Title:

Hand and face somatotopy shown using MRI-safe vibrotactile stimulation with a novel Soft Pneumatic Actuator (SPA)-Skin interface

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Abstract:

The exact somatotopy of the human facial representation in the primary somatosensory cortex (S1) remains debated. One reason that progress has been hampered is due the methodological challenge of how to apply automated vibrotactile stimuli to face areas in a manner that is: 1) reliable despite different curvature depending on the face location; and 2) MR-compatible and free of MR-interference artefacts when applied in the MR head-coil. Here we overcame this challenge by using soft pneumatic actuator (SPA) technology. SPAs are made of a soft silicon material and can be in- or deflated by means of airflow, have a small diameter, and are flexible in structure, enabling good skin contact even on curved body surfaces (as on the face). Here,

we aimed to provide a methodological advance by providing automated tactile vibration stimulation inside the head-coil of the MRI. As a sanity check, we first mapped the well-characterised S1 finger layout using this novel device. We found that tactile stimulation of the fingers elicited characteristic somatotopic finger activations in S1, validating the use of our SPA-setup to map somatotopic representations. Ultimately, we used the device to automatically and systematically deliver somatosensory stimulation to different face locations. We found that the forehead representation was least distance from the representation of the hand. Within the face representation, we found that the lip representation is most distant from the forehead representation, with the chin represented in between. Together our results show that, by providing vibrotactile stimulation using the SPA-technology, we are able to reveal clear somatotopic representational patterns.

Keywords:

Somatosensory, vibrotactile technology, fMRI, face, hand, soft pneumatic actuators

Introduction

Over the past decades, somatotopic mapping had provided us with an increasingly better understanding of our body representations. However, providing tactile stimulation in an MR environment remains challenging. Experimenters commonly use an active movement paradigm (Kolasinski et al., 2016; Schellekens et al., 2018; Zeharia et al., 2015) or manual stroking of body parts (Martuzzi et al., 2014; Sanders et al., 2019; Van Der Zwaag et al., 2015) to probe somatotopic representations. While manual stroking may provide adequate somatosensory cortical signals and movement paradigms may better reflect real-life situations, such paradigms induce participant and experimenter dependent spatiotemporal variance affecting the statistical images. Indeed, the intensity, timing, and body part coverage of active paradigms and manual stimulations may not be consistent and precise. Furthermore, a somatotopic mapping that can distinguish between body parts that are not able to move independently (e.g., certain parts of the face, toes) is impossible using an active movement paradigm. Similarly, manual stroking of different body parts simultaneously, of the face when using a narrow head coil, or of the body when using a full body coil, is challenging. The usage of mechanical vibrotactile devices provides an opportunity to overcome these limitations. However, common vibrotactile elements contain metals or electrical circuits that are mostly not compatible with the MR environment (Yu and Riener, 2006). Stimulating body parts in (or close to) the MR head coil is especially technically demanding given the narrow geometry of the head coil and the safety constraints and imaging artefacts induced by small metal components.

In the past decades, a variety of MR-compatible vibrotactile devices have been developed. Commercially available piezoelectric and piezoceramic devices, for example, are able to deliver vibrotactile stimulation at high frequency ranges at a chosen amplitude. However, these devices mostly still contain some metal components and lead electrical wires

inside the scanner (Puckett et al., 2017; Sanchez-Panchuelo et al., 2010). The electrical wires may be heated by RF pulses if not shielded properly. While this active shielding is sufficient when the stimulators are placed away from the head coil (e.g., on the fingers), they can (in certain cases) induce unwanted signal interference and safety issues when placed closer to, or inside, the MR head coil. Pneumatically driven or air puff devices circumvent issues of such electromagnetic interference and can be made of plastic tubes and MR compatible materials.

The pneumatic devices that have been developed for safe delivery of tactile stimulation to multiple stimulation sites inside the MR head coil are however limited. Indeed, most pneumatically driven devices have been built for providing stimulation to e.g., the fingers or other body parts further away from the head coil (Gallasch et al., 2010; Golaszewski et al., 2002). The Dodecapus was amongst the first pneumatically driven devices build to apply automated tactile stimulation to a range of face locations. Its control system is placed outside the MR environment and air puffs are delivered to specified parts of the face (or other body parts) through long plastic tubes (Huang and Sereno, 2007). The device was extended to deliver punctate tactile stimuli to the face using Von Frey-filaments with a high spatiotemporal accuracy (Dresel et al., 2008). However, in these setups stimulation could only be applied to parts of the face that are exposed (i.e., that are not covered by the head coil). Later, flexible plastic tubes were attached to a facial mask (custom modelled for each subject) to deliver air puffs to different locations of the face (Chen et al., 2017; Huang et al., 2017). With this new implementation the authors were able to reach areas of the face that are covered by the head coil, allowing for a more complete picture of face somatotopy. However, this face mask may not fit in head coils with more narrow geometry and when using participants with larger head sizes. Furthermore, providing air puffs close to the mouth, nose, or eyes may not be comfortable for participants. More recently, the GALILEO SomatosensoryTM was developed. This device can provide tactile stimulation through pressure dynamics in individual stimulators with high

spatiotemporal control (Custead et al., 2017). While this device is very promising and allows the study of stimulation velocity, the stimulators are 6mm in height and may not fit in head coils with very narrow geometry, especially in situations/locations where the spacing between the head coil and parts of the face only persists of a few millimetres. Furthermore, it may not be easy to attach the stimulators to highly curved body surfaces and the device is rather expensive.

