# Assessment of human finger position sense and the effect of vibro-tactile stimulation on proprioceptive acuity

A Dissertation

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# Dedication

This dissertation is dedicated to my family.

# Abstract

Finger position sense, the awareness of where our fingers are in space, is imperative for daily activities requiring manual dexterity, such as typing or opening up a jar. A deficit in this sense, associated with different movement disorders or neurodegenerative diseases would degrade the performance proportional to the amount of deficit. However, there is not yet an objective and quantitative measure of this sense. This partially contributes to the incoherent results about the development of the sense in typically developing children or the effect of tactile input on the sense.

The three projects of this dissertation were designed to address these limitations. Project 1 further developed the finger position sense assessment system originally developed by Block et al. (2019). A new system was modified to accommodate individuals with different hand and finger sizes. It also minimized the effect of any sensory input other than the position sense. Finally, two acuity measures of the sense could be obtained separately: *Bias*, the systematic error, and *Precision*, the random error of the sense.

Project 2 aimed to characterize the finger position sense in typically developing children from 8 to 17, using the system developed in project 1. The development of finger position sense from late childhood to young adulthood could be described as an increase in *precision*, but no significant change in *bias*. In other words, children were more uncertain about their perceptual judgments about their finger positions relative to adults, but their ability to correctly perceive the finger position was already comparable to adults.

Project 3 determined the effect of vibro-tactile stimulation (VTS) on the finger position sense. Healthy young adults were tested using the system from project 1, without and with the VTS applied at one of the two positions on their index finger. In addition, to see if any neurophysiological change would accompany this altered finger position sense, participants' cortical activity was measured. The result revealed that there was a significant location-dependent effect of VTS, with stimulating fingertip increasing *bias* magnitude. Stimulating lateral side of the finger decreased the measure. Cortical response to VTS also increased when participants had VTS on the lateral side of the finger with the opposite being true as well. A possible relationship between the behavioral change and the neurophysiological change was hinted, supporting that the two changes are not independent but the increase in cortical response could be associated with enhanced finger position sense, even at a short-term scale.

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VTS: Vibro-Tactile Stimulation

PSE: Point of Subjective Equality

UA: Uncertainty Area

TD: Typically Developing children

DCD: Developmental Coordination Disorder

SEP: Somatosensory Evoked Potential

HSCL: Human Sensorimotor Control Laboratory

# Introduction

The topic of this cumulative doctoral dissertation concerns the finger position sense – a specific aspect of proprioceptive function. This sense is critical to the precise control of fingers, necessary for different activities such as tool use and object manipulation. Yet, there still doesn't exist an objective and quantitative measure for this sense. Arguments about its course of development are inconclusive. Similarly, the relationship with other sensory input from the finger is not well known. Consequently, three projects of the dissertation are prepared to address these limits. The first project concerned the design and building of a system assessing position sense acuity. The second project used the device and examined the development of proprioceptive acuity in typically developing children. The third project examined if vibro-tactile stimulation of the finger influences proprioceptive acuity.

## Proprioception and fine motor control

Proprioception is defined as the perception of limb position and movement in space (Goldscheider, 1889, 1898; Sherrington, 1907). Proprioceptive signals arise from mechanoreceptors such as muscle spindles, joint capsules, or Golgi tendon organs (Tuthill & Azim, 2018). Along with vision, proprioceptive afferents contribute to different aspects of motor control, such as the fine control of hand and finger movements, which are critical for executing many activities of daily living (Gentilucci et al., 1994; Jones, 1996; Sarlegna & Sainburg, 2009). For example, in planning the reach to grasp a cup on a table, the motor system requires information on the current position of the arm and the hand to plan a goal-directed movement. A movement trajectory, as well as force needed to move the limbs is estimated based on that information. During the reach, the sensory input of the limb position is compared with the expected one, so that the discrepancy between the two is maintained minimal and the goal is achieved successfully.

A deficit or loss of proprioceptive input is considered one factor that negatively impacts coordinated movements, including those of hands and fingers. Loss of proprioception due to damage to the somatosensory cortex accompanied the loss of motor control of the hand (Kato & Izumiyama, 2015). Konczak and Abbruzzese (2013) argued that proprioceptive deficit was associated with the symptoms of musician's dystonia, a motor disorder demonstrating involuntary sustained muscle contractions that hinder effective manipulation of fingers during the play of a musical instrument. Developmental coordination disorder (Tseng et al., 2018), stroke (Hunter & Crome, 2002), or peripheral neuropathy (Gordon et al., 1995; Sainburg et al., 1993) has also been reported to show deficits of proprioception along with impairments of fine motor control. On the other hand, individuals with the aforementioned conditions may show preserved proprioception. Furthermore, relatively intact proprioception in spite of stroke could predict how much individuals recover the upper limb motor function (Broeks et al., 1999; Reding & Potes, 1988). Thus, this complex relationship between proprioception and fine motor control implies that a precise measurement of the sense is required to better understand this relationship.

## Assessing proprioception: Current status and limitations

Despite an understanding of proprioceptive deficits in these populations, current clinical methods used to assess proprioceptive deficits are coarse and rely mainly on subjective clinical impressions (Clark et al., 2015). For instance, determining the severity of proprioceptive deficit in people with stroke relies on clinicians moving a patient's limb segment to two different positions (e.g., flexion and extension) and then asking the patient to discriminate between the two positions (Hillier et al., 2015). Such a method does not have the necessary resolution to evaluate proprioceptive impairment of stroke patients and basically only detects the complete loss of proprioceptive function.

A precise and quantitative assessment of proprioceptive acuity has its own merit. Clinicians could plan for the right amount of rehabilitation training based on quantified proprioceptive deficits. Therefore, researchers within the last decade have attempted to quantify the degree of proprioceptive dysfunction. Outcome measures as well as assessment paradigms to obtain the measures were determined based on the two criteria: 1) which modality of proprioception (position sense vs. motion sense) is tested and 2) which ability (sensitivity vs. acuity) is measured.

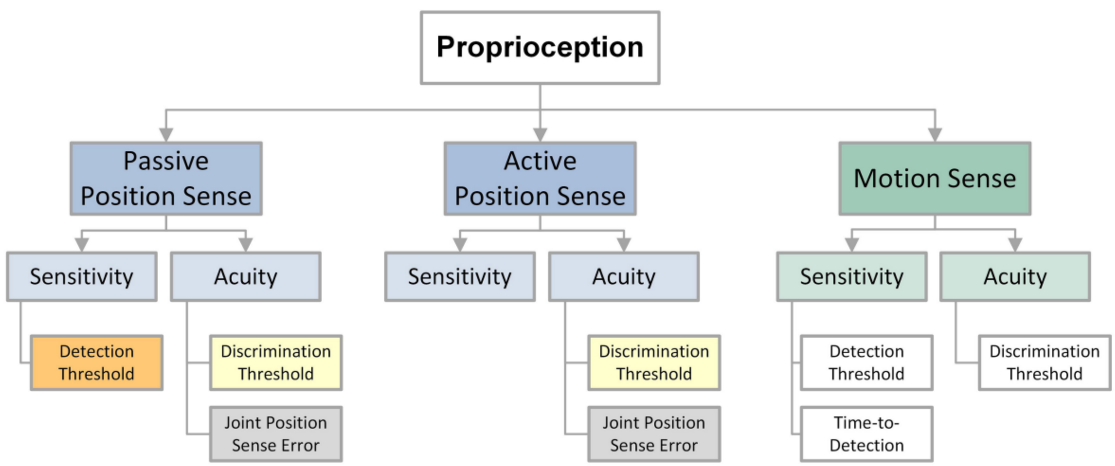


***Figure 1****. An overview of position and motion related proprioceptive assessment outcome measures. For the position sense, tested limb could be moved passively by a robot or an experimenter (passive) or actively by a participant (active). Two measures of the position sense acuity are the discrimination threshold and joint position sense error. Discrimination threshold is the estimated minimum difference at which the participant can discriminate two limb positions. Joint position sense error is the calculated difference between a reference limb position and a matched limb position, measured in distance or angle. Figure is reprinted from Winter et al. (2022).*

Figure 1 describes the outcome measures for different scenarios. In the context of proprioceptive assessment, sensitivity refers to the ability to detect a change in limb position or movement while acuity refers to the ability to discriminate between two different positions or movements. This dissertation focuses on the acuity of finger position sense, and thus relevant assessment paradigms to study the ability will be discussed.

### Assessments to estimate discrimination threshold

The position sense discrimination threshold is the smallest difference between the two detectable limb positions that can be perceived reliably. Assessments to estimate this measure require participants to differentiate the two positions with varying amounts of difference. One example is the assessment with the Wrist robot (Fig. 2). It is a robotic assessment device utilized to determine passive position sense acuity (Cappello et al., 2014; Elangovan et al., 2017) using a 2-alternative forced choice (2AFC) discrimination paradigm. The participant grasps the handle of the robot, and the robot passively flexes the hand to two different angles, the reference, 15 degrees, and the stimulus, defined as an angle larger than the reference angle. After the robot is done moving the wrist to both positions, the participant decides which of the two movements had a larger angular displacement. After a series of comparisons, the discrimination threshold is estimated as the stimulus intensity (the difference between the reference and the stimulus) that had the participant perceive the stimulus to be greater than the reference in degrees with 75% probability.

***Figure 2****. The Wrist robot with a participant tested for her wrist position sense discrimination threshold. The handle flexes the hand at two different angles and the participant indicates which of the two is greater.*

## Assessments to evaluate joint position sense error

These assessments would require participants to match the position or angle of a reference limb with a matching limb either identical (ipsilateral matching tests) or contralateral to the reference limb (contralateral matching tests). Joint position sense error is the difference between the reference limb and the matching limb in angles or distances. Robotic devices such as the Wrist Robot, KINARM (Dukelow et al., 2010), or H-Man Robot (Contu et al., 2017) were developed for the precise evaluation of the error. Simpler manual assessment devices were also developed by the Human Sensorimotor Control Laboratory (Fig. 3).

A B

***Figure 3****. Assessment devices developed by HSCL to evaluate joint position sense error.* ***A****. The device for the wrist joint. A participant matches the previously experienced right wrist joint angle using the same wrist. This is an example of an ipsilateral matching test. Difference between the experienced and the matched wrist angles is the wrist joint position sense error.* ***B****. The device for the elbow joint. A participant matches the right elbow joint angle with the left elbow joint. This is an example of a contralateral matching test.*

During a contralateral matching test, a participant's reference limb is moved to a target position. The contralateral limb of the participant could be moved passively by a robotic device or an experimenter until the participant indicates that the match is achieved. Otherwise, the participant actively moves the limb and stops where the match is made.

For an ipsilateral matching test, the reference limb is moved to a target position, stays for a while, and is moved back to the starting position. Later, the same limb is used to match its previous position voluntarily or passively with the help of a robot.

## An agenda to improve position sense acuity assessments

Robotic devices are typically immobile and not easily integrated in clinical settings. Moreover, using robotic devices *requires extra training* by clinical personnel. These systems are also typically expensive and small clinics or centers cannot afford them. A new assessment method for position sense acuity that is mobile and easily adoptable in many clinical settings can benefit both the clinicians and the patients.

Thixotropic properties of muscle should also be accounted for when measuring joint position sense acuity (Proske & Gandevia, 2012; Proske et al., 1993). The firing of muscle spindles when limbs are relaxed would be influenced by a preceding contraction or lengthening of muscles. This implies that measurements from active position sense matching tests could not control for this trait. A system that fixates the position of the tested limb during the entire assessment may provide a more certain measurement of proprioceptive acuity.

Lastly, it should be noted that the term acuity refers to the sharpness or accuracy of a sense and is defined by two distinct aspects, *bias* and *precision*. For assessing position sense, *bias* refers to the systematic error between the veridical and the perceived limb position, and *precision* refers to the random error between independent repeated responses, representing the amount of uncertainty in a person's perception (ISO, 1994). An effective assessment method should be able to measure the two aspects separately, as a deficit of position sense could be manifested by the impairment of one aspect while the other aspect is intact. For example, Tseng et al. (2018) reported a significant difference in *precision* but not in *bias* between children with DCD and typically developing children. Project 1 of this dissertation thus aimed to develop a new position sense acuity assessment system that would address the points mentioned above.

## Current knowledge of the typical development of limb position sense acuity

The development of human proprioception has not been fully mapped and research findings outlining its time course in typically developing (TD) children have been heterogeneous. For example, several studies reported that a child's proprioceptive acuity reaches adult levels at adolescence (Bairstow & Laszlo, 1981; Hay & Redon, 1997; Laszlo & Bairstow, 1980; Livesey & Parkes, 1995; Sigmundsson et al., 2000) while others contend that proprioceptive development continues throughout adolescence (Goble et al., 2005; Visser & Geuze, 2000). Part of the observed heterogeneity in results is likely owed to differences in methodology with tests having low resolution, not accounting for active motion, or having a small sample size.

Recent work from the Human Sensorimotor Control Laboratory attempted to address some of the limitations of the previous studies and examined developmental changes in elbow and wrist position sense acuity. Using a contralateral joint position matching paradigm, elbow position sense acuity was determined in large cohort of over 300 TD children between the ages of 5-17 years. The results revealed that bias did not change significantly from early childhood to late adolescence, while the precision, the reliability of the perceptual response improves steadily between early childhood and adulthood (Holst-Wolf et al., 2016a). Using a robotic device to passively displace the wrist, a second study tested children's wrist position sense acuity in an ipsilateral position matching task (Marini et al., 2017). The main finding was that wrist proprioceptive acuity continued to develop throughout middle childhood and early adolescence. Adult levels of performance were reached approximately by the age of 12 years. Both studies reported that the development of upper limb position sense between early childhood and adulthood could be characterized as a significant age-dependent increase in precision. Figure 4, for example, shows the data from Holst-Wolf et al. (2016a) that tested elbow joint position sense acuity in TD and young adults, using a manual manipulandum (Fig. 3B). For different elbow joint angles of a reference arm, an age dependent decrease of $SDP_{diff}$, the measure of precision, was evident.

