figs 1a and b) in what is called a ‘Sensor Glove System’. The stimuli generated by active touch of various structures (each structure giving a specific friction sound) can be picked up, amplified and transposed to stereophonic acoustic stimuli by this system. Using the Sensor Glove System, it is possible to train the brain to localise different fingers and identify different textures, allowing use of this alternative sensory feedback for activities of daily living. This principle is used to provide the sensory brain cortex with an alternate sensory input at a time when regenerating nerve fibres have not yet reached the peripheral targets. We have recently, with fMRI technique, demonstrated an audiotactile interaction in persons trained with the Sensor Glove System (Lundborg et al., 2005).

In this controlled, randomised study, subjects were equipped with either a Sensor Glove System within two weeks after surgery and underwent a sensory re-learning programme at this time, or received traditional treatment with sensory re-education starting when some evidence of re-innervation was present in the hand.

## Patients and Methods

The study design was a prospective randomised multicentre study including 6 hand centres in Sweden,(Göteborg, Linköping, Malmö, Stockholm, Uppsala, Örebro), and was approved by the Ethical Committee at Lund, Uppsala, Linköping, Örebro, Göteborg and Stockholm Universities.

The study included 30 consecutive patients over 18 years who were less than two weeks from a complete, clean-cut transection of the median or combined median/ulnar nerves at the wrist or distal forearm level. All patients had given their approved consent. Communication problems due to language or severe psychiatric problems were exclusion criteria. Using sealed envelopes, patients were randomised to receive therapy treatment post-operatively with either the Sensor Glove System early after injury and surgery, or conventional sensory re-education training. Table 1 includes the demographic data of the two study groups.

Twenty-six of the initial 30 patients completed the study, and 14 of these 26 patients (mean age 35 years) used the Sensor Glove System while carrying out conventional rehabilitation following nerve repair, including specific sensory re-education exercises twice daily, from the first postoperative week through the first 3 postoperative months. Twelve patients (mean age 33 years) were randomised to conventional rehabilitation during the first three postoperative months. At the 3 months follow-up, all received information and a home programme about conventional sensory re-education (Dellon, 1981).

**Sensory Re-education Procedures**

*Training with the* Sensor Glove System

Between one and fourteen days after the surgery, training with the Sensor Glove System was initiated. During the immobilisation period, the miniature microphones were attached dorsally with silicone rings on the fingers (Fig 1b) and the patient himself performed passive stimulation and trained to 1) identify four different materials, and 2) localise touch with one of the four materials on the denervated fingers. This was done twice daily for 10-15 minutes. Classic training principles for sensory re-education (Dellon, 1981; Wynn-Parry and Salter, 1976) were used i.e. touch was performed, alternatively with and without looking, while concentrating in a quiet environment. The patient was instructed to concentrate on which material or which finger gave a specific sound. Once the patient was allowed to move the hand freely, the SGS was introduced (Fig 1a). At this point, training with the Sensor Glove also included a period of use of the Sensor Glove during light daily activities for 30 minutes twice daily. Activities were chosen which were appropriate to the mobilisation programme and its restrictions. Training with the SGS finished and “conventional” sensory re-education was introduced when perception of touch/pressure (SWM 4.56) could be detected in the affected area, which was usually three to four months postoperatively. There was follow up 2, 4 and 6 weeks after introduction of the training. Regular check-ups with assessment were performed during the first postoperative year.

*Conventional training*

Classical sensory re-education (Dellon, 1981; Wynn-Parry and Salter, 1976) was used i.e. concentrated perception of different aspects of passive and active touch while watching the touched part of the hand, followed by the same procedure with closed eyes. This was introduced, using a home training programme, when perception of touch/pressure (SWM 4.56) could be detected in the affected area which was usually three to four months postoperatively. Regular check-ups were performed during the first postoperative year.

**Follow-up and Assessment**

Follow up and assessment of hand function was done at 3, 6 and 12 months. This was performed using the ‘’Model Instrument for Outcome After Nerve Repair’, reflecting the summarised outcome from sensory, motor, and pain/discomfort domains (Rosén and Lundborg, 2000; Rosén and Lundborg, 2003). This outcome instrument includes specific assessment of tactile gnosis using the Shape Texture Identification test (STI-test) and static two-point discrimination (s2PD).