An optimal vibrotactile device for MRI usage would be pneumatic such that all components inside the MR environment would consist of MR-safe materials, ensuring that it does not induce any MR interference artefacts and is safe to be placed on the skin, even inside the MR head coil. The control device containing the necessary electronics should be placed outside the MR environment. Further, it should allow good control over vibration frequency and amplitude, enabling both sub- and suprathreshold vibrotactile stimulation. The stimulators itself should be flexible in nature, such that they can be placed on skin surfaces with different curvature. The stimulator should further be small to provide focal stimulation, and narrow, such that it can easily be placed in narrow head coils that are typical for ultra-high field imaging. Lastly, the stimulator should be portable and cost-efficient.

An accurate and detailed somatotopic understanding of the human body will improve our understanding of the somatosensory system and aid our investigation of somatosensory remapping after peripheral body and spinal cord injuries (Corbetta et al., 2002; Flor et al., 1995; Jutzeler et al., 2015; Makin et al., 2015; Moxon et al., 2014; Root et al., 2021). While the gross representation of body parts and fingers in S1 is agreeable across studies, results on the exact somatotopic mapping of the face have been mixed. Contrasting work reports both an inverted (Servos et al., 1999; Yang et al., 1993) and upright somatotopic face representation (Huang and Sereno, 2007; Penfield and Rasmussen, 1950; Root et al., 2021; Roux et al., 2018; Sato et al., 2005; Schwartz et al., 2004). Yet other studies were unable to find clear inverted or upright

representations of face and rather reported more mixed face representations following an ‘onion skin model’ where the nose was represented more inferior in S1 than stimulations on the lower jaw or above the eye (DaSilva et al., 2002; Moulton et al., 2009). To detail the full somatotopic layout of the face an automated face stimulation paradigm and both univariate analysis and multivariate analysis methods that are sensitive to representational overlaps (i.e., representational similarity analysis) are needed.

In this study, we developed a novel tactile stimulation device capable of providing focal and suprathreshold vibrotactile stimulation to the face and other parts of the body. We used soft pneumatic actuator (SPA) skin technology that, unlike common vibrotactile elements, does not contain metals and still provide excellent control over actuation frequencies (Harshal A. Sonar et al., 2019; Sonar and Paik, 2016). SPAs are made of a soft MR-safe silicon material (Dragon Skin 30®, Smooth On Inc., USA) and can be in- or deflated by means of airflow. SPAs have a small (1.4cm) diameter, are soft and flexible in structure, enabling good skin contact even on curved body surfaces (as on the face). Furthermore, the low profile design of the SPA-skin (under 1mm) allows for usage in the narrow geometry of the MR head coil and in narrow bores that are typical for ultra-high field MRI environments. We demonstrated the feasibility of using the SPA-skin-setup for somatotopic mapping in an fMRI study. We hypothesized that tactile stimulation using the SPA-skin would yield robust localised activations in somatosensory areas. We further hypothesized that tactile stimuli of the fingers would elicit characteristic somatotopic finger activations in the primary somatosensory cortex. Lastly, we investigated the somatotopic layout of face, using the device to automatically and systematically deliver somatosensory stimulation inside the head coil.

Materials and methods

Participants

Seventeen healthy participants (mean age $\pm$ s.e.m. = 37.5 ± 4.3 ; 7 females; 2 left-handers) participated in this study. Ethical approval was granted by the Kantonale Ethikkommission Zürich (EK-2018-00937) and written informed consent was obtained prior to study onset. This study is registered on clinicaltrials.gov under the number NCT03772548. As our fingers stimulation experiment was meant as a mere validation of the device and was expected to reveal convincing data in a limited number of participants, we only tested 8 participants for this feasibility aspect of the study. All participants were tested for face somatotopy.

SPA-skin stimulator design

Soft robotics emerged as a new field in robotics over a past decade and has been growing across the applications in medical technologies, personal care, environmental monitoring and entertainment (Bauer et al., 2014; Gibson, 2018; Hawkes et al., 2017; Jafari et al., 2016; Polygerinos et al., 2017). Soft robotics tackles the interactivity and wearability challenges posed to traditional rigid body robotic systems by using soft material based sensors and actuators to replace the traditional sensors and motors. These soft materials enable an inherently safe and mechanically compliant feedback to the environment including a human wearer (Polygerinos et al., 2017, 2015; Pons, 2008; Robertson and Paik, 2017). Wearability of soft technology can further be used to improve traditional haptic communication devices that currently only provide limited wearability due to their bulky and rigid-form factors (Cholewiak and Collins, 2003; Jones, 2011; Yun et al., 2017). Present haptic feedback devices mainly rely on motors and components driven using electromagnetic eccentric mass or piezoelectric motors that have limited wearability due to their bulky rigid mechanisms and cannot be used in

environments prone to electromagnetic interference like the MRI environment (Alahakone and Senanayake, 2009; Cholewiak and Collins, 2003; “Smart Tactor Development Kit,” 2021).