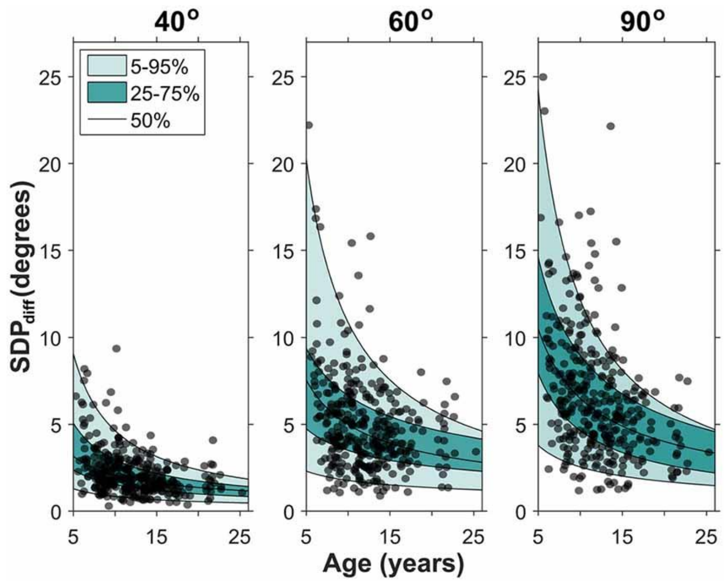


***Figure 4***. *Developmental changes in precision at different target elbow angles. SDP$_{diff}$: standard deviation of the differences between the elbow joint angle of a reference arm (40°, 60° or 90°) and the angle of the matching arm. Each subplot contains the SDP$_{diff}$ values of 334 participants. Figure is reprinted from Holst-Wolf et al. (2016a)*

After investigating the two proximal arm joints, project 2 was set to close the gap in our understanding of the development of upper limb position sense by examining finger position sense as the most distal segment of the arm. This was completed using the assessment device developed for project 1.

## Vibro-tactile stimulation (VTS) and its potential influence on limb position sense acuity

The contribution of mechanoreceptors other than proprioceptors may be also significant for limb position sense. Tsay et al. (2016) proposed that afferent signals from skin and joints may contribute to the estimation of a limb's position in space. Yet, the contribution of cutaneous input to limb position sense, especially tactile input from the mechanoreceptors in skin, is controversial. Clark et al. (1979) concluded that static knee position sense does not depend on sensory input from the skin. Anesthetizing the skin near the knee joint did not influence people's performance in a knee joint position matching task. In contrast, Mildren et al. (2017) reported that reduced cutaneous feedback resulted in increased matching error and variability. Ulkar et al. (2004) have argued that additional tactile input provided through a sleeve-type bracing improved shoulder position sense. It could be hypothesized that the removal of any cutaneous input does not degrade limb position sense, but the augmentation of sensory input, for instance adding a sleeve, might be effective. Therefore, exploring the contribution of external cutaneous input to static limb position sense should be further tested.

Vibro-tactile stimulation is one method to augment the cutaneous input. It is known to alter afferent signals from the vibrated mechanoreceptors in muscles and skin (Bianconi & Van der Meulen, 1963; Brown et al., 1967). Firings of both types of mechanoreceptors contribute to joint position sense (Cohen, 1958; Moberg, 1983). A possible interaction of cutaneous and muscle afferents has been suggested (McCloskey, 1978), further supporting the effect of vibro-tactile stimulation on the joint position sense. The effect was tested for knee joints (Eklund, 1972), elbow joints (Gooey et al., 2000; Tripp et al., 2009), or shoulder joints (Hong et al., 2010). Recently, vibro-tactile stimulus on the unseen target finger was observed to improve the ability of the reaching finger to locate the position of the unseen finger (Mikula et al., 2018). However, this improved ability could be attributed to both enhanced proprioceptive acuity of the target finger and improved motor performance of the reaching finger. Therefore, project 3 aimed to observe the effect of vibro-tactile stimulus solely on static limb position sense, tested at the index finger.

## The neuroanatomy and neurophysiology behind vibro-tactile stimulation

It has been known that afferents of proprioceptors and cutaneous mechanoreceptors are both conveyed to the anterior posterior cortex (Brodmann areas 3, 1 and 2) via the dorsal column – medial lemniscus pathway (Fig. 5).

The ascending fibers originating from tactile mechanoreceptors such as Pacinian and Meissner's corpuscles form synaptic connections with dorsal horn neurons located at the spinal cord of the same level or nearby levels. These neurons project to the lateral cervical nucleus (LCN) at C1 and C2 of the cervical spinal cord via dorsolateral funiculus (DLF). Fibers from the LCN decussate, project to medulla and join medial lemniscus (ML). Later, ML projects to the ventral posterolateral nuclei (VPL) of the thalamus and eventually to the Brodmann area (BA) 3b within the primary somatosensory cortex (Delhaye et al., 2018; Kaas, 2012).

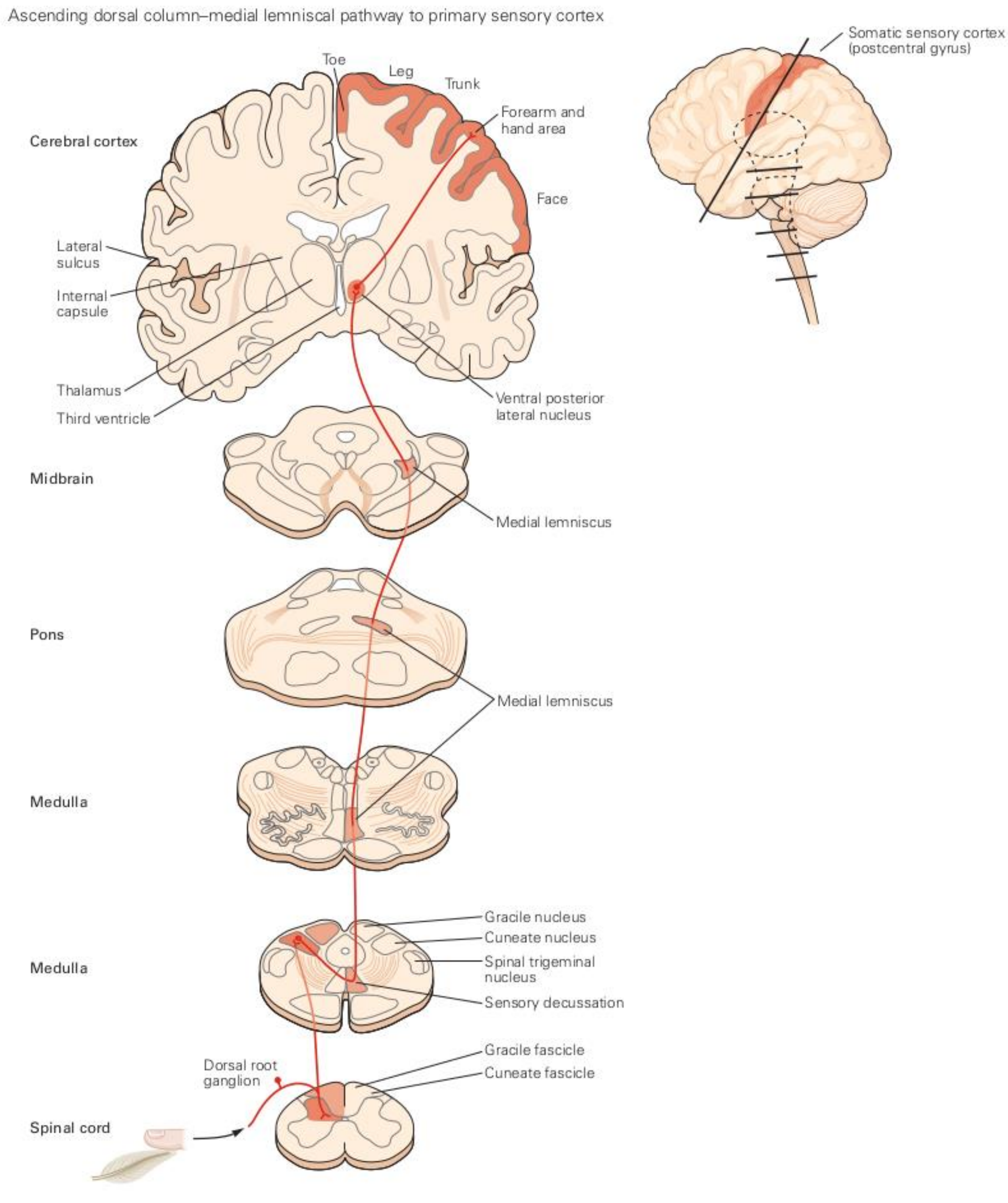


***Figure 5**. A diagram showing the dorsal column – medial lemniscus pathway. Afferents of proprioceptors and cutaneous mechanoreceptors of a finger travel along this pathway to reach the hand area of primary sensory cortex (anterior posterior cortex). Reprinted from Kandel et al. (2021).*

Proprioceptive input, while also conveyed via the dorsal column – medial lemniscus pathway, passes the rostral shell of ventral posterior nuclei and is transmitted to BA 3a in monkeys (Cusick et al., 1985; Padberg et al., 2009) and human beings (Ohye & Narabayashi, 1979; Ohye et al., 1993; Ohye et al., 1989). Disparate cortico-thalamic pathways for two different senses were associated with no convergence of vibro-tactile and proprioceptive input (Ohye et al., 1989). At the cortical level, however, reciprocal connections of the neurons in 3b to those in BA 3a are reported (Burton & Fabri, 1995; Krubitzer & Kaas, 1990). Other studies have observed the multimodal response of the neurons in the primary somatosensory cortex to proprioception and vibration (Cohen et al., 1994; Kim et al., 2015), further supporting the idea that interaction between proprioception and vibro-tactile sense could occur at a higher level. These would increase the feasibility of the effect of VTS on proprioceptive acuity.

## Project 1: Design and develop a system for the objective, quantitative assessment of finger position sense acuity

This project derived from cooperation with Dr. Hannah Block from the Sensorimotor Neurophysiology Laboratory at Indiana University. Her group had developed a tablet-based assessment system (Block et al., 2019; Hoseini et al., 2015) to measure finger position sense.

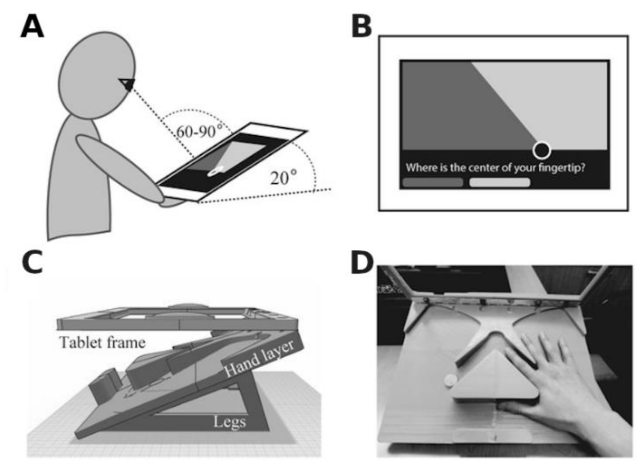


***Figure 6**. The tablet-based finger position sense acuity assessment system developed by Dr. Block and colleagues. **A**. A user would sit in front of an angled tablet with the dominant hand placed underneath it during an assessment. **B**. Assessment display. The circle indicated the position of the metacarpophalangeal joint. The task was to choose one of the two colored areas as the location above the index fingertip. **C**. The design of the stand where the tablet was placed. **D**. A bird-eye view of the tablet stand. Index finger of a user was placed at a pre-defined position. All figures from Block et al. (2019).*

An assessment using the system begins with a user placing the dominant hand at a pre-defined position (Fig. 6). A tablet is placed on top of the hand, presenting a rectangular display divided into two colored areas that appeared on the tablet screen. The user is asked to indicate which of the two areas is placed above the index fingertip. The diagonal line dividing the rectangular display moves closer to the actual index finger position by an initial step size of 15° when the user's response is correct and moves away from the finger when the answer is incorrect. A series of correct responses would move the line closer to the actual index finger position and eventually make the line cross the finger position. When the line crosses the index finger and the user's response is correct, the line changes its movement direction and again approaches the actual index finger position by half of the previous step size. The task was similar to that of a discrimination assessment. Nonetheless, the two stimuli of different modalities (vision and proprioception) were compared, unlike typical proprioceptive discrimination assessments where no visual input is available to a user.

While the system was mobile and simple to operate, there were three limitations.

1) Inter-individual variability in hand/finger size could not be accommodated because a fixed-size tablet was used.
2) The sensitivity of the assessment system was low at 1.25°. Thus, the system could not measure a person's ability to discriminate stimuli with an angular difference below 1.25°.
3) Haptic inputs from the tablet touching the back of a user's hand and the depressions prepared to position the index finger (Fig. 6D) were not controlled.

Consequently, researchers from HSCL agreed to work together with those from the Sensorimotor Neurophysiology Lab. This collaboration begot project 1 of this dissertation, and the focus was to address these limitations and develop a finger position sense acuity assessment system with greater sensitivity.

## Specific aims

**Aim 1**: **Design and develop a device for the assessment of position sense acuity of the index finger that overcomes the limitations of the device by Block et al. (2019)**

**Aim 2**: **Develop and implement new software to measure finger position sense acuity that can determine perceptual *bias* of and *precision*.**

**Aim 3**: **Establish the reliability of the device and assessment procedure.**

## Device description

To accommodate users with different hand and finger sizes, the new assessment system was designed to work with tablets of varying display dimensions. The first generation had bars sliding vertically and horizontally installed on the tablet frame to expand the space for tablet placement. To increase the sensitivity of the system, an adaptive algorithm with a step size of 0.2 ° was implemented. Finally, to reduce the amount of haptic input to the index finger, two pins instead of depressions were used to signal the correct position of the index finger. The entire tablet frame was placed parallel to the hand layer and could slide vertically to adjust different hand thicknesses. A summary of the research and development efforts was published in Oh et al. (2020).