Assessments were performed according to standardised procedures, and s2PD testing was carried out according to the “Moberg Method” (Moberg, 1990), as described by the ASSH and ASHT (ASHT, 1992; ASSH, 1978). The test is carried out in a descending order, starting with 15 mm, to assess the level at which responses were correct (7 out of 10 correct at just blanching of the skin), and were quantified as 0-3 (0= ≥16mm, 1=11-15mm, 2=6-10mm, 3= ≤6mm)(ASHT), 1992).

***Analysis***

A group comparison was done at the 12 months follow up using Mann-Whitney U-test.
To investigate whether the assessed changes in tactile gnosis capacity were true, the minimal level of detectable change (MDC)(Beaton et al., 2001; Stratford et al., 1996) in tactile gnosis capacity was calculated. The MDC yields a threshold—a minimum score—that allows you to be 95% confident that when a change score greater this value is observed, it is likely to indicate a real change in the patient rather than a measurement error. The raw data-scoring in STI-test can be between 0 and 6.  The minimal detectable change for the STI-test, ie. the minimum amount of change that should be observed in the tactile gnosis test between two test occasions to exceed the measurement error of the test instrument,  has been shown in previously published data on test-retest reliability to be 1.3 (Rosén, 2003).

## RESULTS

At the initial assessment, both groups naturally started at zero tactile gnosis (Table 1). The median improvement in STI-testing after 12 months in the patients that had used the Sensor Glove System was 2 (IQR 0-3.25) indicating a true change (score >1.3 in STI-test) from baseline in tactile gnosis (Rosén, 2003). This compares with the control group that showed a median improvement of 0 (IQR 0-0.75) at this time.

Outcome in the sensory, motor and pain/discomfort domains and the ”total score” from the three domains are shown in Table 2. No differences between the groups could be seen after 12 months in ”total score” or in the motor domain. Neither were there any differences between the groups in experienced pain/discomfort. Tactile gnosis outcome was specifically addressed in this study and group comparison (Mann Whitney U-test) at the 12 months follow-up showed significantly better tactile gnosis (p=0.008), as expressed with STI-testing, in the Sensor Glove System group (Table 2 and Fig 2). Two-point discrimination did not demonstrate any difference between the groups. A clear floor effect (most patients could not discriminate between one and two points at 15mm distance) was seen in both groups with test result 16mm or more in 10 cases in the Sensor Glove System group and in 9 cases in the conventional training group (Fig 3).

## DISCUSSION

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The functional reorganisation of cortex after nerve transsection and repair is a rapid process, involving disappearance of the representation corresponding to the denervated body parts and associated expansion of adjacent cortical territories. In such a situation, it is hoped that activation of cortical hand representation might be effective in maintaining the cortical hand map. It is well known that the premotor cortex can be activated by just imaging a movement, so-called “motor imagery” (Jeannerod, 1994; Jeannerod and Frak, 1999; Kosslyn et al., 2001; Lotze et al., 1999).It has been demonstrated that the pattern of somatosensory activation during motor imagery is very similar to the pattern observed during movement execution (Ehrsson et al., 2003) Also, observing movements activates mirror neurons in the frontal cortex (Celnik et al., 2005; Rizzolatti and Craighero, 2004Rizzolatti et al., 1996). Mirror neuron areas have also been shown to be involved in understanding the intention of others (Iacoboni et al., 2005). Reading or listening to action words, related to hand movements, may activate hand representational areas in the motor cortex (Hauk et al., 2004; Pulvermuller, 2005). In respect of ‘sensory imagery’ and involvement of primary sensory cortical areas, a few observations have been reported (Yoo et al., 2003). There are also ways to activate the somatosensory cortex by, for example, observing a bodypart (Keysers et al., 2004) or the hands (Hansson T, 2005) being touched. Several studies also suggests that the SI and SII cortex is related to the mirror neuron system (Avikainen et al., 2002; Mottonen et al., 2005; Yoo et al., 2003). Another possible principle is activation of the somatosensory cortex using a mirror placed transversally in front of the patient with the denervated nerve injured hand hidden behind the mirror and the healthy hand being reflected as an illusion of the injured hand (Moseley, 2004; Ramachandran and Hirstein, 1998; Rosén and Lundborg, 2005). Touching the healthy hand in this situation may give an illusion of touching the injured hand.

Whatever method is chosen there are good reasons to start sensory re-education after nerve repair much earlier than we do today, with the aim of inhibiting, or at least minimising, the reorganisation process in the somatosensory cortex which is induced by the nerve injury. In the very early phase after nerve injury and repair, all of these principles may constitute potential methods to feed the somatosensory cortex with input from the denervated body part.