We developed a novel soft skin like interface (Figure 1): i.e., a soft pneumatic actuator (SPA)-skin that can be driven using pneumatics and is capable of generating plethora of actuation in the range of 10-100 Hz and can be complemented by integrated sensors (Sonar et al., 2019; Sonar et al., 2019; Sonar and Paik, 2016). The SPA-skin is fabricated using silicone material (Dragon Skin 30, Smooth-On Inc., USA) that has similar stiffness as human skin and provides optimal comfort, as is necessary for long duration fMRI studies (Figure 2). The actuator layer, i.e., the SPA, consists of an elastomeric membrane that can be pneumatically inflated with a pressure input (Sonar and Paik, 2016; see Figure 2B). This actuator is fabricated with three thin layers with a total thickness of 500-1000 μm : a middle flexible mask layer (50 μm) to define the actuator’s shape that is sandwiched between two silicone layers. The masking layer is laser cut to obtain the desired shape and is then laminated onto the bottom silicone layer to be encapsulated by a thin top silicone layer. The polypropylene mask adheres to the bottom silicone and ensures that, upon inflation, deformation occurs in the top membrane. It is important to ensure a proper grounding with the skin and attaching the SPA-skin properly at given location without obstructing the inlet pneumatic flow lines.

For any robotic system, sensor feedback plays an important role to ensure an accurate control and understanding of the surrounding environment. The traditionally available pressure or force sensors, needed for providing coherent tactile feedback, work well but like rigid tactile stimulators, these are also limited in their application when they need to be worn by humans, as they often lack the much needed compliance with human body. We have hence developed and integrated possibilities of sensing layers in the SPA-skin that provide localised measurement of interactive forces by virtue of different sensing technologies including active piezo charge sensing (Sonar and Paik, 2016) or passive methods like resistive strain sensor (

Sonar et al., 2019) and soft capacitive skin (Sonar et al., 2018). The sensing layer and the SPA-skin design process tackle this challenge using a finite element based simulation (Agarwal et al., 2017; Moseley et al., 2016) and closed loop feedback control through the sensing layer. This ensures an accurate tactile stimulation even under variable loading conditions or manufacturing variabilities (Sonar and Paik, 2016).

For the fMRI compliant tactile stimulator application we chose a ring shaped SPA design (with a 1.4cm diameter and 2mm inlet tube channel) to maximize the application area on skin while minimizing the volume of air being transferred through the long tubing that helps improving the maximum actuation frequency or bandwidth. The in-house developed setup independently controlled 8 channels that extended to different SPA-skins. The need for long tubing (5m to 6m) limited the amount of air being pushed to the actuators during inflation and then back during the deflation cycle. A careful system design was therefore carried out for each component of the pneumatic supply system (PSS) to achieve maximum bandwidth at 6m tube length and maintaining expected functionality of SPAs at less than 80kPa, as discussed in detail in (Joshi et al., 2021; Joshi and Paik, 2021). This allowed us to stretch the actuation bandwidth up to 15Hz in the current setup. When attempting to reach a bandwidth of 30Hz, we were still able to measure 0.5N of force at 30Hz, which is largely above the perception threshold for the face and fingers.

The SPA-skin was pneumatically controlled through an in-house developed control circuit that was interfaced through a serial communication to the stimulus computer (see Figure 1). The pneumatic controller was composed of the following components: a stimulus computer, a portable air compressor, a portable pneumatic control circuit module, and corresponding pneumatic tubes. An air compressor (Implotex, Germany) provided airflow to a pressure regulator (ITV1050, SMC Corp., USA) that was controlled by the microcontroller in the control circuit. The stimulation intensity could be adjusted using a single pressure regulator and an

array of high-speed solenoid valves which were driven through high-power MOSFET switches and stimulus from the micro-controller.

A portable pneumatic supply line, AC power supply and USB cable for serial communication enabled the primary extension of the controller setup to be placed just outside the RF shielding walls of the fMRI scanner. A 50mm diameter hole in the wall then carried the 5-6m long and 4mm thick tubes to the SPAs that were placed on the face or the fingers. Once connected in this fashion, the system acted as a plug-n-play device that can be easily controlled via the stimulus computer using simple serial commands to turn a given channel on or off at a given frequency. The pressure regulator could be manipulated through the stimulus computer and the working pressure of the pneumatic system could be read in realtime. The build-in limitation of 100kPa operational pressure ensures a delamination free operation of the SPA-skin.

Figure 1: Schematic illustration of the SPA setup. The pneumatic controller was composed of the following components: a stimulus computer, a portable air compressor, a portable pneumatic setup, and pneumatic tubes. Stimulation intensity and frequency could be controlled using a stimulus controlled places in the scanner control room. An air compressor (Implotex, Germany) places in the scanner control room provided airflow to a pressure regulator that was controlled by the microcontroller in the portable pneumatic setup. The stimulation intensity could be adjusted using the pressure regulator and an array of high-speed pneumatic valves which were driven through high-power MOSFET switches and inputs from the micro-controller. A 50mm diameter hole in the RF shielding wall then carried the 5-6m long and 4mm thick tubes to the SPAs that were places on the face or the fingers in the fMRI scanner room.

Experimental paradigm

SPAs were attached to the forehead (~1cm above the eyebrow), above the upper lip, and on the chin (see Figure 2A). These sites were chosen to ensure that an SPA was placed on each of the trigeminal nerves' innervated skin areas. Care was taken to not place SPAs on skin areas that are on the border of trigeminal nerve innervations. To ensure good grounding of the SPAs on

the face, we placed in-house 3D printed plates on top of the SPAs and used a custom-made fabric face mask to apply light pressure to the SPAs (see Figure 2B). Five further SPAs were attached to the fingertips of the left hand using adhesive tape.