The sliding bars of the tablet frame, as well as the sliding frame itself, turned out to be time-consuming to fix the positions. Consequently, the second generation of the system replaced the tablet frame with a layer having only one tablet position adjustment bar. The height of the layer was adjusted by inserting blocks underneath it. For all three projects of this dissertation, this second-generation system was used. The complete system comprised two components: A tablet stand, and a tablet executing the assessment software.

## Tablet stand

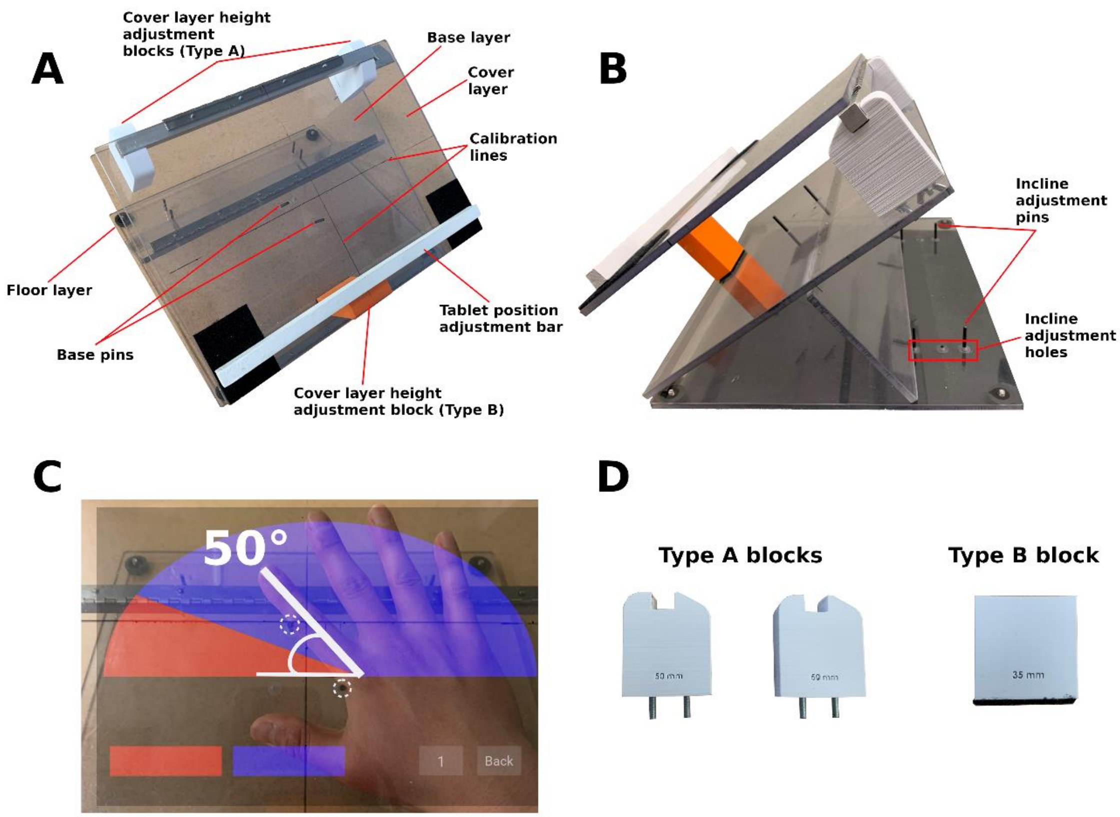


***Figure 7***. *The tablet-based finger position sense acuity assessment system further developed in project 1.* ***A***. *Bird's eye view of the tablet stand with components of the cover layer and the base layer identified.* ***B***. *Side view of the stand with components of the floor layer identified.* ***C***. *A tablet and user's dominant hand placed on the stand. The two base pins (white circles) would ensure the angle between the horizon of the visual display and the index angle to be 50°.* ***D***. *Cover layer height adjustment blocks. Type A blocks are fixed to the top corners of the base layer by closing the screws at the bottom. Type B blocks are fixed to the bottom of the base layer by a Velcro tape attached to it. Height of the blocks varies from 25 mm to 60 mm by the step size of 5 mm.*

The main frame of the tablet stand was assembled with 6mm polycarbonate sheets. Other parts were designed using *SolidWorks* software and 3D-printed using an *Ultimaker Original+ 3D printer* with polyactic acid (PLA) filaments. The stand contained the followings:

1) **Cover layer** is for placing the tablet running the mobile application. The tablet is placed by aligning two intersecting lines on the layer with the corresponding lines of the tablet display. The tablet position adjustment bar would fix the position (Fig. 7A). Tablets from 7 to 12.9 inch display size (17.78 to 32.77 cm) are compatible with the stand.
2) **Base layer** is where the dominant hand of a user is placed. A pair of base pins would be inserted into the holes on the layer (Fig. 7A & C). The pins ensure that the angle between the horizon of the visual display from the tablet and the index finger is 50° (Fig. 7C).
3) **Floor layer** has three pairs of incline adjustment holes (Fig. 7B). The base layer could be elevated from 25° to 35° with an increment of 5°.
4) **The height adjustment blocks** for the tablet support are designed to accommodate hands of different thicknesses and range from 25mm to 60mm with 5mm increments (Fig. 7D). Type A blocks are placed at the top corners of the base layer by closing the screws and type B block is placed at the bottom of the same layer with a Velcro tape attached to it.

## Assessment software

The software was coded using *Python* 3.6 programming language. Once executed, it presented an interactive assessment environment, in which the tablet display was dissected into two colored areas divided by a diagonal line originating from the center of the index metacarpophalangeal (MCP) joint (Fig. 8). The software adjusted the visual display dimensions based on the three anthropometric measures of the user: 1) length of the index finger from MCP joint to the fingertip, 2) center of the MCP joint relative to the edge of the hand, and 3) the width of the finger at the proximal interphalangeal joint. The height of the colored display was determined by the user's finger length so that the bottom of the display crosses the center of the user's MCP joint.

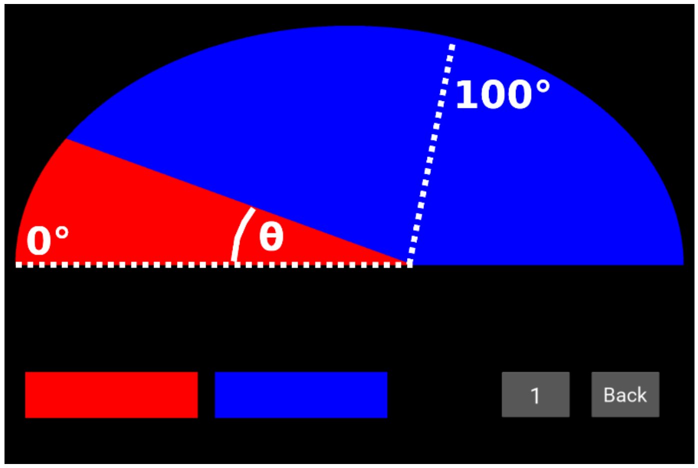


***Figure 8***. *A sample visual display showing a semi-circular shape divided into two colored zones. The area of each zone changed between trials as defined by the inclination angle (θ) of the border between two zones (range: 0° - 100°). For the left-handed participants, the display was flipped with the left-hand index finger positioned at an inclination angle of 130°.*

## Operation of the assessment system

At first, a user completes the Edinburgh Handedness Inventory Questionnaire (Appendix A) to identify the dominant hand, which becomes the tested hand. The anthropometric measures from the index finger of the dominant hand are collected and the dimensions of the test display are calculated accordingly. The user then sits in front of the system and places the dominant hand on the base layer at the above-described test position. The top base pin is removed and a medical tape is used to fix the position of the index finger, preventing finger motion during the assessment. Next, the cover layer with a tablet is placed over the user's hand. Blocks of appropriate height are inserted between the cover and the base layer to assure that the cover layer does not touch the hand.

In each trial, the user views a semicircular display on the screen of the tablet. The semicircle is divided into two sections. Subsequently, the user judges the perceived location of the occluded index finger relative to the colored areas of the visual display (e.g., the finger is under the red or blue area). Based on the judgment, the user presses the button of the same color at the lower portion of the display. The response is coded in two dimensions: 1) area chosen (“left” vs. “right”) and 2) correctness (1: the chosen area is truly above the index fingertip vs. 0: the chosen area is not above the fingertip). The correctness for each trial is used to update the inclination angle (θ) of the border between the two areas for the subsequent trial (possible range: 0º – 100º) using an adaptive *psi-marginal algorithm* (Appendix B). When the user makes a correct perceptual judgment, the border moves towards to the actual finger position as determined by the adaptive algorithm. With an incorrect judgment, the border moves away from the actual finger position. Before testing, the user performs six practice trials to become familiar with the task. The actual testing consists of 50 trials, which take approximately 10 minutes to complete. For left-handed users, base pins are relocated so that left-handers could keep their index finger positioned at 50º relative to the horizon while placing their hands on the tablet stand. The visual display was also flipped so that the increment of θ could occur at the right to the index finger.

## Measurements

The software stores the user responses for the 50 assessment trials. Figure 9 shows the pilot data from a participant. Filled circles indicate that the user correctly judged one’s finger position with respect to the visual display. The hollow circles indicate incorrect judgments. Each response is associated with one trial and the inclination angle (θ) presented during that trial.

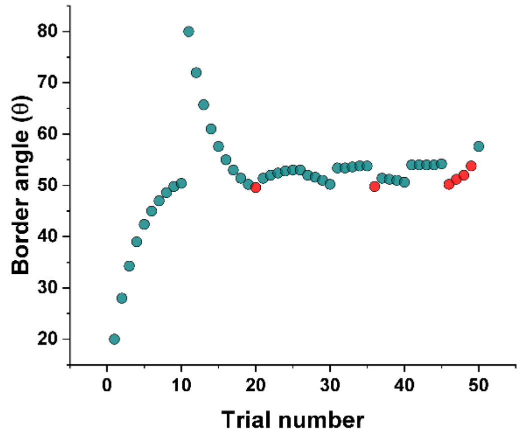


***Figure 9****. A scatter plot depicting the assessment data of a single user. Each data point indicates the inclination angles presented during the assessment. Cyan circles are correct responses and the red circles are incorrect responses.*

Two outcome measures are calculated from the responses: ΔPSE and Uncertainty Area (UA). ΔPSE and UA are the measures of finger position sense *bias* and *precision*, respectively. To obtain the two measures, the response of choosing the left colored area as the index finger position is coded as 1 and 0 otherwise for a right-handed user. For a left-handed user, it is vice versa. Subsequently, these angle-judgment data are fitted to a cumulative log-Weibull function using the Python psignifit4 package (Schütt et al., 2016). The fitted function of one participant's data is presented in Figure 10. Based on the obtained function, the *point of subjective equality* (PSE) is determined as the inclination angle associated with a 50% probability of choosing the left area of the display. Finally, two measures of finger position sense are derived: First, the difference between PSE and the veridical finger position (ΔPSE) was computed as a measure of *bias*. A smaller value of ΔPSE indicates a lower perceptual bias or higher acuity. Second, the corresponding uncertainty area (UA) is determined as the difference between inclination angles at the $25^{th}$ to the $75^{th}$ percentile of judging left. A smaller value of UA indicated an increase in *precision*.

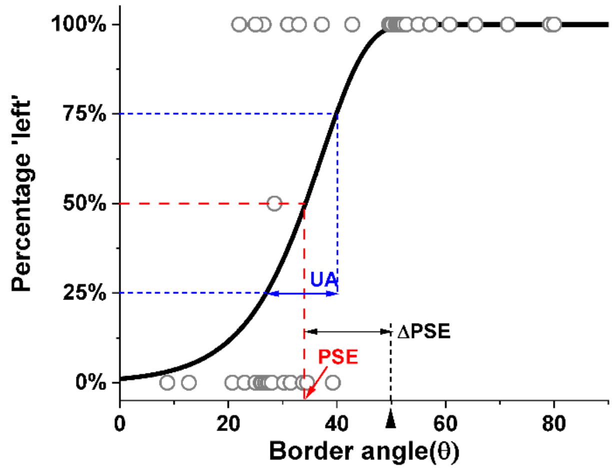


***Figure 10***. *An exemplar psychometric function illustrating how ΔPSE and UA are obtained from the function. Each open circle indicates the percentage of judging the finger position in the "left" zone for a given inclination angle.*

## Reliability of the system

The reliability of the system was established by testing 5 healthy individuals (3 Females; mean age: 25 ± 3.6 years) two times with the interval of 2 days. Participants followed the procedure described above to complete the assessment. To examine how consistent individuals were over the two assessments, intra-class correlation (ICC) was calculated for each measure, ΔPSE and UA. Both reported high ICC values (Table 1), indicating that participants were consistent in their performance on the assessment system.

***Table 1***. *Intra-class correlation coefficients (ICC) for the reliability of the assessment system*

| Measure | ICC | F(4,5) | p-value |
|---|---|---|---|
| ΔPSE | 0.891 | 17.4 | 0.00387 |
| UA | 0.804 | 9.19 | 0.0159 |

## Conclusion

The first aim of the project was to design and develop a system for assessing the index finger position sense acuity. The second aim was to develop and implement an assessment software that objectively and quantitatively measures the two aspects of the sense, *bias* and *precision*. The two aims were achieved after two iterations of R&D efforts, generating a publication and a ready-to-use assessment system. The new system accommodated individuals with diverse hand and finger sizes and demonstrated a measurement sensitivity of 0.2°. Potential haptic input to the index finger was controlled as well. The third aim of the project, establishing the reliability of the system, was achieved by obtaining significant ICC values from users tested multiple times.

It is important to recognize that the system does rely on neural processes of multimodal sensory integration. The assessment requires the user to use proprioceptive signals of the index finger and make judgments on finger position relative to a visual display. Compared to established methods that rely on procedures in which a limb segment is passively displaced, this assessment is simple and does not need a robotic device to displace the limb. The fast and interactive nature of the assessment makes it suitable for examining finger position sense in young children or people with movement deficits due to impaired neuromotor control. This system can generate objective estimates of the finger position sense acuity in 10 minutes. Thus, the system has the potential to be used as a quick diagnostic tool for young children and adults with proprioceptive deficits.