In this study, we utilised the brain´s capacity for audio-tactile interaction so that acoustic information was used as a substitute for missing tactile information (Lundborg et al., 1999). Cortical audiotactile interaction has previously been reported in animal and human studies (Gobbele et al., 2003; Lutkenhoner et al., 2002). The principle is based on the crossmodal capacity of the brain, ie. hearing substitutes for touch. The resemblance in perceptual experience between sound and touch is bridged by the vibratory sense. The Sensor Glove, by using audio-tactile interaction, facilitates relearning once sensation returns to the hand by maintaining a hypothetically better prepared somatosensory cortex for the necessary re-learning process. Our hypothesis was confirmed that maintaining activation of the cortical hand maps, i.e. preserving cortical hand representation in Phase one after the nerve repair (when there was no sensibility in the hand) would facilitate later recovery of functional sensibility (tactile gnosis). Tactile gnosis that was addressed in this study is one of the components of importance for the summarised outcome after nerve repair (Rosén and Lundborg, 2000). We therefore find it reasonable that the tactile gnosis assessment demonstrated improvement while in “total score” , that includes also other components such as motor function and pain problems, the Sensor Glove use had no impact.

In the present study, training with the Sensor Glove System started within the first postoperative days, ie. in a phase of ongoing profound cortical reorganisation, when the cortical hand projection is diminishing, or disappearing, as a result of expanding adjacent cortical areas. A recent fMRI study has shown that acoustic stimuli from the hand, processed by the Sensor Glove System , can activate the somatosensory cortex in healthy individuals who have trained with the equipment (Lundborg et al., 2005) and we hypothesise that this is the case also in nerve injured patients. The findings in this study support such a hypothesis. The Sensor Glove System was used until reinnervation of the hand was obvious. It is not known whether continuing use of the system in Phase 2 would be beneficial. Combination of methods to activate the sensory cortex during Phase one should also be considered.

The Sensor Glove System may also have a use in patients lacking sensibility after lesions in the central nervous system with disturbed body awareness, or due to neurological disease. In respect of nerve injury, our study highlights the need for refinement of sensory re-education programmes, with emphasis on the timing of such programmes in rehabilitation after nerve repair.

**Legends**

Fig 1a and b — Components of the Sensor Glove System, showing a) the Sensor Glove and b) a patient training with miniature microphones attached to a silicone ring on each finger.

Fig 2 — Box plot illustrating results from tactile gnosis assessment with the STI-test

*Note:* Each box encloses 50% of the data with the median value displayed as a line. The top and bottom of each box mark the $90^{th}$ and the $10^{th}$ percentile. Any value outside this range, (outlier) is displayed as an individual point.

Fig 3 — Box plot illustrating results from tactile gnosis assessment with 2PD and a clear “floor effect” i.e. most patients could not discriminate between one and two points at 15 mm distance, meaning that there is low sensitivity to 2PD for this group of patients.

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Table 1 Demographic data

| | Sensor Glove training n=14 | Conventional training n=12 |
|---|---|---|
| Age (mean, range) | 34 (18-64) | 33 (18-66) |
| Gender | 12 males<br>2 females | 5 males<br>7 females |
| Injury | median nerve , 14 | median nerve , 8<br>median and ulnar nerve, 4 |
| Dominant hand injured? | 8 | 8 |

Table 2 Outcome after 3 and 12 months inthe two groups respectively and result from calculation of groupdifference at 12 months follow-up.