Participants viewed a visual display positioned at the head of the scanner bore through a mirror mounted on the head coil. Participants 1-9 were presented with horizontally (for the finger stimulation runs) or vertically (for the face stimulation runs) aligned white circles, corresponding to the different stimulation locations. To cue the participant which location would be stimulated, the circle corresponding to this location turned red 0.8sec prior to stimulation onset and remained red until stimulation offset. Participants 10-17 were cued with the words “Forehead”, “Lips”, “Chin”, and “Thumb” presented in white centred on a black screen. To cue the participant which location would be stimulated, the text cue appeared on the screen 0.8sec prior to stimulation onset and remained on the screen until stimulation offset.

Participants were instructed to attend to the highlighted stimulation location as long as the cue was presented on the screen. Stimulation was presented for 8s at 8Hz with 900ms bursts of stimulation ‘on’ periods followed by a 100ms ‘off’ period to minimise peripheral adaptation. To ensure stable attention during the fMRI runs, stimulations were interrupted in a small percentage of the stimulation blocks (10-20% of trials per run). In these interrupted stimulation trials, stimulation was provided for 4s, after which a 2s silent period was introduced, following by another 2s of stimulation. Care was taken to ensure that the interrupted stimulation trials were equally distributed across the stimulation locations within each run. Participants were instructed to count the number of interrupted stimulation trials and verbally report this at the end of each run.

Since a stronger sensation is expected to lead to a stronger BOLD response, we aimed to match the sensation intensity across stimulation locations prior to the fMRI runs. A stimulation intensity matching task was carried out for the face and finger stimulation runs

separately. First, participants were asked to set the optimal stimulation intensity for a reference location. The forehead location was chosen as a reference for the face stimulation runs, and the little finger was chosen as the reference location for the finger stimulation runs. We chose these stimulation locations as references, since they are innervated by least mechanoreceptors and are therefore likely to be least sensitive (Corniani and Saal, 2020). Participants were instructed that an optimal stimulation intensity would be as strong as possible while remaining focal (i.e., no spread to skin locations not directly underneath the stimulator), comfortable, and stable over the 8s stimulation period (i.e., minimal peripheral adaptation). Participants were asked to respond by means of a button box whether the intensity should be decreased, increased, or should not change. Based on the participants' response the air pressure provided to the SPAs was decreased or increased in steps of 5 kPa (leading to a lower or higher stimulation intensity, respectively) or remained stable. If the participant responded twice in a row that the stimulation intensity should not be changed, the stimulation pressure for the reference location was set at this level for all fMRI tasks. Since the SPAs become fragile when using an air pressure exceeding 80 kPa, this was the maximum pressure setting that could be chosen by participants. The minimum air pressure provided was set at 20 kPa above atmospheric pressure. Once the optimal stimulation intensity was chosen for the reference location, participants were asked to match the stimulation intensity for the other stimulation locations to the stimulation intensity of the reference location. To enable this matching, participants were initially given an 8.8s stimulation trial for the reference location, immediately followed by a stimulation trial of one of the other stimulation locations. Participants were instructed to change the stimulation intensity of the 2nd location to match the stimulation intensity of the reference location as closely as possible. For the face stimulation runs, participants were instructed to match the stimulation intensity of the lips, chin, and thumb to the reference forehead stimulation intensity. For the face stimulation runs, participants were instructed to match the stimulation intensity of

the thumb, index, middle, and ring finger to the reference little finger stimulation intensity. As before, if the participant responded twice that the stimulation intensity should not be changed, the stimulation pressure for this stimulation location was set at this level for all fMRI tasks.

Instructions and stimulations were delivered using Psychtoolbox (v3) implemented in Matlab (v2014b). Matlab then communicated with the Arduino board implemented in the SPA controller set-up via a serial port over a proprietary protocol. Head motion was minimized using over-ear MRI-safe headphones or padded cushions.

A) SPA locations

B) SPA and SPA grounding

Figure 2: SPA locations and grounding on the face. A) SPAs were attached to the forehead, upper lip, chin, and thumb. We either tested the right or the left side of the face and the right or the left thumb. Shaded areas on the face indicate the skin areas innervated by different branches of the trigeminal nerve. B) SPAs were grounded to the face using a custom made fabric mask.

Fingers stimulation runs

The finger stimulation blocked design consisted of 6 conditions: Stimulation conditions for each of the five fingers of the left hand and a rest (no stimulation) condition. The visual cue during the finger stimulation blocks was as described above and presentation of the word “Rest” indicated the rest condition. Each of these 6 conditions had a block duration of 8.8s and was repeated 5 times per run in a counterbalanced order. Each run comprised a different block order and had a duration of 4min and 39.4s. We acquired 4 blocked design runs, with a total duration of 18min and 37.6s.

Face stimulation runs

All face stimulation runs also involved stimulation of the forehead, lips, chin, and thumb. 14 participants were stimulated on the left side of their face and the left thumb. 3 participants were stimulated on the right side of the face and their right thumb. We included thumb stimulation in these runs as the thumb representation borders the face area in S1 (Kikkert et al., 2021, 2016; Kolasinski et al., 2016; Penfield and Rasmussen, 1950; Roux et al., 2018). To uncover face somatotopy we used a blocked design consisting of 5 conditions: Stimulation conditions for each of the three face locations and for the thumb, as well as a rest (no stimulation) condition. The visual cue during the face stimulation blocks were as described above and presentation of the word “Rest” indicated the rest condition. Each of these 5 conditions had a block duration of 8.8s and was repeated 8 times per run in a counterbalanced order. Each run comprised a different block order and had a duration of 6min and 7.4s. We acquired 4 blocked design runs, with a total duration of 24min and 29.6s.