## Deliverable

**Oh, J.,** Mahnan, A., Xu, J., Holst-Wolf, J., Block, H., & Konczak, J. (2020, April). A System for the Objective Assessment of Hand Proprioceptive Function in Pediatric and Adult Populations. In *Frontiers in Biomedical Devices* (Vol. 83549, p. V001T10A016). American Society of Mechanical Engineers.

## Project 2: Characterize the typical development of finger position sense from late childhood to adolescence

### Specific aim

**Characterize finger position sense acuity in a sample of typically developing children, adolescents and young adults**. The assessment system of Project 1 was used to measure ΔPSE and UA of the proprioceptive acuity across the developmental span in children at age between 8 to 17 years and adults ranging from 18 to 35 years. The hypothesis was that there is an age-associated increase in precision and decrease in bias. A significant reduction in UA and/or ΔPSE would verify this aim.

### Methods

#### Participants

A total of 138 child participants (13 left-handed, 76 female, age range: 8 years 6 months ~ 17 years 11 months) were recruited at the 2021 Minnesota State Fair. In addition, 14 adults (2 left-handed, 11 female, age range: 19 years ~ 35 years) from the University of Minnesota participated. All participants had normal or corrected to normal vision and no previous history of neurological disorders. At the time of testing, no participant presented with orthopedic symptoms on their hands that could have influenced perceptual judgment. All adult participants gave written informed consent in accordance with the Declaration of Helsinki. Appropriate parental consent and child assent was obtained before data collection for all child participants. The study was approved by the Institutional Review Board of the University of Minnesota.

## Apparatus

We used the assessment system developed in Project 1. To accommodate different hand sizes of the participants, two tablets were used: Microsoft Surface Go (10.1'' display) and Samsung Galaxy Tab A (8.0'' display).

## Experimental protocol

All participants followed the same experimental protocol described in Project 1: Operation of the system.

## Measurement

Once an assessment was completed, two measures – ΔPSE and UA – were obtained. To calculate the UA value, data were fitted with a Log-Weibull psychometric function using the *Python* psignifit toolbox (Schütt et al., 2015).

## Statistical Analysis

A Shapiro-Wilk test was performed to test the assumption of normality for both data sets of ΔPSE and UA and a Levene's test was conducted to confirm the assumption of homogeneity of variance. Both assumptions were not violated. All child participants were grouped according to chronological age in bins of a size of 2 years. This was the smallest bin size that assured an approximately equal number of children per bin. Adult participants (18 ~ 35 years) formed a single group. To determine age-dependent changes in ΔPSE and UA a two-way (AGE by GENDER; AGE had 6 levels and GENDER had 2 levels) Analysis of Variance (ANOVA) was performed for each outcome measure. Age groups that are significantly different from the adult group could reveal at what age range the adult level of ΔPSE or UA is achieved. Yielding a significant main effect for AGE triggered a post-hoc analysis using Tukey's HSD test to determine at what age bin the outcome measures differed significantly from those of adults.

## Results

### Bias did not change significantly from late childhood to early adulthood

The data in Figure 11 delineate the observed age-associated changes in ΔPSE, showing both individual and grouped data. Across the tested age range, the difference between the perceived and the physical index finger position was distributed around zero degrees (Fig. 11A). There was no age-dependent trend in estimating the index finger position towards the thumb or the middle finger across the tested age range. The slope of a linear fit on the data (Fig. 11A, red line) was 0.29 (p-value = 0.044), but the fit explained only 2 % of the variability of ΔPSE ($R^2_{adjusted}$ = 0.02).

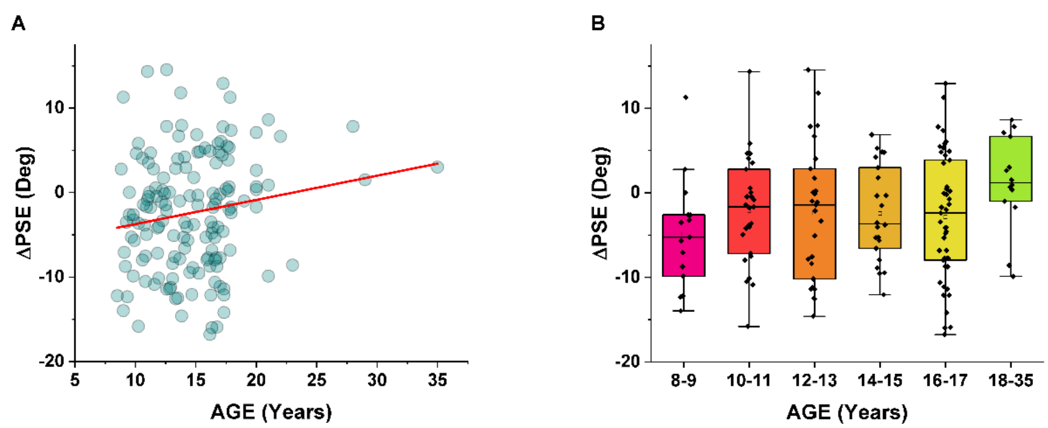


***Figure 11***. *ΔPSE values plotted across chronological age.* ***A***. *ΔPSE of all participants are plotted against chronological age. A perfect finger position match would have ΔPSE value of zero. A negative value indicates the perceived finger position to be closer to the thumb, and a positive value indicates the opposite. The red line indicates the linear fit of the data.* ***B***. *Boxplots for ΔPSE. No age group was significantly different from the adult group.*

A subsequent two-way ANOVA on ΔPSE with the factors AGE and GENDER yielded neither significant main effects (chronological age: $F_{5, 140}$ = 1.26, p-value = 0.28; gender: $F_{1, 140}$ = 0.86, p-value = 0.35) nor a significant interaction ($F_{5, 140}$ = 0.72, p-value = 0.61).

The number of participants per group as well as the group average of ΔPSE is described in Table 2.

***Table 2**. ΔPSE means and standard deviations (SD) by age group*

| AGE (years) | 8-9 (N = 15) | 10-11 (N = 27) | 12-13 (N = 27) | 14-15 (N = 22) | 16-17 (N = 47) | 18-35 (N = 14) |
|---|---|---|---|---|---|---|
| mean (SD) | -4.87° (± 6.53°) | -2.11° (± 6.35°) | -2.38° (± 7.96°) | -2.44° (± 5.63°) | -2.86° (± 7.41°) | 1.30° (± 5.56°) |

## Precision increased from late childhood to early adulthood

The individual data for UA revealed an age-related trend between the tested age range of 8 and 35 years (Fig. 12A). The inverse root model introduced in Marini et al. (2017) was used to fit the data. The fit explained 12 % of the variability of UA ($R^2_{adjusted} = 0.118$).

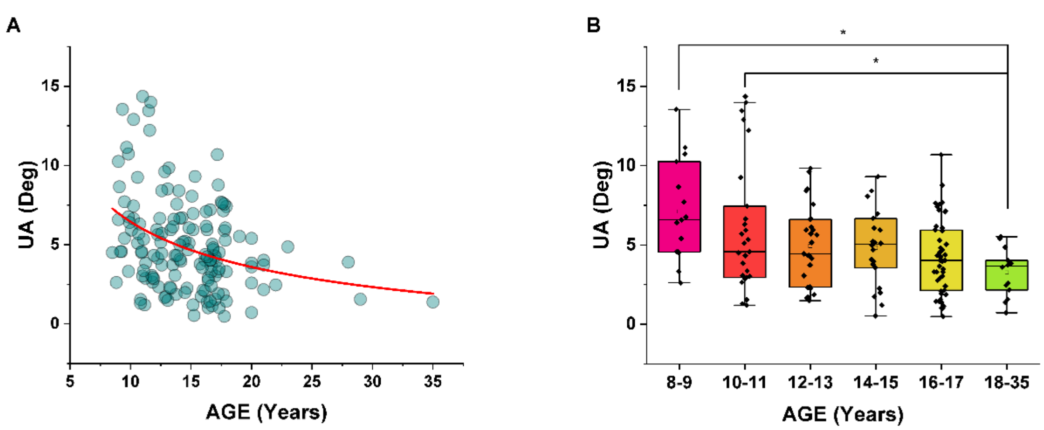


***Figure 12**. UA values plotted across chronological age. **A**. UA of all participants are plotted against chronological age. Participants with less variability in perceptual judgments of their index finger position would generate smaller value of UA. The red line is the inverse root fit on the data. **B**. Boxplots of UA. Two age groups, 8-9 years old and 10-11 years old were significantly different from Early Adulthood in terms of UA, the measure of precision. *: $p < 0.05$*

To examine any systematic developmental changes in precision, a two-way ANOVA of UA with the factors AGE and GENDER was performed. The effect for AGE was significant ($F_{5, 140} = 3.92$, p-value = 0.002), while the main effect for GENDER ($F_{1, 140}$ =

0.19, p-value = 0.67) and interaction effect ($F_{5, 140}$ = 0.85, p-value = 0.52) did not reach significance. A subsequent post-hoc analysis applying Tukey's HSD showed that UA at the age groups of 8-9 years (Mean = 7.12°, SD = 3.18°) and 10-11 years (Mean = 5.95°, SD = 4.08°) were significantly different from adults (Mean = 3.27°, SD = 1.5°, Fig. 12B).

***Table 3***. *UA means and standard deviations (SD) by age group*

| AGE (years) | 8-9 (N = 15) | 10-11 (N = 27) | 12-13 (N = 27) | 14-15 (N = 22) | 16-17 (N = 47) | 18-35 (N = 14) |
|---|---|---|---|---|---|---|
| mean (SD) | 7.12° (± 3.18°) | 5.95° (± 4.08°) | 4.93° (± 4.84°) | 4.84° (± 2.37°) | 4.22° (± 2.36°) | 3.27° (± 1.50°) |

## Discussion

This study concerned the development of proprioception. It is the first study to report systematic data on the typical development of finger position sense during late childhood and adolescence. We applied a fast, child appropriate, novel psychophysical test that yielded objective measures of proprioceptive *bias* and *precision* and collected data of a large cohort of TD and young adults. The main findings are: First, development of finger position sense from late childhood to early adulthood can be characterized as an age-dependent increase in *precision* with UA values reaching adult levels at approximately 12 years. In other words, the variability in perceptual judgment decreases with age. Second, typical development between late childhood to adulthood is not characterized by a systematic change in *bias* as measured by ΔPSE.

The results of this study on finger position sense are consistent with those of previous studies that examined position sense development of the wrist (Marini et al., 2017) or elbow (Holst-Wolf et al., 2016b). These reports showed that from late childhood the development of wrist and elbow position sense follows a similar developmental path than the one shown for finger position sense. With respect to position sense precision, the observable range at all three major upper limb segments was comparable across arm joints and did not reveal a proximal-to-distal gradient. The reported mean magnitudes of precision ranged between 7-9.6° in late childhood, dropped to 4.8-5° in adolescence and plateaued to approximately 4° in adulthood.

With respect to *bias*, we found no significant directionality in *bias* of finger position sense. If there were signs of an age-related change in bias, we would have observed that children at a particular age show either a tendency to perceive finger position closer to the thumb or to one's middle finger. However, our cross-sectional data provide no evidence that typical development from late childhood shows such shifts in bias (see Fig. 11B). A significant increasing linear fit on ΔPSE data might signal that across age from 8 to 17 years old, the tendency to perceive the index finger closer to the thumb would be weakened. However, given the variability of ΔPSE values, of which only 2% is explained by the fit, such a conclusion could not be made too soon. At the other end of the life-span, age-related shifts in bias have been reported for haptic perception in older adults and people with Parkinson's disease (Konczak et al., 2012). At present, we do not know, whether the development of proprioceptive acuity during the first years of early childhood is characterized as a development toward a smaller bias with older children exhibiting lower position sense thresholds than younger children. Unfortunately, there are no comprehensive data on children younger than 5 years.

## Neural changes underlying the development of finger position sense

Proprioception and motor control are intricately linked. Proprioceptive afferents are used by the nervous system to regulate muscle tone, spinal stretch reflexes, and postural reflexes. Moreover, cerebro-cerebellar and somatosensory motor cortical networks process proprioceptive signals for voluntary motor control. It is firmly established that the networks undergo structural and functional changes during development. Yet, the neural mechanisms underlying proprioceptive development in humans are not fully delineated. Based on current neurophysiological knowledge one should consider if there are features of neural development that can be consistent with the markers of proprioceptive development observed here. It is unlikely that morphological changes in proprioceptive mechanoreceptors can explain such perceptual development, because muscle spindles are not going through significant morphological changes after 3 years of age in humans (Österlund et al., 2011). However, there is evidence of an age-related increased sensitivity of the muscle spindles represented as increased stretch reflex responses from 7 to 11 years (Grosset et al., 2007). Improved muscle spindle sensitivity will result in afferent signals that allow the proprioceptive system to differentiate between smaller differences in finger position, which could translate in more precise perceptual judgments.

It is further known that functional organization associated with proprioceptive information processing undergoes development that lasts into late adolescence. Investigating how tibialis anterior muscle vibration evokes the perception of illusory movement revealed that adult patterns of cortical activation were already present in early adolescence in the core regions of the associated proprioceptive processing network (Cignetti et al., 2016). However, the functional connectivity topology of the network comprising cingulate, prefrontal and ventrolateral cortices, basal ganglia and thalamus was larger in children at early adolescence and had narrowed in late adolescence to the level of adults. In summary, there is converging evidence that the observed age-related changes in proprioception from late childhood and adolescence to adulthood are not explained by structural changes in the peripheral nervous system (e.g., tract myelination or mechanoreceptors), but by functional changes in the associated subcortical and cortical central networks.

