Towards cot-side mapping of the somatomotor cortex in preterm and term infants with wearable high-density diffuse optical tomography

Elisabetta Maria Frijia[a,b], Hubin Zhao[a,b,c] Liam Collins-Jones[a,b], Greg Smith[d], Nicholas L. Everdell[d], Topun Austin[b] and Robert J. Cooper[a,b]

[a]*DOT-HUB, Department of Medical Physics and Biomedical Engineering, University College London, London, WC1E 6BT, UK*
[b]*neoLAB, Cambridge University NHS Foundation Trust, Cambridge, CB2 OQQ, UK*
[c]*James Watt School of Engineering, University of Glasgow, Glasgow, G12 8QQ, UK*
[d]*Gowerlabs Ltd., Department of Medical Physics and Biomedical Engineering, University College London, London, WC1E 6BT, UK*
elisabetta.frijia.18@ucl.ac.uk

Abstract: We are translating wearable HD-DOT to the neonatal clinic to investigate healthy and brain-injured infants and establish a model of the developmental trajectory of the infant sensorimotor system.

1. Introduction

Neonatal brain injuries often occur at birth or in the very early days of life, and brain-injured newborns often go on to develop cerebral palsy. Cerebral palsy (CP) is a group of permanent movement disorders and is the most common movement disability of childhood [1]. Even if there is no cure for CP, early diagnosis is critical for treatments that can potentially improve an infant's long-term motor ability. Therapy should be undertaken during the first few weeks and months of life when the brain is at its most adaptable. The majority of infants with CP are not formally diagnosed until 1 or 2 years-of-age. At present, there is a lack of methodology that can provide early and objective assessment of neuromotor development. The parts of the brain that control movement and receive somatosensory input have a disrupted organization in subjects with cerebral palsy. Monitoring this disruption in the infant using functional neuroimaging could improve our understanding of the emergence of CP, and potentially aid early diagnosis.

At present, no technology can provide high resolution and motion tolerance needed to map the infant sensorimotor system at the cot-side. Most fNIRS fibre-based devices only permit the acquisition of ~20-100 sparse channels [2], and the placement of high numbers of optical fibres is challenging, particularly for newborn subjects. The ANIMATE systems developed at DOT-HUB consist of wearable HD-DOT modules designed specifically for neonatal applications. The introduction of these lightweight, wearable HD-DOT technologies allows a higher channel density and therefore higher accuracy and spatial resolution than has previously been possible in this population.

2. Methods

2.1 The ANIMATE HD-DOT systems

The ANIMATE systems are a series of wearable, lightweight HD-DOT technologies based on the Gowerlabs LUMO platform that are designed to map the somatomotor cortex of the neonate. We have developed a series of different mechanical designs (Fig. 1(a,b)) that seek to miniaturize the system footprint, reduce the weight and provide an encapsulation that is cleanable and/or disposable and therefore suitable for the clinical environment. A key feature of these designs is that they can easily conform to the highly curved infant scalp. In ANIMATE v1 multilayer flex-rigid PCBs are implemented to produce modules of 2 or 3 hexagonal units (Fig. 1(a)). Each unit is equipped with 3 dual-wavelength LEDs (735 nm and 850 nm) sources and 4 silicon photodiodes detectors, and provides within-unit source-detector separations (SDS) of 10 mm and 20 mm. Board-to-board connectors are built in to each dual or tri-hex DOT module on flexible PCB tabs to allow different DOT modules to be connected together in various configurations. The ANIMATE v2 system (Fig. 1(b)) is also made of independent modules based on flex-rigid PCB. The number of sources and detectors and intra-unit source-detector separation are the same as ANIMATE v1, but by using a switch-back, stacked board design, each module can be connected by a short, robust and shielded cable to create a daisy-chain of modules without increasing the module footprint. This design was constructed to optimise for robustness and permit clinical handling in the neonatal clinic. In both systems (v1 and v2), the units are encapsulated in cleanable and/or disposable rubber manifolds that are suitable for the clinical environment. The layout configuration of both system consists of up to 12 hexagonal units that provide a total of 36 sources and 48 detectors and allow ~600 measurement channels per wavelength (Fig. 2(b)).