MRI acquisition

MRI data was acquired using a Philips 3 tesla Ingenia system (Best, The Netherlands). Data of participants 1-9 was collected using a 32-channel head coil and data of participants 10-18 was collected using a 15-channel head coil. fMRI data was acquired using an echo-planar-imaging (EPI) sequence with partial brain coverage: 36 sagittal slices were centred on the postcentral gyrus with coverage over the thalamus and brainstem. We used the following parameters: 2.3mm³ spatial resolution, TR: 2200ms, TE: 30ms, flip angle: 82°, SENSE factor: 2.1, 36 slices. We acquired 127 and 167 volumes for the finger and face stimulation runs, respectively. Anatomical T1-weighted images for participants 1-9 were acquired using the following acquisition parameters: TR = 7.7 ms, TE = 3.6 ms, flip angle = 8°, voxel size = 1

mm isotropic, transversal slices = 160. Anatomical T1-weighted images for participants 10-17 were acquired using the following acquisition parameters: 0.7mm³ spatial resolution, TR: 9.3ms, TE: 4.4ms, flip angle: 8°.

MRI analysis

fMRI analysis was implemented using tools from FSL v6.0 (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki>) in combination with the RSA toolbox (Nili et al., 2014; Wesselink and Maimon-Mor, 2017) and in-house scripts developed using Matlab (R2018a). Cortical surface analysis and visualisations were realised using Freesurfer (<https://surfer.nmr.mgh.harvard.edu/>; Dale et al., 1999; Fischl et al., 2001).

Preprocessing and image coregistration

Common preprocessing steps were applied to each individual fMRI run using FSL's Expert Analysis Tool FEAT (version 6.0; <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FEAT>). The following preprocessing steps were included: motion correction using MCFLIRT (Jenkinson et al., 2002), brain extraction using automated brain extraction tool BET (Smith, 2002), spatial smoothing using a 2.3mm full-width-at-half-maximum (FWHM) Gaussian kernel, and high-pass temporal filtering using a cut-off of 90s.

Image coregistration was done in separate, visually inspected, steps. For each participant, a midspace (i.e., an average space in which images are minimally reoriented) was calculated between the 4 face stimulation blocked design runs and, if the fingers were also tested, between the four finger stimulation blocked design runs. We then transformed all fMRI data to these functional midspaces using purely rigid probability mapping in ANTs. Next, we registered each participant's midspace to the T1-weighted image, initially using 7 degrees of freedom and the mutual information cost function, and then optimised using boundary based

registration (BBR; Greve and Fischl, 2009). Each coregistration step was visually inspected and, if needed, manually optimised using blink comparison in Freeview. Structural images were transformed to Montreal Neurological Institute (MNI) standard space using nonlinear registration (FNIRT).

Univariate analysis

First-level parameter estimates were computed using a voxel-based general linear model (GLM) based on the gamma hemodynamic response function and its temporal derivatives. Time series statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction. To reduce noise artifacts, CSF and WM scan wise time series were added to the model as nuisance regressors. Data were further assessed for excessive motion, and volumes with an estimated absolute mean displacement $> 1.15\text{mm}$ (half of the functional voxel size) were scrubbed. Contrasts were defined for each stimulation condition versus rest, for overall face or finger stimulation conditions versus rest, and for each stimulation condition versus all other stimulation conditions. We then used a fixed effects higher-level analysis to average across the finger stimulation runs and across the face stimulation runs separately for each individual participant. Z-statistic images were thresholded using clusters determined by $Z > 2.3$ and $p < .05$ family-wise-error-corrected cluster significance thresholding was applied.

To visualise inter-participant consistency of somatotopic finger and face selective representations, we calculated cortical activation probability maps. Cortical surface projections were constructed from participant's T1-weighted images. Each participant's cortical surface was inflated into a sphere and aligned to the Freesurfer 2D average atlas using sulcal depth and curvature information. The thresholded stimulation site selective (i.e., condition versus all other stimulation conditions) contrast maps from each participant's fixed effects higher-level

analysis were resampled to the Freesurfer 2D average atlas and binarised. We then calculated finger-specific and face part specific inter-participant probability maps.

Lastly, to visualise which brain areas were activated during overall face and fingers stimulation, whole-brain group averages were assessed for the stimulation of all fingers versus rest and stimulation of all face locations versus rest contrasts. Group-level analysis was performed for the finger and face stimulations runs separately using FMRIB's Local Analysis of Fixed and Mixed Effects (Woolrich et al., 2004), respectively. Data collected for individuals of whom we tested the right side of the face was flipped on the midsagittal plane before conducted group analysis to ensure that the tested hemisphere was consistently aligned. Z-statistic images were thresholded using clusters determined by $Z > 3.1$ and $p < .05$ family-wise-error-corrected cluster significance thresholding was applied. To visualise the group average activity maps, statistical parametric activity maps were projected to the Freesurfer 2D average atlas brain.