## Limitations of the study and its method

The assessment could control for potential contribution of motion sense in measuring position sense by fixing the hand and finger position. While the assessment did not rely on joint displacement, it requires to make a perceptual judgment about finger position sense through another sensory modality, vision. That is, a perceptual judgment about joint position requires to the simultaneous processing of proprioceptive and visual signals. Consequently, it does not reflect “pure” proprioception, but relies on the processing of bimodal sensory information. Still, this study differs from previous studies that investigated the ability to integrate visual and proprioceptive information. Typically, studies with such an aim would introduce a target represented with two different modalities- vision and proprioception (Gori et al., 2008; King et al., 2010). The two modalities would each provide information about the target to be identified. This study does not have a target provided in different modalities. Rather, each sensory input constitutes a unique stimulus to compare with one another. Consequently, change in children’s ability to integrate vision with position sense could not be an explanation to our finding.

Another issue raised in proprioceptive testing concerns the potential confound of working memory that arise in traditional ipsilateral matching tasks. In ipsilateral matching an observer experiences a distinct joint position before the joint will be rotated to a second position, and then subsequently judges the first against the second joint position. This procedure requires the observer to “hold” the first position in working memory in order to make a judgment. Given that spatial cognition and working memory also develop through childhood, any such tests have a potential confound. Thus, it is an advantage of the present method that the judgment about finger position is made current and does not rely on spatial working memory.

Finally, the child appropriateness of the test should be discussed. Knowing that especially younger children have a limited attention span and may have difficulty focusing over a longer period of time, it is important that the test keeps the child’s attention and is quick. In comparison to traditional psychophysical procedures, the current test is relatively fast (< 10 minutes) and is simple to understand. Nevertheless, it does require attentional focus and we found in the current study that children younger than 8 years old may not be able to hold such focus to successfully complete the test.

## Conclusion

The aim of project 2 was to delineate the typical development of finger position sense. Using a new assessment tool, we determined finger position sense acuity in a large cross-sectional sample of 138 children from 8 to 17 years of age. We found no evidence that children in this age range exhibit age-related changes in position sense bias. Measures of *bias*, the systematic error between the person’s perception and the veridical finger position are already comparable to the adult level at the age of 8 years. Our data show that *precision*, the amount of uncertainty in the person's perception, still undergoes development between late childhoods to adulthood. Children under twelve exhibited a significantly greater UA than adults while adolescent children (13-17 years) exhibited no significant differences when compared to adults. This implies that the typical development of finger position sense from late childhood to adulthood is characterized as an age-dependent increase in proprioceptive precision and not as a change in bias. The current assessment system and the large database on typical development of finger position sense generated in this study will enable future work on pediatric populations and patients with suspected proprioceptive dysfunction.

## Deliverable

### Submitted journal article

Oh, J., Mahnan, A., Xu, J., Block, H., & Konczak, J. (2022). The typical development of finger position sense from late childhood to adolescence. Submitted to *Journal of Motor Behavior*.

## Project 3: Examine the effect of vibro-tactile stimulation on the finger position sense acuity

Project 3 aimed to observe the effect of VTS on static limb position sense. Particularly, VTS at the fingertip was expected to enhance or sharpen the sense, leading to decreased amount of *bias*. The rationale for this assumption was based on a previous report on how VTS assisted people in improving the localization of targets. Mikula et al. (2018) asked participants to reach target positions signaled by the left index fingertip placed underneath a reflective mirror. The two experimental conditions all participants experienced were: 1) vibration was applied on the index fingertip before reaching and 2) no stimulation at the left index fingertip. The vibration resulted in a significantly less error compared to its absence. An error was defined as the horizontal distance between the actual target position and the reached position. Researchers argued that additional tactile input enhanced the localization of the proprioceptive target. Consequently, a result similar to this finding was anticipated: VTS on the index fingertip may reduce the amount of *bias*.

It is still not known if VTS applied to any other area of the index finger may result in a similar reduction of *bias* or not. This is certainly a point to consider when one is interested in augmenting proprioception or substituting touch for impaired proprioception by VTS. Mikula et al. (2018) did not apply VTS to any other region of the target finger. VTS on any area of the finger may have generated the same finding. This was considered, however, unlikely based on the distribution of cutaneous mechanoreceptors in a hand. Fingertip has the highest density of receptors compared to any other area (Ciano & Beatty, 2022). Therefore, a more acceptable expectation was that the effect of

VTS on the finger position sense acuity would be weaker or none when applied to any area other than the fingertip. To explore this idea, project 3 also prepared another index finger area to stimulate. The lateral side of the index finger between the metacarpophalangeal (MCP) joint and the proximal interphalangeal (PIP) joint was targeted (Fig. 13B).

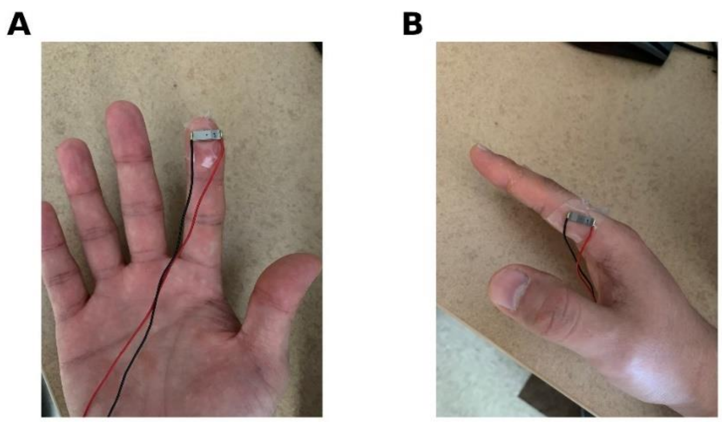


***Figure 13****. Two positions of vibro-tactile stimulation.* ***A****. The tip of the Index finger.* ***B****. The radial side of the index finger between the metacarpophalangeal joint and the proximal interphalangeal joint.*

Project 3 also sought to determine if there is a cortical change associated with the altered finger position sense. Proprioception, touch, pressure, or vibration are different modalities of somatosensation processed in the somatosensory cortex. Consequently, a change in proprioceptive acuity could be represented by the altered excitability of the somatosensory cortex.

One established method to observe the response of the somatosensory cortex is recording somatosensory evoked potentials (SEPs) and quantifying characteristic measures from the recording (Cracco & Cracco, 1976; Giblin, 1964). Upper limb SEP recording involves the electrical stimulation of the median nerve near a person's wrist. Recordings from the electrodes placed over the scalp, specifically the area over the somatosensory cortex area, would reveal characteristic peaks at different time points after the onset of a stimulus. Figure 14 shows an example of SEP. Different peaks, both positive and negative, are indicated with corresponding scalp images that show activation levels of different cortical areas. Peaks are named after their directions and the time they appear. For example, P45 in figure 14 is a positive peak that appears around 45 milliseconds after the onset of the stimulus. N60 in the same figure is a negative peak at 60 milliseconds.

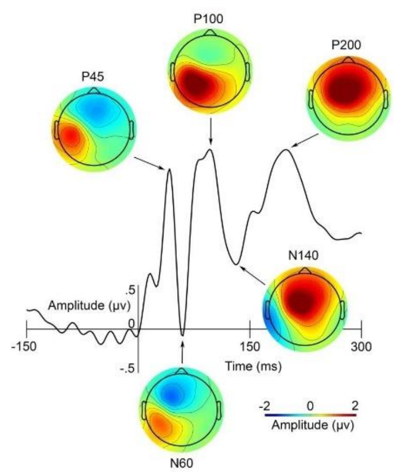


***Figure 14****. An example image of SEP showing peaks at different time points. The time zero indicates the onset of stimulation. Peaks are named after their directions and time since the onset of stimulus. For example, P100 indicates a positive peak that appears near 100 milliseconds after the presentation of stimulus. Figure reprinted from Miller et al. (2019).*

## Use of P100 as a measure of somatosensory processing

VTS was chosen as the means to evoke cortical responses because it is known to influence proprioception (Krueger et al., 2017; Risi et al., 2019). In the past, researchers tested VTS of different frequencies and reported that the first two distinct peaks within 200 milliseconds after the onset of vibration are P50 and P100 (Hämäläinen et al., 1990), both in the hemisphere contralateral to the stimulated side.

According to Desmedt and Robertson (1977), P50 is an *early* component (peaks 18-70 milliseconds post-stimulus) whereas P100 is a *mid-latency* component (70 to 200 milliseconds post-stimulus). In particular, mid-latency components are thought to be serving conscious somatosensory processing (Arnfred, 2005; Desmedt & Robertson, 1977; Eimer & Forster, 2003; Kida et al., 2004; Kida et al., 2006; Schubert et al., 2006). A group of researchers further suggested that components after 80 milliseconds might indicate the integration of sensory information (Tanaka et al., 2008). The focus of project 3 was on the perceptual experience of the index finger position. Consequently, SEP component relevant to conscious processing, P100, was chosen as the measure of the somatosensory cortex response to a stimulus.

### P100 changes relevant to enhanced proprioception

Studies on SEPs of individuals with specific training designed to develop sensorimotor skills suggested that the response of the somatosensory cortex could be altered by such pieces of training (Bulut et al., 2003; Iwadate et al., 2005) with experienced athletes having shorter latencies or greater amplitudes of peaks as a sign of improved skills. Yamashiro et al. (2013) described how baseball players who practiced their hand and finger movements extensively showed shorter P100 latency, or the time between the stimulus onset and the peak, compared to other athletes such as swimmers or sprinters. These studies imply that features of P100 may change with long-term training that aims to enhance limb position sense. The change could be observed even in a short-term training. A single session training of using a hand-shaped tool to pick up balloons resulted in an increase in P100 amplitude among healthy individuals (Miller et al., 2019). Therefore, project 3 aimed to examine if latency or amplitude of P100 would be altered as a sign of temporarily enhanced somatosensory processing, expected from the potential integration of tactile and proprioceptive inputs.

## Specific aims

**Aim 1**: **Determine the effect of VTS on finger position sense acuity based on its application site**. The hypothesis is that VTS on the fingertip will decrease ΔPSE and ΔUA significantly while the stimulation on the lateral side will not result in such a change. A significant location-dependent effect of VTS would verify Aim 1.

**Aim 2**: **Delineate the effect of VTS on the neural activation patterns of the somatosensory cortex and associate it with possible perceptual changes as measured by ΔPSE and UA.** The hypothesis is that experiencing repeated VTS associated with the finger position estimation task will change P100 latency and/or amplitude. A significant increase in amplitude or decrease in latency would verify Aim2. The relationship between the altered latency or amplitude and the change in the behavioral measures will be examined to further support that observed neural changes are associated with the behavioral change.

## Methods

### Participants

33 healthy individuals (21 Females; mean age: 22.9 ± 3.3 years; 2 left-handed) were recruited from the University of Minnesota. All participants had normal or corrected to normal vision and no previous history of neurological disorders. At the time of testing, no participant presented with orthopedic symptoms on their hands that could have influenced perceptual judgment. All adult participants gave written informed consent in

accordance with the Declaration of Helsinki. The study was approved by the Institutional Review Board of the University of Minnesota.

## Apparatus

The assessment system described in Project 1 is used to monitor proprioceptive acuity before and after the intervention. Microsoft Surface Go (10.1'' display) was used.

To provide vibro-tactile stimulation, a piezo actuator (Fig. 15B) attached to a high-voltage piezoelectric driver (BOS 1901 by Boréas Technologies, Bromont, Canada) was used. The dimension of the actuator was 12 x 4 x 1.8 mm.

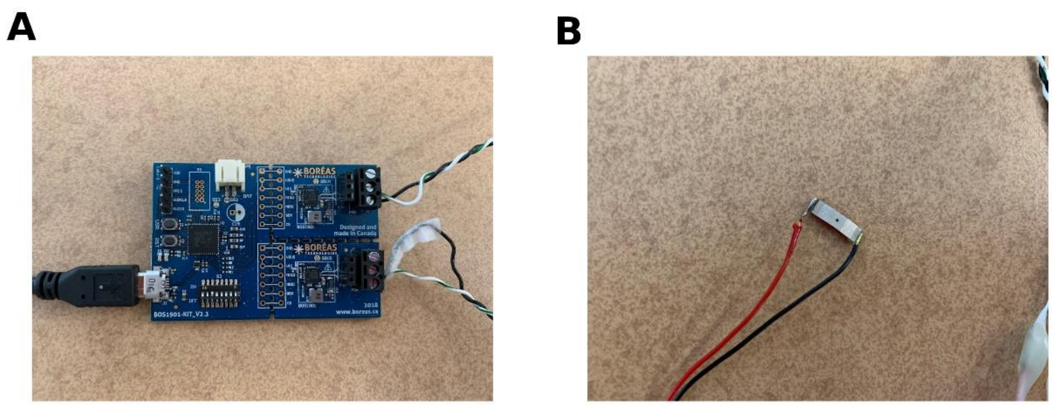


***Figure 15****. Devices used for vibro-tactile stimulation.* ***A****. High voltage piezoelectric driver (BOS1901). The cord on the left was connected to a mobile laptop.* ***B****. Piezo actuator attached to one of the two positions of the index finger.*

EEG was recorded using a DC amplifier (ANT Neuro, Hengelo, Netherlands). The amplifier was connected to a mobile laptop and a 64 channel EEG cap (Waveguard by ANT Neuro). The signal was recorded from 63 Ag/AgCl pallet electrodes mounted on the cap according to the extended 10-20 international EEG system and was monitored online through *eego*$^{TM}$ *software*. The ground electrode was placed on AFz. Skin impedances were kept under 20kΩ and the sampling frequency during recording was 500 Hz.

Experimental protocol

The study employed had a single treatment of VTS at one of the two sites. The first site was the area between the MCP joint and the PIP joint of the index finger. The second site was the fingertip. The site for each participant was predetermined by a random assignment.