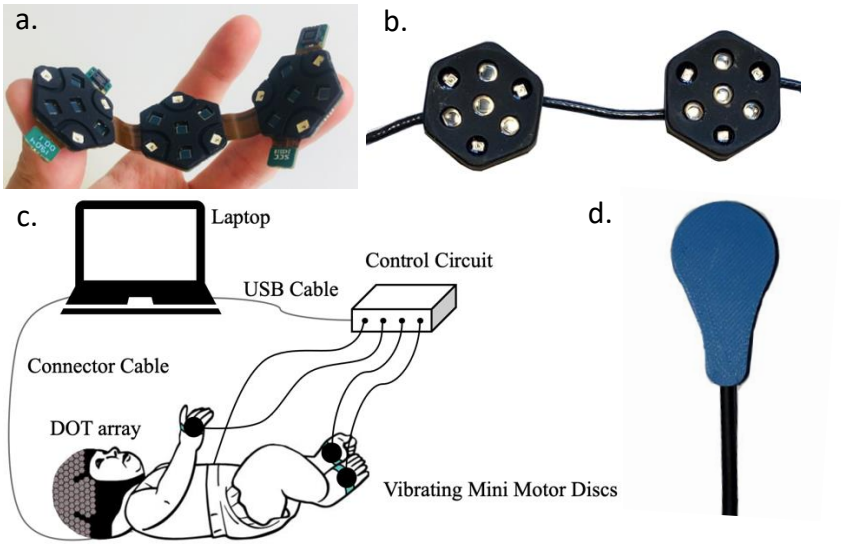

Fig. 1. ANIMATE v1 triple-hexagonal module design (a). ANIMATE v2 connected hexagonal modules (b). Infant DOT sensorimotor imaging arrangement (c). Silicone encapsulation of the vibrating DC micro motor (d).

2.2 Sensorimotor Mapping Paradigm

To map the sensory and motor cortices of the newborn at the cot-side, we must first develop an appropriate stimulation paradigm. Several studies have shown that tactile stimulation is a reliable method to evoke a functional response in the somatosensory cortex [3–5]. We have therefore developed a custom vibrotactile stimulation system to elicit somatosensory responses in the infant. A soft, flexible stimulation band containing a vibrating DC micro motor will provide vibrotactile stimulation controlled via a PC (Fig. 1(c)). The vibrating motors are switched on and off via a custom, USB-serial-controlled circuit based on a low-cost, 4-channel USB relay.

The functional organization of the motor cortex will be mapped by performing a motor stimulation of multiple parts of the body. Given that infants are clearly incapable of undertaking a specified motor paradigm, motor activation will be achieved by monitoring spontaneous, self-driven infant movement, or via passive movement of limbs. Spontaneous movements of the infant will be tracked using a 3D inertial motion tracking system. These motion capture devices (Notch (https://wearnotch.com)) are lightweight and will be placed on each limb to capture and record relative upper and lower limb movements based on three-axis acceleration data and three- axis gyroscope data. A secondary motion capture system based on video recording will also be used.

Each experiment will be divided in two phases. The first will involve the somatosensory stimulation of each limb using the vibrotactile system. During the second phase, the infants will be left free to move in their cot while the motion tracking systems will monitor their limb movements to enable functional imaging of the motor cortex. In order to interpret and correlate an HRF signal to a specific limb, we will extract features of the motion tracking data to be used to encode events in a general linear model of the HD-DOT data. By combining the tracking data and video monitoring of the movements it will be possible to aid clinical assessment of movement itself, alongside our neuroimaging investigation of the motor cortex.

2.3 Phantom validation

In order to validate the ANIMATE systems and demonstrate their capacity to image to sensorimotor cortex in infants, a novel, anatomically accurate dynamic phantom has been realised. This tissue-mimicking phantom is electrically activated with precisely controlled thermochromic targets positioned at the location of the primary motor cortex. Three-dimensional images of the activation of the targets within the phantom were obtained with the ANIMATE v1 system. Recordings were taken from both hemispheres by placing the array (which consisted of two tri-hex and three dual-hex modules) in a flexible cap (EasyCap, Germany) over the top surface of the phantom directly above the two targets, covering the left and right motor sensorimotor cortices symmetrically (Fig. 2(a)).

3. Results

Preliminary results obtained using the dynamic phantom are shown in Fig. 2(d,e). As shown from the three-dimensional reconstructed volume images the system detected and localized the discrete regions of absorption located at a certain depth below the phantom scalp surface over the location of the targets. The Euclidean separation

between the centre of mass and the centre of the rod target volume was evaluated. The offsets for the 735 nm wavelength are 5.83 and 3.68 mm for the left and the right hemisphere respectively and similarly for the 850 nm wavelength the values are 6.91 and 2.59 mm. Using the images shown in Fig. 2(d,e) we calculated the FWHM of the perturbation in x (left-right), y (anterior-posterior) and z (inferior-superior) at 735 nm. The values obtained were 12.59, 12.04 and 10.52 mm respectively for the left hemisphere target, and 12.14, 16.38 and 17.68 mm for the right hemisphere target. The dimensions of the thermochromic target in these dimensions were 8.0, 8.0 and 8.0 mm respectively.