Representational similarity analysis

A fuller description of somatotopic representations can be obtained by taking into account the entire fine-grained activity pattern of stimulated finger or face parts. Representational dissimilarity was therefore estimated between fingers or between face locations using the cross-validated squared Mahalanobis distance (or crossnobis distance; Nili et al., 2014; Wesselink and Maimon-Mor, 2017b). We closely followed previously described procedures (Kikkert et al., 2021; Wesselink et al., 2019).

We first defined an anatomical S1 hand and an S1 face ROI using the probabilistic Brodmann area parcellation provided by recon-all in Freesurfer. Each participant's cortical parcellations for Brodmann areas 1, 2, 3a and 3b were converted to volumetric space and merged to form a single S1 mask. Next, any holes in these converted masks were filled and the

non-zero voxels in the mask were mean dilated. We restricted this S1 mask such that it spanned a 2cm strip medial/lateral to the anatomical location of the hand knob to form the S1 hand ROI (Yousry et al., 1997). The S1 area inferior to this S1 hand ROI was then extracted to form the S1 face ROI.

We computed the dissimilarity between the activity patterns measured for each pair of stimulation conditions within the S1 hand or S1 face ROI for the fingers and face stimulation runs, respectively. We extracted the voxel-wise parameter estimates (betas) and the model fit residuals under the ROI and prewhitened the betas using the model fit residuals. We then calculated the cross-validated squared Mahalanobis distances between each pair of conditions, using the four runs as independent crossvalidation folds, and averaged the resulting distances across the folds.

The dissimilarity values for all pairs of conditions were initially assembled in a representational dissimilarity matrix (RDM), with a width and height corresponding to the number of conditions (i.e., a 5x5 RDM for the finger stimulation runs and a 4x4 RDM for the face stimulation runs). Since the RDM is mirrored across the diagonal with meaningless 0's on the diagonal, all statistical analysis was conducted on the unique values of the RDM (10 unique values for the finger stimulation runs and 6 unique values for the face stimulation runs). Finally, we performed multidimensional scaling (MDS) to visualise the dissimilarity structure of the RDM in an intuitive manner. MDS projects the higher-dimensional RDM into a lower-dimensional space, while preserving the inter-condition dissimilarity values as well as possible (Borg and Groenen, 2005). MDS was performed for each individual participant and then averaged per group after Procrustes alignment to remove arbitrary rotation induced by MDS.

We estimated the strength of the representation or “representational separability” by averaging the unique off-diagonal values of the RDM. If it is impossible to statistically differentiate between conditions (i.e., when a parameter is not represented in the ROI), the

expected value of the distance estimate would be 0. If it is possible to distinguish between activity patterns this value will be larger than 0. To further ensure that our S1 face ROIs contained face information, we created a cerebral spinal fluid (CSF) ROI that would not contain somatotopic face information. We then repeated our face RSA analysis in this ROI and statistically compared the separability of the CSF ROI to the separability in the S1 face ROI.

Statistics

Statistical analysis was carried out using SPSS (v25). Non-parametric statistical testing was used for analysis of the finger stimulation data. Parametric statistical analysis was carried out for the face stimulation data after checking for normality using the Shapiro-wilk test. Non-parametric statistical testing in case of normality violations. All testing was two-tailed and we used the Benjamini-Hochberg procedure to control the false discovery rate with $q < 0.05$.

Data availability

Full details of the experimental protocol are available on clinicaltrials.gov under the number NCT03772548. Data is shared on <link will be made available upon publication>.

Results

In the current study, we aimed to validate the use of our newly developed SPA-setup for somatotopic mapping using fMRI, we first explored whether SPA tactile stimulation would elicit characteristic finger representations in S1. Next, we used our SPA setup to uncover the somatotopic layout of the face in S1.

Vibrotactile SPA stimulation induces activity in somatosensory processing areas

We first examined activity elicited by tactile stimulation applied on the fingers (Figure 3A) and on the face (Figure 3B) using our SPA setup. As expected, we found that both stimulation on the fingers and on the face activated S1 and secondary somatosensory cortex (S2) contralateral to the stimulation site. Ipsilateral S1 and S2 activity was less widespread for both the fingers and face stimulation. Note that a direct comparison with regards to level of activity between the finger and face stimulation runs is not accurate here given that activity elicited by fingers stimulation was only tested on a subset of 8 participants and fixed effects modelling was used to create the group activity map in Figure 3A. In contrast, 17 participants were tested to examine activity elicited by face stimulation and mixed effects modelling was used to create the group activity map in Figure 3B. Importantly, following the classical layout of the homunculus (Penfield and Rasmussen, 1950), fingers stimulation activity was superior to the face stimulation activity in S1.

Figure 3: Brain activity in the contralateral hemisphere during sensory stimulation using SPA technology.

Both fingers (A) and face (B) stimulation elicited activity in S1 and secondary somatosensory cortex. Consistent with previous reports and the classical layout of the homunculus, face stimulation elicited activity inferior to the hand representation. White arrows indicate the central sulcus. P = posterior, A = anterior.