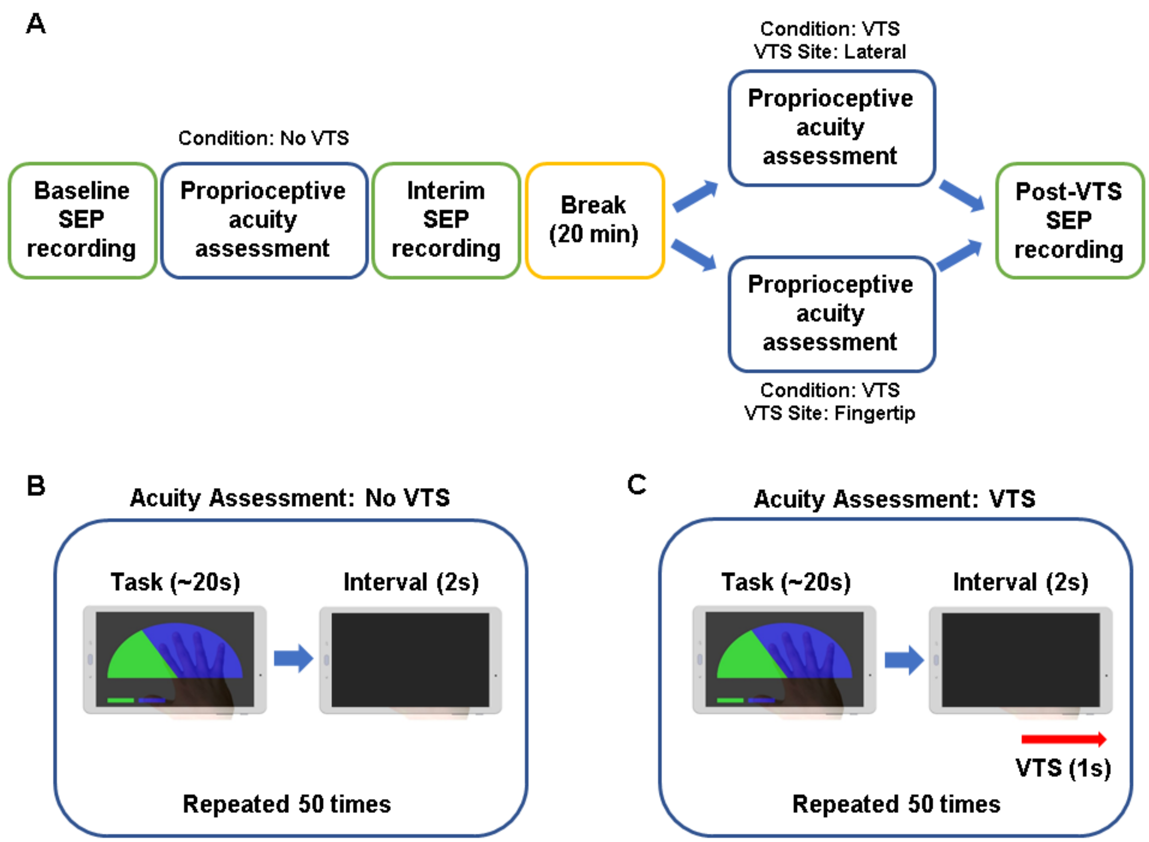


***Figure 16**. Schematic descriptions of the study procedure. **A**. All participants went through the same procedure up to a 20-minute break. After the break, each participant completed the acuity assessment with VTS applied at one of the two locations, followed by the post-VTS Somatosensory Evoked Potential (SEP) recording. **B**. During the assessment without VTS, each judgment task was followed by a 2 second interval and this was repeated 50 times. **C**. The assessment with VTS was similar to the baseline measurement except a 1 second VTS on the finger during the second half of the 2 second interval.*

The experiment took place at the HSCL, University of Minnesota. Participants sat on a comfortable chair and had the piezo actuator placed on the tip of the dominant hand's index finger to begin with the baseline SEP recording.

## SEP recording

Each recording presented VTS a hundred times. A 300Hz sine wave modulated with a rectangular signal was used for stimulation. The frequency was set to target the stimulation of Pacinian corpuscles (Bolanowski Jr & Zwislocki, 1984; Vallbo & Johansson, 1984). The stimulus duration was 20 ms, and the interstimulus interval (ISI) was 1000ms. During the recording, participants placed their stimulated hand and forearm on a table with the palm facing upward and relaxed. There were in total three SEP recordings: baseline, after the finger position assessment (Interim), and after the assessment with VTS (Post-VTS).

## Proprioceptive acuity measurement

Acuity assessment without VTS followed the protocol described in Project 1. When VTS was applied, the protocol was adapted from the original one. During the 2-second interval between two perceptual judgment trials, VTS of 30 Hz sine wave at the designated position was provided for the last second (Fig. 16).

## Measurement

Similar to the first two projects, two behavioral measures – ΔPSE and UA – were obtained from the data. For each participant, $\Delta PSE_{NV}$ and $UA_{NV}$ were acquired from the assessment without VTS and $\Delta PSE_{V}$, $UA_{V}$ from the assessment with VTS. ΔPSE values reflected the direction of finger position sense *bias* by different signs, shadowing the pure change in the magnitude of the *bias*. To observe the effect of VTS on the magnitude of *bias*, |ΔPSE|, the absolute values of ΔPSE were derived.

The two EEG measures, P100 latency and amplitude, were obtained after each EEG recording was preprocessed. The preprocessing procedure involved:

1) Signals were band-pass filtered. The lower cut-off frequency was set to 1Hz to address possible slow drift. The upper cut-off frequency was set to 40 Hz. Filtering was done using a zero-phase Finite Impulse Response (FIR) filter. With the 40Hz cut-off frequency, power line noise was filtered as well.
2) Each channel was re-referenced to the common average of all electrodes.
3) Segments of EEG recordings from 250 ms before the onset of VTS to 250 ms after the onset were extracted as data epochs. The mean of 250 ms preceding the stimulus was used as the baseline for epochs.
4) Independent Component Analysis (ICA) was performed with *picard* algorithm (Ablin et al., 2018) on all EEG channels. ICA was used to filter out potential artifacts from the signal.
5) An automated procedure to identify the independent components (IC) not categorized as brain signals, *ICLabel* (Pion-Tonachini et al., 2019), was implemented. Muscle artifacts arising from gulping or eye blinks could be effectively removed.
6) New EEG signals were reconstructed from the remaining IC's to extract two EEG measures: P100 latency and amplitude.

P100 was defined as the mean event-related potential (ERP) amplitude of 100 recordings from CP3 or CP4 (for left-handed participants) from 80 to 110 ms post-stimulus onset. CP3 and 4 are electrodes over the centro-parietal scalp region. Its amplitude corresponds to the positive voltage value of the peak, and its latency is the time between the onset of VTS and the peak.

### Statistical analysis

The effect of VTS on the finger position sense bias was analyzed in two different ways. To check if the direction of bias was influenced by VTS, a linear mixed model was fitted on ΔPSE data using two fixed effects: *VTS Condition* (No VTS vs. VTS) and *VTS Site* (“Fingertip” vs. “Lateral” side of the index finger). Random intercept at the *participant* level was included in the model, accounting for the repeated measurements of the same participants. To check if the magnitude of the *bias* was associated with VTS, another linear mixed model with the same configuration was fitted on |ΔPSE| data. To examine whether finger position sense *precision* was influenced by VTS or not, another linear mixed model with the same fixed and random effects was fitted on UA data.

For the two EEG measures from the electrode of interest, linear mixed models were fitted with *Time* (Baseline vs. Post-VTS) and *VTS Site* as the fixed effects and *participant* as the random effect. The distribution of residuals, as well as the random effects of all fitted models, were tested with the Shapiro-Wilk test to account for the normal distribution of the two. When a model violated the normality assumption, appropriate measures such as the transformation of the response variables were taken.

## Results

### VTS location did not have any directional effect on the finger position sense *bias*

To observe any stimulation site dependent change in ΔPSE, the scatterplot of the raw data was prepared (Fig. 17A). The line of equality, where $\Delta PSE_{NV}$ and $\Delta PSE_{V}$ are identical, was presented as a solid diagonal line.

Data showed a linear trend along this line with no distinction by *VTS Site* (see Table 4 for group means and standard errors). For example, if the reduction of the finger position sense *bias* did occur with the application of VTS, data points should be placed near the dotted line that indicates $\Delta PSE_V = 0°$, or the perceived finger position during the VTS condition coming near the veridical finger position. Neither VTS sites demonstrated such a trend.

***Table 4***. *Group means and standard errors (SE) of ΔPSE by VTS Site at two conditions.*

| | Fingertip | | Lateral | |
|---|---|---|---|---|
| | No VTS | VTS | No VTS | VTS |
| ΔPSE mean (SE) | 2.13° (1.23°) | 1.85° (2.08°) | 2.26° (1.88°) | 1.36° (1.56°) |

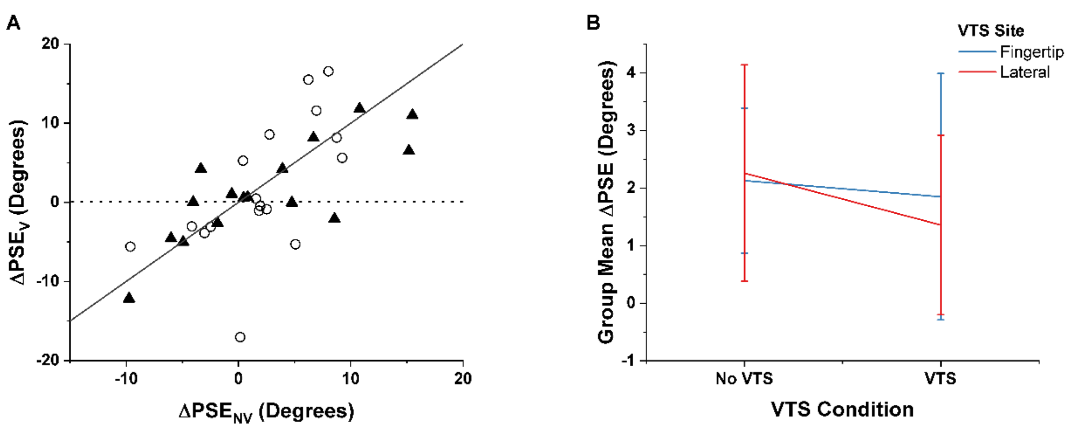


***Figure 17***. *Plots of ΔPSE data.* ***A***. *The scatterplot showing the relationship between $\Delta PSE_{NV}$ and $\Delta PSE_V$ based on VTS Site. Hollow circles indicate data of fingertip VTS group and solid triangles indicate lateral VTS group. The solid diagonal line is the line of equality. Data points show a linear trend along this line. The dotted line indicates $\Delta PSE_{NV} = 0°$. More data points would be aligned along this dotted line if the estimated finger positions during the VTS condition were closer to the veridical one than by those at No VTS condition.* ***B***. *The interaction plot of group mean ΔPSE values. VTS at both the fingertip and the lateral side of the index finger decreased group mean ΔPSE from no VTS condition to VTS condition, but this was not statistically significant. Error bars indicate SEs.*

A subsequent linear mixed model with VTS *Condition* and *VTS Site* showed no significant fixed effect as well as a significant interaction of the two (Table 5). This implied that VTS did not have a location-associated influence on the direction of perceived finger position.

*Table 5*. Type III Analysis of Variance Table of the mixed effects model on ΔPSE data with Satterthwaite's method.

| | Sum sq | Mean sq | NumDF | DenDF | F | p-value |
|---|---|---|---|---|---|---|
| Condition | 5.7567 | 5.7567 | 1 | 31 | 0.3548 | 0.5557 |
| VTS Site | 0.1088 | 0.10884 | 1 | 31 | 0.0067 | 0.9353 |
| Condition x VTS Site | 1.6122 | 1.6122 | 1 | 31 | 0.0994 | 0.7547 |

Fingertip VTS was associated with an increase in position sense *bias* magnitude while lateral finger VTS showed the opposite trend

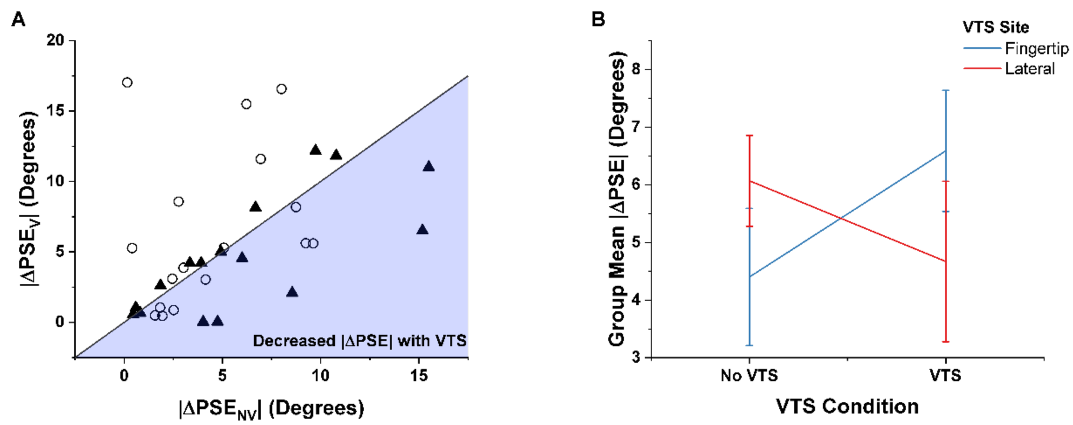


***Figure 18***. *Plots of |ΔPSE| data.* ***A***. *The scatterplot showing the relationship between* $|\Delta PSE_{NV}|$ *and* $|\Delta PSE_V|$ *based on VTS Site (symbol notation same as Figure 17). The shaded area represents decreased |ΔPSE| with VTS.* ***B***. *The interaction plot of group mean |ΔPSE| values. The crossover interaction shows that lateral VTS decreased mean |ΔPSE| of the group while the opposite was observed for fingertip VTS group. This interaction was statistically significant. Error bars indicate SEs.*

|ΔPSE| data showed a different trend (Fig. 18). Particularly, |ΔPSE| group mean increased from No VTS condition to VTS condition for fingertip VTS group while it was the opposite for the lateral finger VTS group (Table 6).