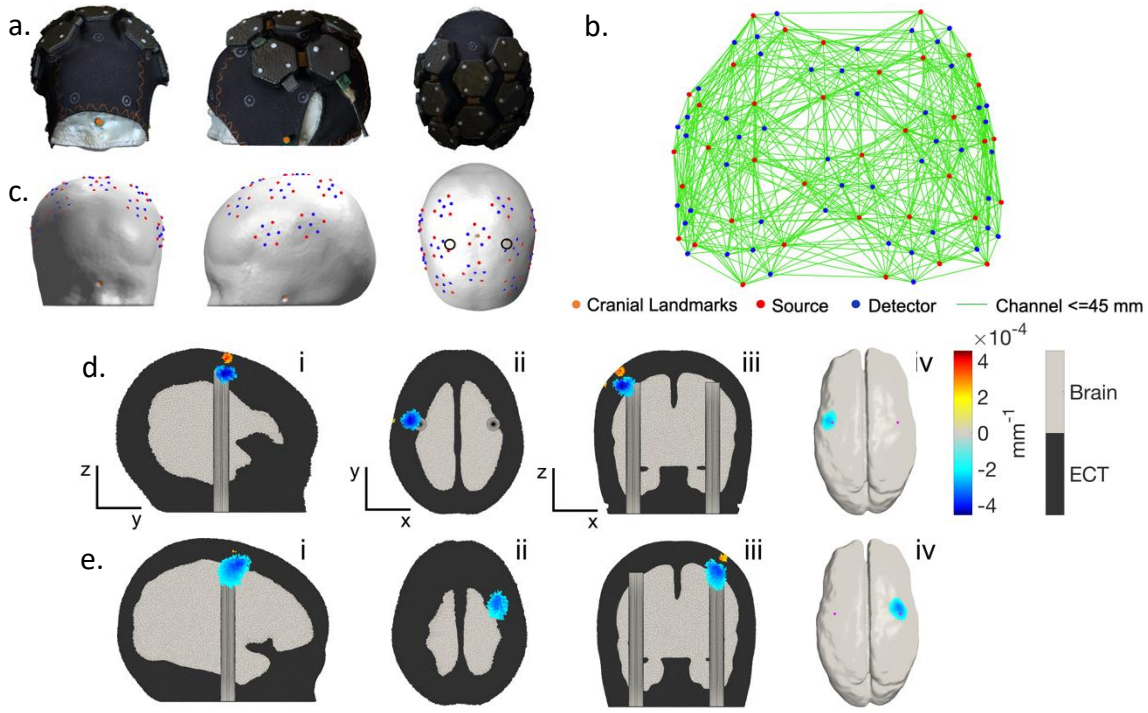

Fig. 2. (a) Frontal, lateral, and superior views of the ANIMATE v1 system placed on the dynamic phantom. (b) 3D channel layout from the above. (c) Optode positions registered to the anatomical atlas model. Volumetric and grey-matter surface images of changes in absorption coefficient at 735 nm (λ_1) displayed for the left (d) and the right (e) hemisphere activations. Each image is thresholded at 50% of the maximum absolute signal deviation found in the volume. The sub-panels in each row show the volume images in sagittal section (i), transverse section (ii), and coronal section (iii), and an extraction of the grey-matter surface (iv).

4. Conclusion

We are working towards translation of wearable HD-DOT to the neonatal clinic to map the sensorimotor system in healthy and brain-injured infants. We have developed two different HD-DOT systems, both specifically for neonatal clinical applications. Each has different mechanical advantages, but both are lightweight, low-profile and provide high-density sampling. Phantom validation of the v1 system demonstrates that the spatial localization and resolution of the system should be sufficient to resolve functional activation in response to the stimulation of each limb in the newborn infant. Our goal is to optimise the design of our sensorimotor paradigm to map brain function during vibrotactile stimulation and during natural movement. Translating these technologies to the neonatal clinic will enable imaging at the cot-side throughout the perinatal period, allowing us to investigate novel imaging markers of motor dysfunction and cerebral palsy.

5. References

[1] S. McIntyre, C. Morgan, K. Walker, and I. Novak, "Cerebral palsy-Don't delay," *Dev. Disabil. Res. Rev.*, vol. 17, no. 2, pp. 114–129, 2011.

[2] F. Scholkmann *et al.*, "A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology," *NeuroImage*, vol. 85. pp. 6–27, 15-Jan-2014.

[3] C. Habermehl *et al.*, "Somatosensory activation of two fingers can be discriminated with ultrahigh-density diffuse optical tomography," *Neuroimage*, vol. 59, no. 4, pp. 3201–3211, Feb. 2012.

[4] S. P. Koch, "High-resolution optical functional mapping of the human somatosensory cortex," *Front. Neuroenergetics*, 2010.

[5] C. Stippich *et al.*, "Somatotopic mapping of the human primary somatosensory cortex by fully automated tactile stimulation using functional magnetic resonance imaging," *Neurosci Lett*, vol. 277, no. 1,pp. 25-8, 17-Dec-1999.