**Tactile and Auditory psychophysics experiments for LEAP3**

**1. Tactile psychophysics experiments**

* 1. Background

The proposed work is based a battery of vibrotactile tasks that was developed to objectively assess low-level tactile function in pediatric cohorts (including those with neurodevelopmental disorders). The tasks are reliant on GABAergic function and have been validated between children and adults (Puts et al., 2013). In particular, in prior work we have shown that reduced GABA levels are associated with abnormal vibrotactile detection thresholds (Puts et al., 2016), and we and others have shown that children with ASD show abnormal detection threshold, abnormal modulation of detection threshold (a measure of feedforward inhibition/sensory gating) and abnormal amplitude discrimination threshold (Puts et al., 2014; Tavassoli et al., 2016). Finally, our recent work (under review) shows that abnormal tactile function strongly correlates with clinical scores of sensory hypersensitivity and touch avoidance, and potentially allows for separation based on diagnosis (ASD and ADHD).

* 1. Approach

All stimulation will be applied on the left index and middle finger using a Cortical Metrics vibrotactile device. Visual feedback will be provided to indicate intervals, no right/wrong feedback will be given. Each task is preceded by three practice trials.

* + 1. *Required equipment*

The stimulator to be used is a Cortical Metrics Braingauge Pro. The Braingauge Pro has two probes located on a mouse-like device that can present stimuli (with m-accuracy and ms-accuracy) to the index and middle fingers. Control and user interface are run through the Braingauge app. Raw data can be extracted and analyzed. The device is connected to a laptop through USB. The UI is child friendly and responses can be obtained using a wired mouse. In addition to the Braingauge Pro, sites require a PC desktop or laptop with internet connectivity, with at least two free USB ports, a screen, and a wired mouse.

* + 1. *Tasks*

Static and Dynamic Detection threshold (~15 min)

Static Detection threshold will be measured under four conditions. Modulating detection threshold is thought to provide a measure of feed-forward inhibition.

*Baseline:* In the baseline task, participants have to judge on which of two fingers they received a stimulus (25 Hz, 500 ms, starting amplitude 20 m, 35 trials).

*Short-paired (SP-DT) and long-paired (LP-DT):* In the second and third task, each of the trials as presented in the baseline measure (also 30 trials), is preceded by a brief (40 ms) sub-threshold (3 m) stimulus thought to engage inhibitory interneurons therefore modulating threshold. Our current data suggests that children with ASD get better when there is a pre-stimulus present. The pre-pulse is presented either 30 ms (short; SP-DT) or 100 ms (long, LP-DT) prior to the test stimulus

The baseline and paired tasks are 2-alternative forced choice task with staircase tracking. Responses are made using the right hand on a mouse button. The left mouse button corresponds to the left middle finger, the right mouse button to the left index finger. Participants are asked to indicate on which finger they felt a stimulus.

*Dynamic:* In the dynamic detection threshold task, stimulus level starts at zero or at twenty m. In half the trials, children have to press a button when they feel the stimulus (dynamic-UP) and in half the trials kids have to indicate when they stop feeling the stimulus (dynamic-DOWN, 10 trials per condition). Participants are asked to press a button (indicating which finger, as above) as soon as they feel the stimulus.

*Primary outcome measures*

1. Detection thresholds for the baseline, SP-DT, LP-DT, dynamic-UP and dynamic-DOWN tasks. For the first three, threshold is calculated based on the average of the last 5 trials. For the dynamic tasks, threshold is calculated based on the average of correctly answered trials.
2. Difference metrics. Absolute and percentage difference between baseline and all other thresholds will be calculated.
3. A confidence measure for each condition (based on Response Time for each trial for each condition).

*Secondary outcome measures*

1. D-prime to assess finger preference
2. Average and variability in Response Time
3. Accuracy (by fitting a power law curve)

Amplitude discrimination with and without an adaptation component (~7 min)

Amplitude discrimination with- and without adaptation can be used to measuring adaptation/habituation and have been linked to lateral inhibition. We find that amplitude discrimination is impaired in ASD and that children with ASD do not adapt. Participants are asked to discriminate which of two stimuli is the strongest.

*Sequential amplitude discrimination:* Two sequential stimuli are applied (25 Hz, all supra-threshold, 500 ms duration, 500 ms ISI, 30 trials) and participants are asked which finger received the strongest stimulus.

*Simultaneous amplitude discrimination:* Same parameters, but stimuli are applied simultaneously.

*Simultaneous amplitude discrimination with adaptation:* The instruction is the same, but each trial is preceded by an 'adapting' stimulus (100 m, 1 second, 500 ms ISI) which modulates perception of the two subsequent stimuli, making people better, or worse.

All tasks are 2-alternative forced choice task with staircase tracking. Responses are made using the right hand on a mouse button. The left mouse button corresponds to the left middle finger, the right mouse button to the left index finger. Participants are asked to indicate which finger received the strongest stimulus.

*Primary outcome measures*

1. Amplitude discrimination thresholds for each task. Threshold is calculated based on the average intensity of the last 5 trials.
2. Difference metrics. Absolute and percentage difference between simultaneous and sequential threshold, and between simultaneous with- and without adaptation thresholds will be calculated.
3. A confidence measure for each condition (based on Response Time for each trial for each condition).