| Model Instrument for Outcome After Nerve Repair* | | Median outcome 3 months postoperatively (interquartilerange) | | Median outcome after 12 months (interquartile range) | | Group dif after 12 months (Mann-Whitney) p-value |
|---|---|---|---|---|---|---|
| | | Sensor Glove Training n=13 | Conventional Training n=12 | Sensor Glove Training n=14 | Conventional Training n=12 | |
| Sensory domain, 0-1 | Perception of touch, SWM, score 0-1 | 0.27 (0.05-0.27) | 0.20 (0.07-0.32) | 0.60 (0.53-0.73) | 0.56 (0.4-0.73) | *0.77* |
| | Tactile gnosis, 2PD, score 0-1 | 0 (0-0) | 0 (0-0) | 0 (0-0.17) | 0 (0-0.17) | *0.84* |
| | Tactile gnosis, STI-test, score 0-1 | 0 (0-0) | 0 (0-0) | 0.33 (0-0.5) | 0 (0-0.09) | ***0.008*** |
| | Dexterity, Sollerman test (#4,#8,#10) score 0-1 | 0.33 (0.17-0.42) | 0.17 (0.08-0.25) | 0.58 (0.33-0.67) | 0.42 (0.21-0.58) | *0.10* |
| | | 0.15 (0.08-0.18) | 0.08 (0.06-0.13) | 0.37 (0.22-0.55) | 0.31 (0.16-0.35) | *0.12* |
| Motor domain, 0-1 | Muscle function, MMT score 0-1 | 0.4 (0.18-0.65) | 0.2 (0-0.77) | 1 (0.6-1) | 0.8 (0.8-0.8) | *0.19* |
| | Grip strength, Jamar score 0-1 | 0.37 (0.27-0.57) | 0.29 (0.15-0.58) | 0.77 (0.65-0.88) | 0.72 (0.58-0.83) | *0.54* |
| | | 0.45 (0.28-0.59) | 0.31 (0.16-0.51) | 0.83 (0.68-0.90) | 0.77 (0.64-0.86) | *0.38* |
| Pain/discomfort domain, 0-1 | Cold intolerance, Subjective rating score 0-1 | 0.67 (0.33-0.75) | 0.67 (0.67-0.92) | 0.33 (0-1) | 0.33 (0.17-0.67) | *0.75* |
| | Hyperaesthesia, Subjective rating score 0-1 | 0.67 (0.33-1) | 0.67 (0.33-1) | 1 (0.33-1) | 1 (0.67-1) | *0.62* |
| | | 0.5 (0.33-0.88) | 0.67 (0.54-0.84) | 0.67 (0.33-0.84) | 0.67 (0.5-0.84) | *0.99* |

| | | | | | |
|---|---|---|---|---|---|
| **Total score 0-3** | 1.3(0.9-1.4) | 1.1(1-1.4) | 1.9(1.2-2.3) | 1.7(1.5-1.9) | *0.28* |

- The scoring system for this model instrument (Rosén and Lundborg, 2000) is based on a calculation of the quotes between
- obtained results in each subtest and the ”normal” result. This quote can be a value between 0 and 1. Result in sensory, motor and
- pain/discomfort domains are the mean quotes of included subtetsts. ”Total score” (0-3), 3 meaning full recovery with normal
- sensory and motor function and no pain/discomfort, is the summarized mean-scores from the three domains.