Finger representations

We hypothesized that if our SPA technology is reliable in mapping somatotopic representations, then we should observe typical finger somatotopy in the S1 hand area. Since the S1 hand representation contains a characteristic layout of finger selective representations that is relatively consistent across individuals, we first explored finger selective representations. We contrasted activity elicited during each finger stimulation against activity during stimulation of all other fingers and binarized the resulting finger selective maps. We then created inter-participant probability maps representing the number of participants exhibiting specific finger selectivity (i.e., using a winner-take-all approach) for each vertex in S1. These maps exhibited, as expected, that finger selectivity was not perfectly consistent across participants (Figure 4A; Kolasinski et al., 2016). Indeed, a given vertex was found to have finger selectivity selective for different fingers across participants. We did however observe a characteristic gradient of finger preference progressing from the thumb, for which inter-subject probability was highest lateral of the S1 hand area, to the little finger, for which inter-subject probability was highest medial of the S1 hand area. Qualitative inspection

suggests that inter-participant consistency was highest for the thumb and lowest for the little finger representation.

Next, we explored a 2nd somatotopic principle that is known to be consistent across individuals: the pattern of overlap between finger representations. We examined this intricate relationship between finger representations using representational similarity analysis. We found a typical pattern of inter-finger representational distances where neighbouring fingers have relatively lower representational distances compared to fingers that are further apart. Furthermore, fingers that we use more frequently together in daily life (e.g., the ring and little fingers) had lower representational distances compared to fingers we use more separately in daily life (e.g., the thumb and index fingers (Ejaz et al., 2015)). This inter-finger representational distance pattern found using SPA tactile stimulation of fingers (Figure 4B) was highly similar to the inter-finger representational distance patterns that we and others have described previously in fMRI experiments using individual finger movements (Ejaz et al., 2015; Kikkert et al., 2021, 2016; Sanders et al., 2019; Wesselink et al., 2019) or individual finger tactile stimulation (Sanders et al., 2019). The inter-finger representational distances were averaged across finger pairs within each participant to obtain an estimate for average inter-finger representational separability (see Figure 5C), or ‘representation strength’. We found that inter-finger separability in the S1 hand area was greater than 0 ($Z = -2.52$, $p = 0.01$), showing that the S1 hand area contained information about individual finger representations. Furthermore, there was significant greater separability in the S1 hand area compared to a control cerebral spinal fluid (CSF) ROI that would not be expected to contain finger specific information ($Z = -2.52$, $p = 0.01$). Together, our results demonstrate that our SPA setup can be used to reliably map the well characterised somatotopic layout of the hand.

Figure 4: SPA stimulation uncovers typical finger somatotopy. A) inter-participant probability maps of finger selective representations. Colours indicate the number of participants (ranging from 1 (red) till 8 (blue)) who demonstrated finger selectivity for a given vertex. Typical finger selectivity is characterised by a progression of finger selectivity from the thumb (laterally) to the little finger (medially). We observed a characteristic gradient of finger preference progressing from the thumb, for which inter-subject probability was highest lateral of the S1 hand area, to the little finger, for which inter-subject probability was highest medial of the S1 hand area. Qualitative inspection suggests that inter-participant consistency was lowest for the little finger representation and highest for the thumb representation. The white arrow indicates the central sulcus. A = anterior; P = posterior. B) Two-dimensional projection of the representational structure of inter-finger distances. Inter-finger distance is reflected by the distance in the two dimensions. Individual fingers are represented by different colours: thumb = red; index finger = yellow; middle finger = green; ring finger = blue; little finger = purple. By stimulating fingers using SPA technology, we found a classical and frequently reported inter-finger distance pattern in the hand area of S1. Ellipses represent the between-participants standard error after Procrustes alignment.

Face representations

One advantage of our SPA setup is that, unlike most commercially available vibrotactile devices, it is able to provide vibrotactile stimulation to localised areas of the face (i.e., in the MRI head coil) without causing any imaging artefacts or safety issues. We made use of this advantage by examining the somatotopic layout of the face using our SPA setup. First, as for the fingers, we created inter-participant probability maps of forehead, lip, chin, and thumb selective representations (Figure 5A). The resulting inter-participant probability maps represent the number of participants exhibiting selectivity (i.e., using a winner-take-all principle) for a specific stimulation site for each vertex in S1. Qualitative inspection suggests

that the selective thumb and lip activity was more consistent across participants compared to the forehead and chin. Furthermore, stimulation site selective activity was more consistent across participants in the contralateral compared to the ipsilateral hemisphere.

We used RSA in the S1 face area to investigate representational distances between stimulation sites (i.e., between the forehead, lip, chin and thumb) that were stimulated during the face stimulation runs (Figure 5B). The averaged representational distances (i.e., separability) between face sites (i.e., excluding the face-thumb distances) were markedly lower compared to the representational distances found between fingers in the S1 hand area (Figure 5C; $Z = -2.52$, $p = 0.01$). However, we found a clear pattern of inter-face site representational distances in the S1 face area revealing that the forehead had the lowest representational distance from the thumb. The chin had more representational distance from the thumb than the forehead, and the lips was most distant from the thumb.

We found that inter-face site (i.e., excluding the face-thumb distances) separability in the S1 face area was greater than 0 (Figure 5C; $t_{(16)} = 5.84$, $p < 0.001$), indicating that the S1 face area contained information about face sites. Separability between face sites was not significantly greater than 0 in a CSF ROI ($t_{(16)} = -0.25$, $p = 0.81$). Furthermore, there was significant greater separability in the S1 face area than in a control CSF ROI ($t_{(16)} = -6.00$, $p < 0.001$).