*Table 6*. Group means and standard errors (SE) of |ΔPSE| by VTS Site at two conditions.

| | Fingertip | | Lateral | |
|---|---|---|---|---|
| | No VTS | VTS | No VTS | VTS |
| \|ΔPSE\| mean (SE) | 4.40° (0.77°) | 6.59° (1.35°) | 6.07° (1.19°) | 4.67° (1.05°) |

As |ΔPSE| data followed a non-normal distribution, an appropriate transformation was done. The best estimate of the transformation exponent of the Box-cox transformation (λ) was calculated. Transformation followed an adapted formula of the original form of the Box-cox transformation, which was simply calculating the original values to the power of the exponent (Eq. 1).

$$y_i^{(\lambda)} = y_i^{\lambda} \qquad \textit{Eq. 1}$$

λ with the highest likelihood was 0.5, so the transformed data were the square roots of the original data. A linear mixed model was fitted to this transformed data. The model output showed that the interaction of VTS *Condition* and *VTS Site* was statistically significant (Table 7), with the group mean of |ΔPSE| increasing from No VTS to VTS condition when VTS was applied to the lateral side of the index finger and vice versa.

This was contrary to the hypothesis outlined in Aim 1 that fingertip VTS would increase the finger position sense acuity by reducing the systematic error, *bias*. In fact, lateral finger VTS was associated with the decrease in the group mean of systematic error's magnitude.

***Table 7****. Type III Analysis of Variance Table of the mixed effects model on transformed |ΔPSE| data with Satterthwaite's method. *: p < 0.05*

| | Sum sq | Mean sq | NumDF | DenDF | F | p-value |
|---|---|---|---|---|---|---|
| Condition | 0.00022 | 0.00022 | 1 | 31 | 0.0004 | 0.9838 |
| VTS Site | 0.01924 | 0.01924 | 1 | 31 | 0.0367 | 0.8493 |
| Condition x VTS Site | 2.36429 | 2.36429 | 1 | 31 | 4.5115 | 0.0418* |

Finger position sense *precision* was not influenced by VTS

UA, the measure of *precision*, did not show a VTS dependent change, not to mention any location-dependent change. When $UA_{NV}$ and $UA_{V}$ data were plotted simultaneously, data were spread across the line of equality (Fig. 19A).

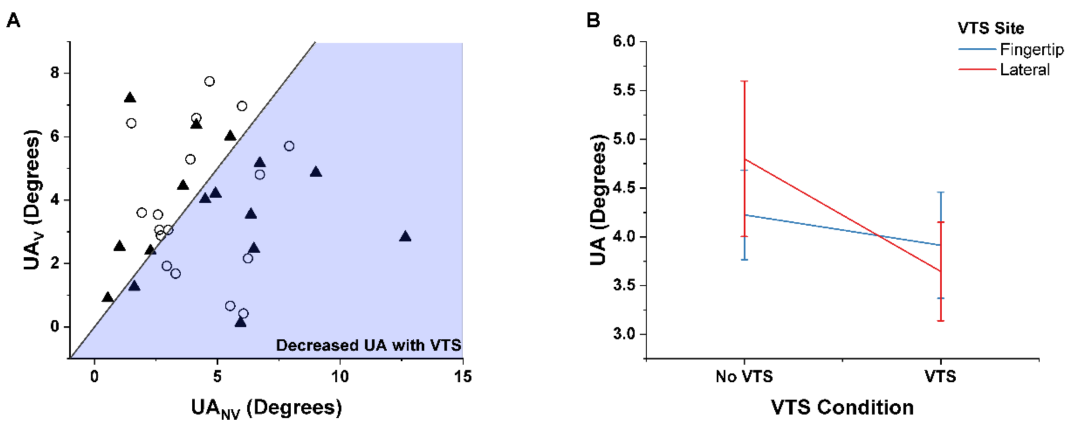


***Figure 19***. *Plots of UA data.* ***A***. *The scatterplot showing the relationship between $UA_{NV}$ and $UA_{V}$ based on the VTS Site (symbol notation same as Figure 17). The shaded area represents decreased UA with VTS.* ***B***. *The interaction plot of UA data. Both VTS Sites decreased UA from No VTS to VTS condition, but this was not statistically significant. Error bars indicate SEs.*

***Table 8***. *Group means and standard errors (SE) of UA by VTS site at two conditions.*

| | Fingertip | | Lateral | |
|---|---|---|---|---|
| | No VTS | VTS | No VTS | VTS |
| UA mean (SE) | 4.23° (0.46°) | 3.91° (0.55°) | 4.80° (0.80°) | 3.64° (0.51°) |

A subsequent linear mixed model reported no significant interaction effect of VTS *Condition* and *VTS Site* along with no significant fixed effect (Table 9).

***Table 9**. Type III Analysis of Variance Table of the mixed effects model on UA data with Satterthwaite's method.*

| | Sum sq | Mean sq | NumDF | DenDF | F | p-value |
|---|---|---|---|---|---|---|
| Condition | 8.8699 | 8.8699 | 1 | 31 | 1.6937 | 0.2027 |
| VTS Site | 0.3318 | 0.3318 | 1 | 31 | 0.0634 | 0.8029 |
| Condition x VTS Site | 2.9285 | 2.9285 | 1 | 31 | 0.5592 | 0.4602 |

## Contralateral P100 amplitude increased following lateral finger VTS

Two participants declined to complete ERP recordings due to time pressure. Figure 20 shows the processed ERPs of CP3, the electrode over the contralateral anterior parietal lobe. The lateral finger VTS group (Fig. 20A) revealed an increase of P100 amplitude from baseline (black line) to Post-VTS recording (red line) while the fingertip VTS group did not (Fig. 20B). Both groups did not differ in terms of P100 latency, showing similar latency values across the recording sessions.

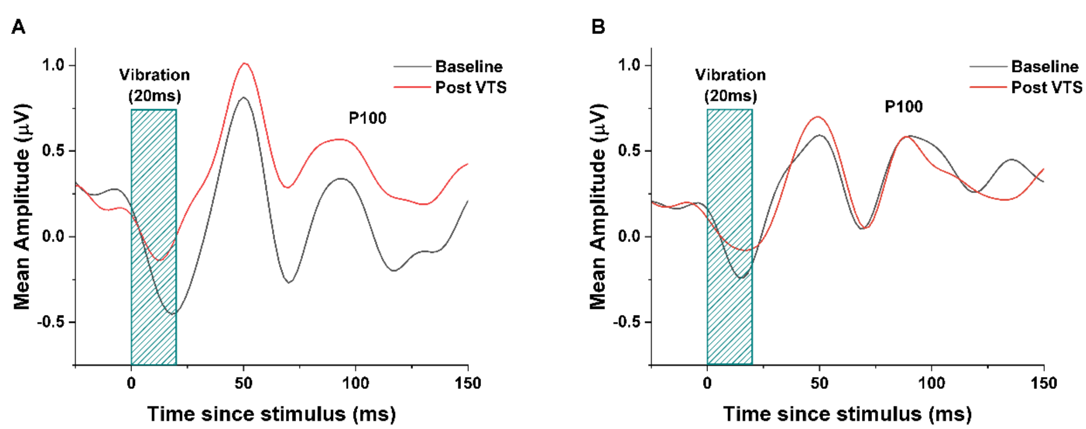


***Figure 20**. Plots of ERPs recorded from CP3/4 averaged at the group level Cyan shaded regions indicate the periods (0 ~ 20ms) when the vibration was applied to the finger. **A**. Data of lateral finger VTS group. The amplitude of P100 was greater at the post-VTS recording than at the baseline. **B**. Data of fingertip VTS group. The amplitude of P100 did not show distinctive difference between the two recordings.*

Individual data of P100 amplitude show that the lateral VTS group demonstrated an increase in amplitude from the baseline SEP recording to the post-VTS recording while the fingertip VTS group showed an opposite trend. Group mean interaction plot shows this trend as well (Fig. 21). Individual data of P100 latency show that both groups decreased the latency from the baseline to the post-VTS recording (Fig. 22). Group level means of P100 amplitude and latency are provided in table 10.

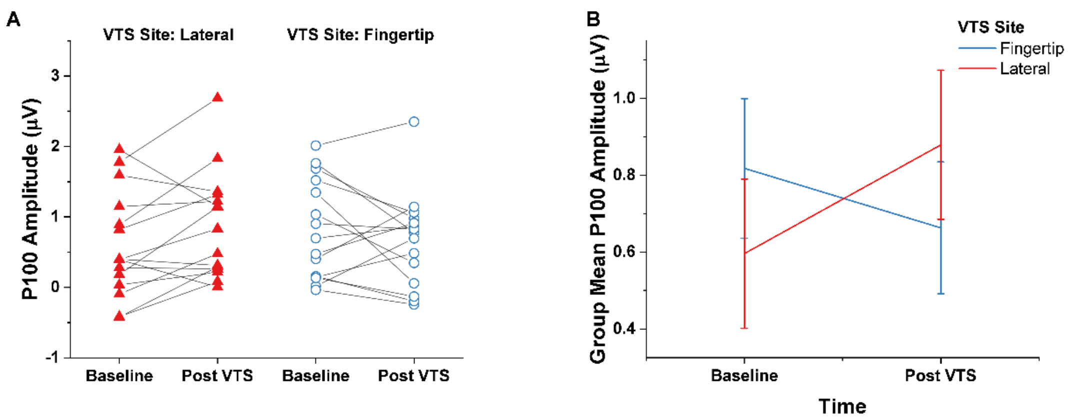


***Figure 21***. *Plots of P100 amplitude.* ***A***. *Individual data delineating how P100 amplitude of the participants, based on VTS Site changed from baseline SEP recording to post VTS one.* ***B***. *A crossover interaction of the group mean P100 Amplitude was observed with the lateral finger VTS group increasing the amplitude and the fingertip VTS group decreasing it. This interaction was statistically significant. Error bars indicate SEs.*

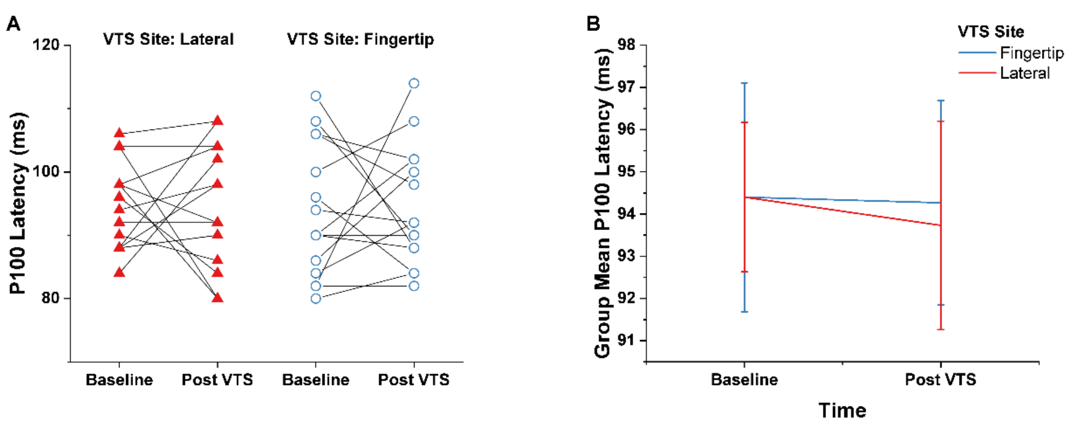


***Figure 22***. *Plots of P100 latency.* ***A***. *Individual data delineating how P100 latency of the participants, based on VTS Site change from baseline SEP recording to post VTS one.* ***B***. *Both the lateral finger VTS group and the fingertip VTS group decreased P100 latency, but this was not statistically significant. Error bars indicate SEs.*

***Table 10****. Group means and standard errors (SE) of contralateral P100 amplitude and latency at CP3/4 by VTS Site at two recording times.*

| | Fingertip | | Lateral | |
|---|---|---|---|---|
| | Baseline | Post-VTS | Baseline | Post-VTS |
| P100 Amplitude (µV) | 0.818 (0.182) | 0.663 (0.171) | 0.596 (0.194) | 0.879 (0.194) |
| P100 Latency (ms) | 94.4 (2.71) | 94.267 (2.42) | 94.4 (1.77) | 93.733 (2.47) |

To analyze if this graphical representation was statistically significant, linear mixed models were fitted to the two measures of contralateral P100, amplitude and latency. A model fitted on the amplitude data showed that the interaction of *Time* and *VTS Site* was significant (Table 11). The group with lateral finger VTS during the finger position sense assessment showed an increase in P100 amplitude from baseline to post-VTS SEP recordings while it was the opposite for the other group. Another model fitted on the latency data from the same electrode revealed no significant interaction effect as well as no significant fixed effect (Table 12).

***Table 11****. Type III Analysis of Variance Table of the mixed effects model on contralateral P100 amplitude at CP3/4 with Satterthwaite's method. *: $p < 0.05$*

| | Sum sq | Mean sq | NumDF | DenDF | F | p-value |
|---|---|---|---|---|---|---|
| Time | 0.05625 | 0.05625 | 1 | 28.489 | 0.3517 | 0.55785 |
| VTS Site | 0.00042 | 0.00042 | 1 | 29.184 | 0.0026 | 0.95968 |
| Time x VTS Site | 0.70585 | 0.70585 | 1 | 28.489 | 4.4131 | 0.04463* |

***Table 12****. Type III Analysis of Variance Table of the mixed effects model on contralateral P100 latency at CP3/4 with Satterthwaite's method.*

| | Sum sq | Mean sq | NumDF | DenDF | F | p-value |
|---|---|---|---|---|---|---|
| Time | 3.1503 | 3.1503 | 1 | 26.090 | 0.0351 | 0.8529 |
| VTS Site | 19.4195 | 19.4195 | 1 | 26.113 | 0.2161 | 0.6459 |
| Time x VTS Site | 14.8723 | 14.8723 | 1 | 26.090 | 0.1655 | 0.6874 |

### A relationship between the behavioral and the neurophysiological measures

Behavioral and neurophysiological measures showed significant *VTS Site* dependent changes. To check if such changes were related, the two measures were examined together. For each participant, the following two measures were derived:

1) change in contralateral P100 amplitude at CP3 from baseline to post-VTS SEP recordings
2) change in |ΔPSE| from No VTS condition to VTS condition

Figure 22 shows the scatterplots of the two groups. Four quadrants could be defined from plots: 1) Both |ΔPSE| and P100 amplitude increased, 2) |ΔPSE| decreased and P100 amplitude increased, 3) Both |ΔPSE| and P100 amplitude decreased, and 4) |ΔPSE| increased and P100 amplitude decreased. Based on the findings of each measure, it was hypothesized that the increase in P100 amplitude could be associated with the decrease in |ΔPSE| and vice versa. From the scatterplots, more data points were expected to be placed in the second quadrant for the lateral VTS group and in the fourth quadrant for the fingertip VTS group.