Fig 1a

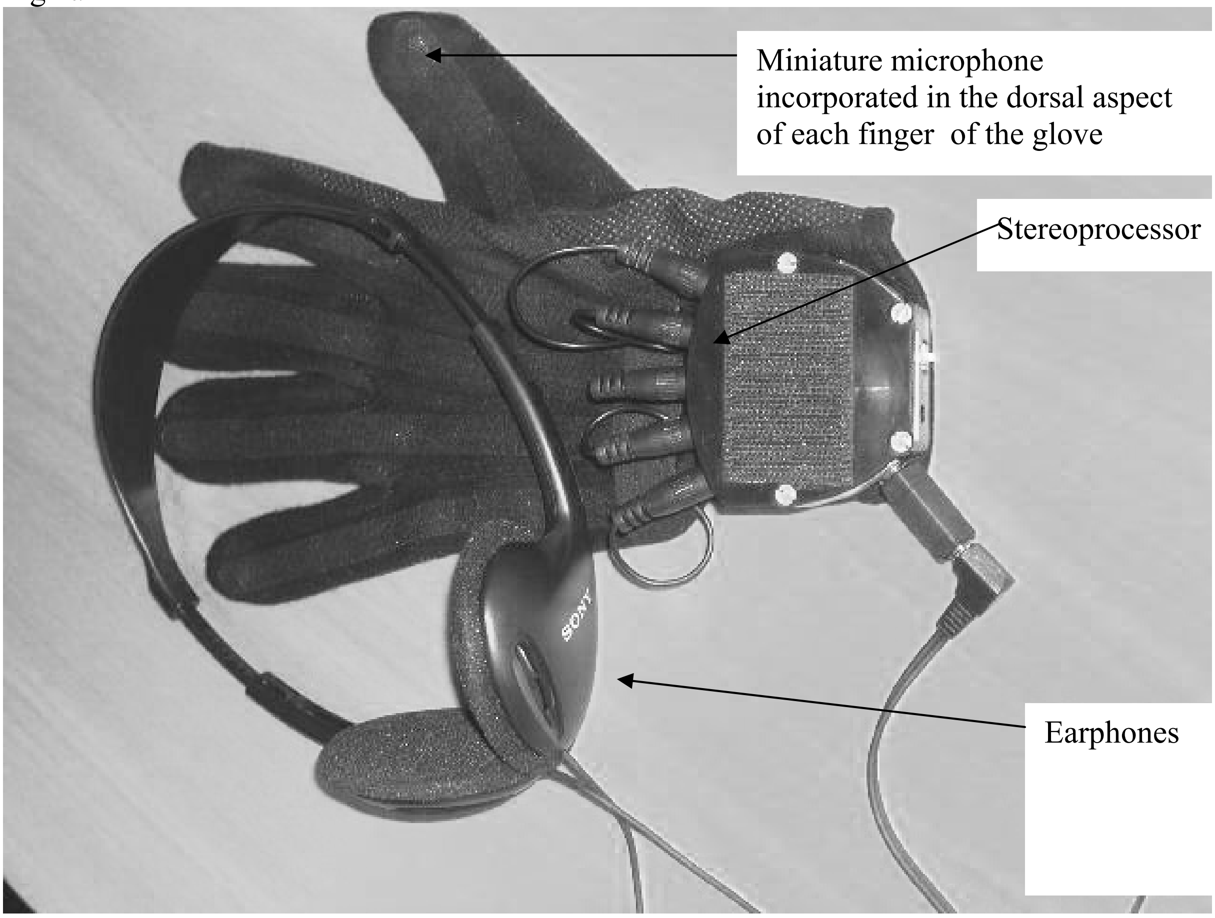
Miniature microphone incorporated in the dorsal aspect of each finger of the glove
Stereoprocessor
Earphones
SONY

Fig 1b

Score STI-test

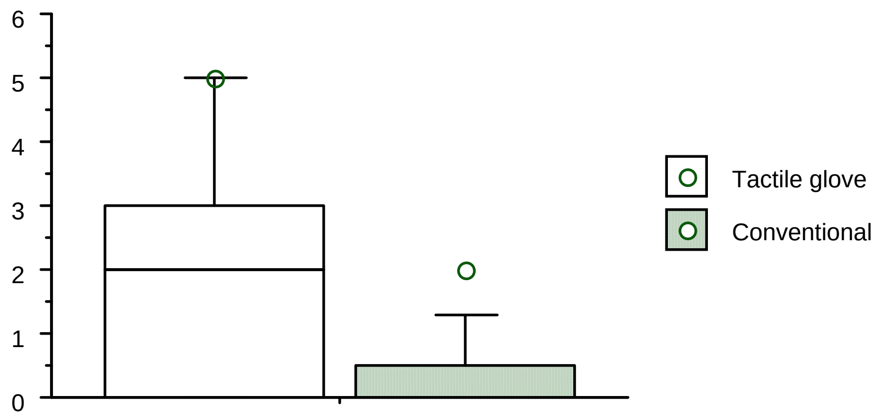


Fig 2

2PD, mm

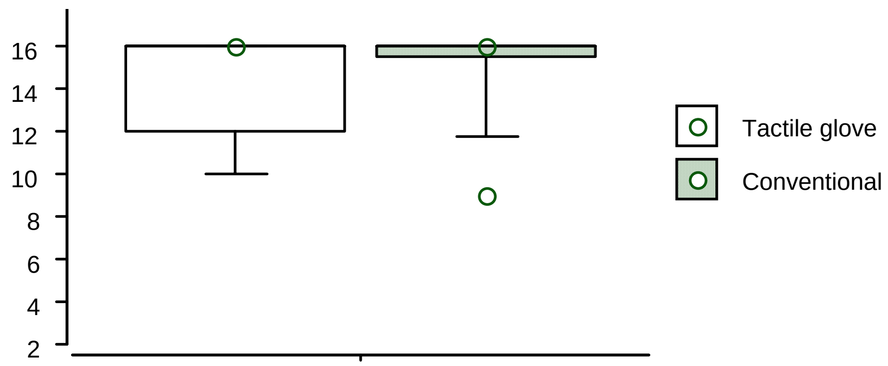


Fig 3