# Notes

**Abstract**

* Background
  + Proprioception is important for planning and control of limb posture and movement
  + Clinical tests to assess proprioception aren’t good
    - Ordinal
  + New way to quantify proprioception (continuous ratio scale)
    - Based in signal detection theory of sensory psychophysics
* Methods
  + Detect displacement – or force perturbation robotically applied to arm in two-interval, two-alternative forced-choice task
  + Logistic psychometric function parameterize detection of limb perturbation
    - Shape of function determined by:
      * Signal detection theory
      * Variability of responses about that threshold
  + Use auditory tone discrimination task to control for possible deficits in comprehension, attention, and memory deficits
* Results
  + All but one stroke survivor was competent on auditory training test
  + Those with clinically defined proprioceptive deficits had higher detection thresholds and exhibited greater response variability than those without proprioceptive deficits
* Conclusion
  + This approach is sensitive to small changes in proprioceptive detection of hand motions

**Background**

* More than 50% of stroke survivors exhibit somatosensory deficits that negatively impact quality of life and rehabilitation outcome
* Proprioception is important for both feedforward and feedback control
* Clinical assessments of proprioception currently suffer poor reliability
* Automated tests are better than clinical measures, but require subjects to actively match stationary limb or the motion of one limb with the other
* To determine how deficits in proprioceptive perception contribute to motor control deficits, it seems necessary to assess proprioceptive perception within the moving limb itself, rather than across limbs
* Task focuses on kinesthetic proprioception by requiring people to detect small position or force perturbations applied to one hand within the context of a two-interval two-alternative forced choice test
* Task made to evaluate the ability of the new technique to discriminate individuals with proprioceptive deficits from those without
  + Repeated assessment >1 wk apart for test-retest reliability
    - Excellent agreement with initial testing
    - Subtle learning effect across days of practice