*Secondary outcome measures*

1. D-prime to assess finger preference
2. Average and variability in response time
3. Accuracy
4. **Simultaneous and backward auditory masking**

2.2. Background

Similar to the vibrotactile paradigms, we aim to use an auditory detection task, which includes modulation of auditory detection to probe sensory gating. The tasks involve absolute auditory threshold, and two additional conditions with both backward and forward masking (known to engage thalamocortical sensory gating mechanisms and modulate perception of auditory tones. These tasks are based upon prior work (Rosen et al., 2009; Wright et al., 1997) that have established that this work is appropriate for pediatric cohorts.

2.2. Approach

*2.2.1. Required equipment*

All sites will need a computer with audio output, an over-ear headphone, and a wired mouse for responses.

*2.2.2. Task (~10 min)*

Auditory tone detection thresholds will be determined under three conditions, quiet, simultaneous masking, and backward masking, using adaptive tracking. A 2AFC approach will be used. Measurements will be made for the right ear. For each condition, an adaptive procedure (PEST) will be used to track 75% correct by varying the amplitude of a 20 ms 1 kHz tone (the test tone). The maximum step size will be 8.6 dB between trials. Three suprathreshold stimuli will be applied as a practice for each condition.

In each individual trial, there will be two intervals, indicated visually by a flashing blinking light and a number (1, or 2; the original paper used faces opening their mouth, but this is a social construct best to avoid in ASD). The participant needs to indicate whether the test tone occurred in synchrony with the first (left) or second (right) flashing light.

In the quiet condition, no additional noise bursts are given, and thus allows for determining absolute auditory amplitude detection threshold for the test tone. In the two masking conditions, in both intervals, 300 ms bursts of masking noise will be given (bandpass 0.6-1.4 kHz at 40 dB SPL (ISI 340 ms). In the simultaneous masking condition, the probe will occur 200 ms after mask onset. In the backward masking condition, the probe occurs 20 ms prior to the start of the masking (no overlap). All stimuli are gated with a 10 ms cosine wave envelop (ramp up and down) and each condition will consist of 40 trials per task (~8 min of testing)

*Primary outcome measures*

1. Auditory detection thresholds for each task. Threshold is calculated based on the average intensity of the last 5 trials.
2. Difference metrics. Absolute and percentage difference between Quiet and backward, and between Quiet, and Simultaneous masking thresholds.
3. A confidence measure (based on Response Time for each trial).

*Secondary outcome measures*

1. D-prime to assess order preference
2. Average and variability in response time
3. Accuracy
4. **Visual processing of local and global content in goal-directed and spontaneous vision**
   1. Background

The assessment of visual perception is based on a task developed by Campana et al (Campana et al., 2016) . This study predicts that global visual information is perceived faster than local visual information and that global information is encoded regardless of task-demand. Finally, the authors suggest that spontaneous vision is dominated by global visual percepts. The spontaneous task will be utilized for this study. The debate concerning visual perception in ASD is often described by children with ASD showing superior local, but inferior global visual perception (Van der Hallen et al., 2019), and indeed, studies suggest that children with ASD have poorer sensory information gating (e.g. information flow from local to global) with prior work suggesting that children with ASD may be more detail oriented e.g. (Blaser et al., 2014; Gliga et al., 2015).

* 1. Approach
     1. Required equipment
     2. Task

Stimuli consist of circular textures (diameter 7.4o angle) made of oriented lines (line length 0.18o, distance between lines 0.2 o, 36 o line on the radius) will be presented on a uniform gray background. Each texture consists of lines of random orientation, with a central rectangular area where lines are approximately aligned along a given orientation (the ‘local’ orientation). The central rectangle has its own orientation (the ‘global’ orientation). Local and global orientations are chosen from 4 angles with an angular difference between global and local of 45, for a total of 8 combinations of orientations. Difference coherence parameters will be used (high = very coherent lines, low = random lines, 4 coherence values). The global shape will be entirely defined by the distribution of a single local feature (local lines) meaning there is no contour. Further, local and global orientation derive from the same physical level (orientation).

Each trial starts with a fixation cross presented for 0.6-0.7 s, followed by a stimulus presented on an LCD screen (60 Hz, resolution 1680 x 1050 pixels, screen size 43.6 x 27.1 cm) at a viewing distance of 70 cm. The stimulus will be presented until a participant responds or a maximum of 2 s. Responses are matched to a button box with 4 potential answers (four potential orientations presented at the beginning of each block). After response, there will be a delay of 1.8-2.2 s before a new trial.

*Spontaneous condition*

In the spontaneous condition (which is always first), participants are instructed to report the orientation they spontaneously perceive when viewing the stimulus. Participants will be instructed that there is no wrong answer and a ‘no impression’ was also an option. Participants are not instructed of the global or local distinction, but rather, are trained on the four orientations as colored lines of size intermediate between global and local lines and then tested on 12 practice stimuli with congruent local and global lines. Trials during the experiment consisted of 50% congruent and 50% incongruent stimuli.

*Instructed condition*

In this condition, participants re told which representation to report on (local or global). In the global task, participants are instructed to report the orientation of the homogeneous shape. In the local task they are instructed to report the general orientation of individual lines.

*Outcome measures*