The expected relationship between the behavioral and the neurophysiological measures was not evident. Eight out of fifteen participants from the lateral VTS group both increased P100 amplitude and decreased |ΔPSE| with VTS (Fig. 23A, blue rectangular area). When Pearson's chi-squared test was performed on the contingency table generated from the number of data points in four quadrants, the number of data points in the second quadrant did not reach a statistical significance ($\chi^2(1)= 2.8125$, $p=0.094$). For the fingertip VTS group, only 4 out of 15 participants showed increased |ΔPSE| and decreased P100 amplitude. Pearson's chi-squared test showed that all four categories did not significantly differ in terms of the number of data points ($\chi^2(1) = 0.9375$, $p=0.3329$).

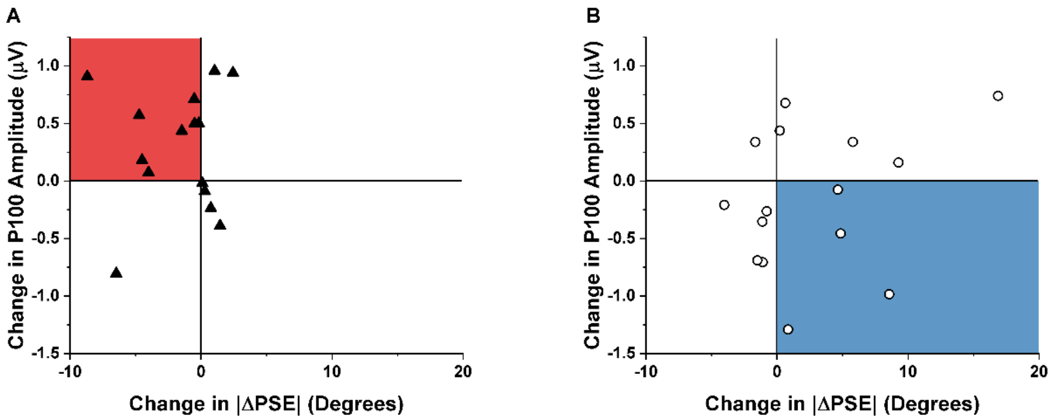


***Figure 23***. *Scatterplots of the change in P100 amplitude aginst the change in |ΔPSE|. A positive value along any axis would indicate an increase of the corresponding measure and vice versa. A. The plot for lateral VTS group.Data points in the red area decreased bias magnitude and increased P100 amplitude. B. The plot for fingertip VTS group. Data points in the blue area increased bias magnitude and decreased P100 amplitude.*

## Discussion

This project examined if VTS applied during the assessment of finger position sense would alter the acuity of that sense. In particular, the effect of VTS on the acuity of the sense was assumed to be dependent on the location of VTS. It was hypothesized that the stimulation of the fingertip would decrease the measure of *bias* (the systematic error) and *precision* (the random error) of the sense. In addition, this project aimed to examine if a change in cortical response to a somatosensory signal may follow the application of VTS during a limb position sense assessment. The original expectation was that P100 latency, the time between the onset of stimulation and the characteristic peak near 100 milliseconds observed from a SEP recording, would be shortened as a sign of temporarily enhanced somatosensory processing.

Results showed that VTS on the index fingertip was not associated with enhancing the finger position sense acuity. When the magnitude of finger position sense *bias* was analyzed, VTS on the fingertip increased the group mean of |ΔPSE| while the stimulation on the lateral side decreased it. Finger position sense *precision*, another aspect of the acuity of the sense was not influenced by the location of VTS.

In terms of cortical measures, the group mean of P100 amplitude measured at CP3, the electrode placed over the contralateral somatosensory cortex, changed with VTS. The lateral finger VTS group showed increased P100 amplitude after experiencing VTS. In contrast, participants who had VTS on their index fingertips showed a decrease in P100. P100 latency did not show any significant VTS location-associated change.

Separate results of analyzing behavioral and electro-cortical measures suggested that the increase of P100 amplitude could be related to the decrease of |ΔPSE| while the decrease of P100 amplitude could be associated with the increase of |ΔPSE|. The chi-square statistics were not statistically significant. Yet, it is notable that half of the participants from the lateral finger VTS group (8 out of 15) showed a simultaneous decrease in |ΔPSE| and an increase in P100 amplitude.

## Finger position sense *bias* is facilitated by the VTS on the lateral side of the index finger, but not by the one on the fingertip

Increased finger position sense *bias* magnitude of the fingertip VTS group may seem to contradict the previous report on the effect of VTS on goal-directed reaching movements (Mikula et al., 2018). However, as Ingram et al. (2019) noted, the accuracy of a reaching task relies on both proprioception of the limb that moves, and the work of the internal model (Kawato, 1999; Wolpert et al., 1995) that generates a motor command based on the positions of the target limb and the reaching limb. Reduced reaching error to the stimulated target cannot entirely be attributed to the effect of VTS on the position sense acuity. The motor command for the reaching movement may have been updated continuously over a series of trials, resulting in reduced overall error.

One possible explanation is that VTS applied to the fingertip interfered with sensing the index finger position. Refshauge et al. (2003) reported that electrically stimulating the index fingertip or stroking the tip of an adjacent finger (thumb or middle finger) with a brush significantly impaired the ability to detect the passively applied flexion movement at the proximal interphalangeal joint of the index finger. VTS at 300 Hz applied to the tip of the middle finger demonstrated a similar outcome, suggesting that if stimulation beyond a certain threshold is applied on or near the tested limb, it is recognized as *noise* (Weerakkody et al., 2007). Based on the result of this project, a lower frequency (30Hz) VTS adjacent to the tested limb could be construed as a noise to the correct estimation of the limb position. A relatively-low frequency VTS repeatedly applied could have induced the suppression of Meissner corpuscles induced cutaneous input used in the proprioceptive judgment about the index finger position. It could be hypothesized that the cutaneous input of the index finger is coming from the entire finger, with weights proportional to the density of the receptors. Fingertip has the greatest density of Meissner corpuscles (Ciano & Beatty, 2022), so compromised cutaneous input from the fingertip could lead to a greater dependence on the input from the lateral or the medial side of the finger. This could have resulted in greater $|\Delta PSE|$ values with VTS. On the other hand, lateral finger VTS tuned down the cutaneous input from the lateral side of the finger and increased the dependence on the fingertip input.

Nevertheless, it should be noted that this effect may not be universal. In my study, nine participants of the fingertip VTS group (n=16) decreased |ΔPSE| and 6 of the lateral finger VTS group (n=17) increased |ΔPSE|. Varying levels of tactile sensitivities among individuals associated with the density of Meissner's corpuscles (Ciano & Beatty, 2022) or their experience (Cohen et al., 2011) could be a factor that explains why several individuals were not influenced. In addition, the transformation of the response variable in the fitted model indicates individual variability in processing VTS-induced sensory input along with proprioceptive one. The effect of VTS on finger position sense acuity may be nonlinear, and exploring characteristics that determine this nonlinearity should be the work of future studies.

### A short-term enhancement of somatosensory signal processing may be associated with the increased finger position sense acuity

The significant interaction of *VTS Condition* and *VTS Site* on the contralateral P100 amplitude at CP3 showed that relative to the baseline value, P100 amplitude increased for the lateral finger VTS group while it was the opposite for the fingertip VTS group. Habituation of cutaneous receptors at the fingertip is not likely to explain the group mean decrease of P100 amplitude. The frequency and the duration of stimulus used for SEP recording (300Hz, 20ms) were different from the one used during the finger position sense assessment (30Hz, 1000ms). Given that Meissner's corpuscles and Pacinian corpuscles are most responsive to different frequency ranges that do not overlap, the primary source of ERP recordings would be the activation of Pacinian corpuscles.

It could be suggested that temporarily enhanced index finger position sense acuity was reflected through increased P100 amplitude. Different trainings enhancing proprioception are found to increase cortical activity beyond the training intervention. Children with hemiplegic cerebral palsy, after going through constraint-induced movement therapy, showed significantly higher P100 amplitude elicited by tactile stimulation of their index fingers, along with improved clinical function (Jobst et al., 2022). A similar study showed that training tailored to increase muscle strength and walking performance of children with cerebral palsy also demonstrated a significant increase in somatosensory cortical activity after the training (Bergwell et al., 2022). In the current study, more than half of the lateral VTS group demonstrated decreased |ΔPSE| and increased P100 amplitude. Although this number was not statistically significant, it too suggests that the increase of P100 amplitude may be related to temporarily-enhanced proprioceptive acuity or somatosensory processing in general.

The neurophysiology underlying P100 also proposes that the increased P100 amplitude could reflect the multisensory experience, or possibly the integration of proprioceptive and tactile inputs which contributed to the decrease of |ΔPSE|. P100 of SEP was suggested to have its origin in the secondary somatosensory cortex (SII), or the posterior parietal cortex (Barba et al., 2004; Forss et al., 1994; Kany & Treede, 1997). SII was noted as a potential site for the integration of different senses, particularly tactile and proprioception both in macaque monkeys (Fitzgerald et al., 2004) and humans (Hsiao, 2008). Similar is true for the posterior parietal cortex (Bolognini & Maravita, 2007; Limanowski & Blankenburg, 2016). As mentioned in the introduction, tactile and proprioceptive inputs project to separate areas of the primary somatosensory cortex (SI). Yet, the projections from SI to SII indicate that the two sensory inputs are potentially integrated at SII. A change in the perceptual experience of those senses may be represented by a corresponding cortical response of SII or the feature of P100. In project

3, such a change would be the short-term decrease of |ΔPSE| from the lateral finger VTS.

## Conclusion

This project presents the effect of VTS on finger position sense acuity and the neural processing of somatosensory signals. Data show that VTS applied on the fingertip increased the magnitude of systematic error while the stimulus presented at the lateral side of the index finger decreased it. There was no direction-specific influence of VTS applied to the lateral side of the finger, meaning that people's perceived finger position did not significantly move toward the lateral side. In addition, there was no effect of VTS on the *precision* of the finger position sense. This implies that VTS of 30 Hz applied at the index finger, regardless of its location, did not influence the consistency of perceptual judgments. In terms of cortical changes, experiencing repeated VTS on the lateral side during the finger position sense acuity assessment was associated with a significant increase in P100 amplitude. This finding implies that VTS on the lateral side of the index finger may enhanced somatosensory processing. The finding could add to the continued research on the possible means to augment the sense of individuals with proprioceptive deficits. To increase the finger position sense acuity with VTS, the fingertip could be avoided and the lateral side could be targeted.

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# Appendix

## A. Adapted handedness questionnaire

| **Handedness** | **Which hand do you prefer?** | | |
|---|---|---|---|
| | **right** | **left** | **no preference** |
| Writing | | | |
| Drawing | | | |
| Throwing | | | |
| Using scissors | | | |
| Using a toothbrush | | | |
| Using a knife without a fork | | | |
| Using a spoon | | | |
| Using a broom (upper hand) | | | |
| Opening a box (removing a lid) | | | |
| Holding a computer mouse (or using touchpad/touchscreen) | | | |
| Holding a key to unlock a door | | | |
| Holding a hammer | | | |
| Holding a brush or comb | | | |
| Holding a cup while drinking | | | |
| **Totals:** | | | |

## B. Psi-marginal adaptive method

For each trial of an assessment, the inclination angle was determined by the Psi-marginal adaptive method. The Psi-marginal method (Prins, 2013) is a Bayesian inference algorithm for psychophysical threshold estimation. According to the method, a Gumbel (Eq. 2) function characterizes the mechanism that decides one's performance to the stimulus intensity (*x*). α is a threshold parameter and β is a slope parameter for the function.

$$F_G = 1 - exp(10^{\beta(x-\alpha)}) \qquad \textit{Eq. 2}$$

*F* is a mental process, and thus is not directly observable. Therefore, *F* is inferred by the trend of responses. For a stimulus intensity *x*, the probability of observing a positive response is given by a probability function ψ.

$$\psi(x;\ \alpha,\beta,\gamma,\lambda) = \ \gamma + (1-\gamma-\lambda)F_G(x;\ \alpha,\beta) \qquad \textit{Eq. 3}$$

γ is the guess rate, the reciprocal of the number of possible choices. Given that there are two possible choices, γ = 0.5. λ is the lapse rate, which is the probability of making an unintended erroneous choice.

Each of α, β, and λ has its own prior distribution and the initial value to begin with. Consequently, joint posterior distribution of the three parameters, given a response and a stimulus intensity can be calculated (Eqs. 4 and 5).

$$p(\alpha,\beta,\lambda;x,r_{correct}) \propto L(\alpha,\beta,\lambda;x) * p(\alpha,\beta,\lambda) \qquad \textit{Eq. 4}$$

$$p(\alpha,\beta,\lambda;x,r_{incorrect}) = 1 - p(\alpha,\beta,\lambda;x,r_{correct}) \qquad \textit{Eq. 5}$$

With λ marginalized out, the entropy of the joint posterior distribution is calculated for all possible pairs of a stimulus intensity and a response. The inclination angle with the lowest expected entropy was presented for the next trial.

$$H = -\sum_{\alpha}\sum_{\beta} p\,(\alpha, \beta; x, r) log_2 p(\alpha, \beta; x, r) \quad \textit{Eq. 6}$$

The first inclination angle was 30° angular difference from the index finger in the actual assessment. For a right hand user, the first angle was 30° to the left. In order to prevent any directional bias in the user's response, two algorithms were implemented separately for the two opposite directions. The stimuli direction changed after the first ten trials, then alternated for every five trials. Each direction had twenty-five trials.