**Methods**

* 16 stroke survivors , 16 age matched (+- 5) controls
* 7 stroke had clinically determined proprioceptive deficits (SS-P)
* All stroke with proprioceptive deficits had tactile deficits as well
* Clinical assessments
  + Visual field/visual search evaluation
  + Upper extremity Fugel-Meyer
  + Modified Ashworth scale
  + Hand dynamometer grip strength
  + Proprioception (shoulder, elbow, wrist, and MCP joints)
    - Up and down test
      * Intact – brisk and accurate
      * Impaired – unable to respond with confidence
      * Absent – unable to determine position
    - Two point discrimination test
* Experimental procedure
  + Subjects wore a wrist brace (commented to handle) to prevent motion to the shoulder and elbow (????)
  + Opaque screen occluded vision of shoulder, arm, and robot
* Training task (tone discrimination)
  + Evaluate subject ability to comprehend multistep instruction, concentrate, and use working memory
  + 24 trials (2 tones/trial), 3s observation intervals in close succession
    - One interval (at random) was constant pitch (500 Hz tone) embedded in auditory white noise
    - Other interval was conspicuously rising pitch embedded within white noise
    - Indicate whether first or second noise masked the rising pitch
* Primary experiment: arm movement detection
  + 14 SS (7 impaired/absent proprioception) and 11 NIC participated
  + Test ability to detect hand displacements of various magnitudes in a series of 130 trials in center of arm’s reachable workspace
  + Hand displacement = separate sum-of sinusoids in X and Y directions
  + Each trial = 2 observations with 3 s of auditory white noise and intervening 1s of silence
    - One interval – perturbation
    - Other interval – no perturbation
  + Asked whether first or second noise masked the hand motion
    - Such an odd way of asking interval hand moved
  + Fixed set of 9 perturbation magnitudes (0 – 1 cm)
    - Each perturbation presented between 10 and 20 times in pseudo random order
  + Test-retest reliability
    - 7 SS and 5 NIC returned >1 wk later for repeat testing
* Supplemental experiment: hand force detection
  + Quantify detection of force-perturbation applied to hand
  + 7 SS (3 impaired or absent proprioception) and 7 NIC
  + Detect sum of sinusoid force perturbation
  + 130 trials
  + Robot generate specific temporal pattern of desired force vectors regardless of hand position
  + Stimulus detection driven by controlled hand-force perturbation
  + 9 perturbation magnitudes (0 – 2.5 N)
* Data analysis
  + Training task probed if participants were unable to complete discrimination task because of inability to follow multi-step direction, working memory impairment, and/or attention deficits
    - Auditory system intact or not
  + Analyzed with equal-variance Gaussian model of two-alternative forced-choice task
    - Equal variances, but different means
  + Probability of a positive difference (equation 1)
  + Discarded first 4 training trials to account for initial task learning (??)
  + Calculate P\_c = percentage of remaining 20 trials with correct responses
  + Limit of acceptable performance
    - If sensation variance increase 50% or more compared to NIC
  + Minimum acceptable performance threshold of 80.4%
  + Training task performance <= 80% indicated potential concerns with participants ability to perform two-alternative forced-choice task
  + Motion detection task
    - Measure hand path length during perturbation and averaged across trails, within perturbation magnitude, for each participant
    - Quantify reaction forces induced by imposed motion with hand force bias and variability
      * Hand force bias = average magnitude of horizontal planar hand force during perturbation
    - Test hypothesis that spasticity would manifest as increased arm stiffness in response to imposed robotic perturbation
  + Characterize proprioceptive sensitivity using detection threshold [DT] (minimum magnitude of displacement (or force) that subjects begin to detect reliably when comparing to no-perturbation condition
  + Acuity of proprioceptive sensation using choice uncertainty (CU) to quantify variability of individuals response about detection threshold
  + Each participant, each perturbation magnitude, and each day, calculate P\_correct
    - % of trials correctly identified
    - P\_correct at 0 magnitude = 0.5
    - Fit cumulative-normal psychometric function to P\_correct of each 9 perturbation magnitudes using a non-linear optimization for each participant %%
  + DT – perturbation magnitude at which fitted curve passed through 75% likelihood
  + CU – one SD of underlying normal distribution
    - CU low when function is steep (skinny Gaussian)
    - CU high when function is flat (fat Gaussian)
  + Fit constraints
    - 1. DT – CU > 0
      * Ensure P(0) close to 0.5
    - 2. CU > 0.002cm
      * Handle situations where subject respond with perfect accuracy at and above some perturbation magnitude
* Statistical hypothesis testing
  + ANOVA w/ post-hoc Bonferroni t-test to evaluate effect of proprioceptive integrity
    - Group X DT and CU
  + Repeated-measures ANOVA to test repeatability of psychophysical assessment of limb proprioceptive integrity
    - DT + CU X Day
      * Group and session as fixed factors
      * Subject as within group random factor
  + SS – linear regression to evaluate correlation between DT+CU and performance on audition task
    - Multiple linear regression to evaluate correlation between DT+CU and clinical measures (FM, MAS, Grip)
  + Supplemental experiment
    - One-way ANOVA to compare DT,CU across 3 groups