Figure 5: Face somatotopy uncovered using SPA stimulation. A) Inter-participant somatotopic probability face maps. Colours indicate the number of participants (ranging from 1 (red) till 17 (blue)) who demonstrated face part or thumb selectivity for a given vertex (i.e., stronger activity compared to the other stimulation sites). Qualitative inspection suggests that inter-participant consistency contralaterally was lowest for the forehead representation and highest for the thumb representation. Furthermore, inter-participant consistency was higher in contralateral, compared to ipsilateral S1. White arrows indicate the central sulcus. A = anterior; P = posterior. B) Two-dimensional projection of the representational structure of inter-stimulation site distances. Inter-stimulation site distance is reflected by the distance in the two dimensions. Individual stimulation sites are represented by different colours: thumb = red; chin = yellow; forehead = green; upper lip = blue. Ellipses represent the between-participants standard error after Procrustes alignment. C) Separability (i.e., average dissimilarity), or ‘representation strength’, for the fingers in the S1 hand area, for the face in the S1 face area, and for cerebral spinal fluid (calculated between face stimulation sites). There was significant separability (i.e., great than 0) for the fingers in the S1 hand area and for the face in the S1 face area. No significant separability was found in a control CSF ROI. Furthermore, separability for the fingers in the S1 hand area and for the face in the S1 face area was greater than separability in the control CSF ROI. Lastly, separability was higher for the fingers in the S1 hand area compared to separability in in the S1 face area. * = $p < 0.05$; *** = $p < 0.001$

Discussion

Providing somatosensory stimulation in an MR environment is challenging. Our results show that somatosensory representations can be mapped using new SPA technology that is MR-compatible and can be used within the MR head coil without causing artefacts. Using our SPA setup, we found a typical somatotopic layout of participants' fingers, both in terms of the gradient of finger selectivity and the inter-finger representational distance pattern. This validates the use of our SPA setup for mapping somatotopic representations.

We further probed face somatotopy using automated tactile stimulation to the forehead, lips, and chin – 3 face sites that are innervated by different branches of the trigeminal nerve. Representational distances between the face sites were drastically reduced compared to the representational distances between the fingers. Our face somatotopy results did not support a clear inverted or straight-up representation of the face. Our univariate analysis revealed a great degree of inter-participant variability of face-site selective representations. While the location of the thumb and lip representations were relatively stable across participants, the forehead and chin representations were much less stable. Potentially, the low density of mechanoreceptors in the chin and forehead may have led to lower BOLD activations, causing them to be 'overshadowed' by the thumb and lip representations in this winner-take-all analysis. We attempted to control for variability in sensed intensity using our intensity matching task. Mechanoreceptor innervation in the skin of a given body part is suggested to be directly linked to size of S1 representation (Catani, 2017; Penfield and Rasmussen, 1950). It is therefore likely that the forehead and chin are represented less prominently in S1 compared to the thumb and lip and may therefore not 'win' in winner-take-all univariate stimulation site selective analysis. Indeed, we suggest that it is more appropriate in the study of face somatotopy to use an analysis method that does not adhere to such a winner-take-all principle and instead is sensitive to representational overlap or representational distances between face parts. Using RSA, we

revealed that the forehead was least distance to the thumb representation, followed by the chin representation, and lastly by the lip representation. These results are in line with, and extend the results of, a recent study using RSA and movements of the forehead, nose, lips, and tongue to study face somatotopy in S1. As in our study, Root et al. (2021) reported that the forehead neighboured the hand representation. They further found that the nose closely neighboured the forehead representation and that the lips were furthest from the forehead representation. Root et al. (2021) could not disentangle the lips and chin representation, due to the nature of their movement task. As such, we extend their results by showing that the chin representation is in-between the lip and forehead representation in S1.

The aim of this study was to construct a simple MR-compatible pneumatic vibrotactile device for implementation in somatotopic mapping experiments. While pneumatic tactile stimulators are highly applicable in studies investigating somatotopy, especially when investigating body part representations in or nearby the MR head coil, they generally have a smaller frequency range and more limited actuation control compared to piezoelectric devices. Due to the length of our plastic tubes, our SPA setup can provide accurate control of frequencies up to 35Hz. While this stimulation frequency is reasonable for somatotopic mapping experiments, it may not be ideal when investigating neural responses to stimulation of specific mechanoreceptors. Furthermore, while our SPA setup can stimulate suprathreshold, its stimulation amplitude is limited due to the nature of the SPA material. As such, it is not suitable for studies requiring highly intense sensations on skin surfaces with low innervation of mechanoreceptors (e.g., on the neck or ankle). Furthermore, the pneumatic supply system components (tubing resistance, compressibility and inertia of the oscillating air, conductance of various components) and the extent of grounding force with which the SPA is fixed to the stimulation site influences the exact amount of skin indentation. The overall control system is optimized using the process presented in Joshi et al., (2021) for individual components.

Together our results show that, by providing vibrotactile stimulation using the SPA-technology, we are able to reveal clear somatotopic representational patterns of different body parts. Given that in our SPA-setup, all materials in the MRI scanner room are non-metallic, no MR safety and image quality certifications are required when using this device. SPAs are small and can easily be attached to different sites of the body. The SPA setup is flexible, easy-to-implement, precise, portable, fast and offers a cost-effective solution in comparison to commercially available devices that often induce artefacts, are highly expensive, require active shielding, or hardware modifications.

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Competing interests

The authors declare that no current competing interests exist.

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