**Results**

* No participants exhibited visual field deficits or hemispatial neglect
  + SS-P and SS+P two samples t-test found no difference in spasticity as quantified by MAS
  + All participants (besides 1) scored >= 80%
    - SS 04 = 70% (+ excluded from further statistical analyses)
* Primary experiment: arm movement detection
  + Perturbation strength influenced path length (duh)
  + No effect of group or interaction between factors
  + Thus, robot imposed repeatable displacements despite large differences in spasticity across groups
    - Hand displacements in experiment much smaller than that used for MAS
  + Separate repeated measures ANOVA revealed mean hand force varied systematically across groups, but not across displacement magnitudes
    - Two SS groups produced more average force against the robot’s handle than did the control group
      * Post-hoc showed no significant correlation between mean hand force and MAS score
    - within-trial variability of hand force depended systematically on perturbation magnitude and did not vary across groups
    - no correlation found between variability of hand force and MAS
  + Cumulative Gaussian fit well
  + All participants readily detected large 1cm displacements and responded with chance accuracy at low perturbation magnitudes
    - Responses varied markedly across groups for moderate perturbation magnitudes
  + SS – linear regression found no correlation between either DT or CU and UEFM, MAS, or Hand grip
  + One-way ANOVA of day 1
    - Main effect of group on DT
      * Post-hoc: higher threshold in SS-P relative to NIC and SS+P
  + One-way ANOVA
    - Main effect of group on choice uncertainty
      * Post-hoc: higher choice uncertainty in the SS-P group relative to NIC and SS+P
  + Outcomes of previous ANOVA’s replicated with day 2 data (Two-way repeated-measures ANOVA)
    - Main effect of group on DT
    - Main effect of testing day on DT
      * No interaction
    - Post-hoc Bonferroni t-test due to higher thresholds in SS-P relative to NIC and SS+P
  + Strong correlation between DT across days
    - DT decreased ~0.04 cm from day1 to day2 (seem in all groups)
      * Learning effect
  + Two-way repeated measures ANOVA
    - Main effect of group on choice uncertainty
      * No effect of testing day or interaction between factors
    - Collapse across days
      * Bonferroni t-test revealed group effect due to higher choice uncertainty in SS-P group relative to NIC and SS+P groups
    - Test-retest only modest correlation of CU (r = 0.54)
  + For subjects who performed above criterion on the auditory training task, linear regression found no correlation between training task performance and either DT or CU
    - SS04 may have had deficits unrelated to proprioceptive integrity
  + For NIC subjects, linear regression between DT and CU values
    - No correlation (r^2 = 0.07)
    - Interesting
  + For all subjects, all NIC and SS+P were enclosed within 99.9% isolikelihood contour whereas all SS-P data resided outside this same contour
* Supplemental experiment: hand force detection
  + Assessed participants ability to detect range of hand force perturbation in 2AFC experiment (same thing???)
  + Determine whether a hand force detection task might also be sensitive to proprioceptive deficits in small cohort of stroke survivors
  + Fit cumulative Gaussian functions x magnitude of perturbation
  + ANOVA
    - Main effect of group on hand force DT
      * Post-hoc: higher detection threshold in SS-P group relative to NIC and SS+P
  + ANOVA
    - Main effect of group on CU
      * Post-hoc Bonferroni: higher uncertainty in SS-P relative to SS+P
        + But not between SS-P and NIC (??)
      * Choice uncertainty values in SS+P and NIC did not differ from each other
  + DT x CU
    - Iso-likelihood contour could separate SS with proprioceptive deficits from those without
      * 1 SS+P had a value close to SS-P
      * All SS-P were outside contour (95%)
* These two “experiments” suggest that controlled displacements may provide a better assessment of proprioceptive integrity than force perturbation when using this approach

**Discussion**

* Current clinical tests lack resolution to detect small differences in proprioceptive integrity
* Variation observed in DT and CU values were largely due to participant group membership, although a subtle learning effect was evident across sessions in all participant groups
* Comparison to the “up or down” test of upper extremity proprioception
  + Limited in that there are only 3 possible grades of proprioception: intact, impaired, and absent
  + Robotic test introduced yields a pair of ratiometric performance variables
    - When plotted with normative performance can indicate the likelihood of proprioceptive impairment in the tested limb as well as a quantitative measure of impairment
  + Ceiling effect
    - One reason – unavoidable production of secondary sensory cues by clinician as they move limb up or down (especially shoulder)
      * Affect posture of trunk, clothing shift, head movement
    - All SS-P performed poorly on robotic test even those with “intact” proprioception at elbow/shoulder
  + Robotic test specifically designed to quantify proprioceptive sensitivity to horizontal planar perturbation similar to those currently used in ongoing studies of robotic interventions
* Comparison to other instrumented tests of upper extremity proprioception
  + Paradigm 1: one arm moved passively, subject match with opposite arm
    - Tests assess integrity of entire neuromuscular control arc spanning both limbs
    - Up to 20% of stroke survivors exhibit proprioceptive deficits in ipsilesional arm
    - And some stroke survivors exhibit subtle motor deficits in ipsilesional arm
    - Limb matching tests can confound proprioceptive deficits in the arm under evaluation with sensory and motor deficits in matching limb
    - -
    - Carey and colleagues test
      * Examiner move unseen wrist to specified location, subject indicate perceived wrist angle by aligning goniometric pointer with imagined line between middle of wrist and index finger
      * Only assess position sense at wrist, lack automation, doesn’t evaluate sense of limb motion
  + Paradigm 2 – participant indicate verbally when they detect motion in slow moving arm or when moving limb’s position matches a previously presented position
    - Improve via acoustic/white noise to mask noise from manipulandum
  + Paradigm 3 – this study
    - Only moved one limb, only used other limb to answer
    - Arm stretched over a range of positions and velocities
    - Subjects asked to relax arm so motor deficits “didn’t” come into play
    - Acoustic noise to mask potential robot noises
* Limitations
  + Robots are costly both in terms of time for intervention and money
  + 2AFC task
    - Must commit sensory stimuli to memory and then recall later for comparison
    - Used auditory discrimination task to screen out participants with unapt cognitive abilities
  + Lack of correlation between our two outcome variables (DT,CU) and two common measures of motor impairment (FM and MAS)
    - Future study determine extent to which proprioceptive integrity is predictive of other important behavioral characteristics (function and arm use post stroke)
    - Increased understanding of relationship between proprioceptive deficits and deficits in control of limb posture and movement maybe prove useful in identifying patients for sensory stimulation
  + Overall small sample size
    - Additional testing refine normative distribution for DT and CU in NIC individuals
* Conclusions
  + This test provides a measure of proprioceptive integrity on a continuous scale that is sensitive to small changes in performance
  + “Thus, the robotic assessment described here can characterize proprioceptive deficits post-stroke with a resolution superior to that of a common clinical test of proprioception.”

# Comments

* Why the auditory noise in between arm discrimination trials?
* Where is screen for response?
* Don’t fully understand how supplemental experiment different from main experiment
  + All subjects always displaced same amount, no matter how much resistance they applied, but during force, the displacement will depend on how much resistance they applied
* Signal detection theory?
* Main effect of testing day X DT, but no interaction
* -
* Why did they do this study?
  + Clinical measures of proprioception are unspecific and can be excelled at even with clear deficits
  + Need a more reliable way to measure proprioception
* What’s their interpretation of the results?
  + Their two methods (displacement and force) are sensitive to small changes in proprioceptive abilities and should be used to more accurately characterize proprioceptive deficits
* Do I agree with their interpretation?
  + Yes, their methods provide a more detailed description of the proprioceptive abilities of people, but I think methods could be refined a little
  + Why?
    - Pretty much anything on a continuous scale is going to give better results than something on an ordinal scale
* -
* Key take-aways
  + Clinical measures suck because they aren’t sensitive to small changes. The robotic tasks here are more sensitive and provide a continuous scale of levels of proprioceptive impairment
* -
* Are the statistical analyses appropriate for the question asked?
  + Yes
* What’s the big picture?
  + Clinical tests suck, this robotic task is much more accurate and can be used to provide clinicians with a score relative to healthy age-matched controls

# Questions

* How does one get from y/n answers to logistic function?
  + Look up
  + Read chapter 1 (and 2) of Gesheider
  + Put on hold, get Monday?
* Does stroke typically come with auditory deficits?
  + Read
* Difference between positional movement and force perturbation?
  + There is a difference
* How familiar with clinical assessments?
  + General idea of what they are
  + What the scores mean
* Classification of SS-P or SS+P groups
  + Sensory part of fugel-meyer ?
  + Just up down test
* Wrist brace
* Noise during primary experiment used to drown out sounds of motors, correct?
* Sum of sinusoids
* Supplemental experiment – Aren’t force and displacement related
* Why testing spasticity?
* Fitting normal cumulative psychometric functions
  + What they are
  + What the differences
  + When to apply which one
* Fitting of cumulative Gaussian fits
  + Figure 3A
* Likelihood contour graphs
  + What data used to get lines
* Feel like with some of these studies it’s almost confirming that the clinical tests are sufficient to determine general state of proprioception