2013

Measuring the spatiotemporal profiles of neuronal activity and bold in early visual cortex using high resolution fMRI

Mark M. Schira
University of Wollongong, mschira@uow.edu.au

Michael Breakspear
Queensland Institute of Medical Research

K M. Aquino
University of Sydney

Measuring the spatiotemporal profiles of neuronal activity and bold in early visual cortex using high resolution fMRI

Abstract

Abstract presented at the Australian Neuroscience Society Inc 33rd Annual Meeting, 3-6 Feb 2013, Melbourne, Australia

Keywords

spatiotemporal, profiles, neuronal, activity, bold, early, visual, cortex, high, measuring, resolution, fmri

Publication Details

Schira, M. M., Breakspear, M. & Aquino, K. M. (2013). Measuring the spatiotemporal profiles of neuronal activity and bold in early visual cortex using high resolution fMRI. 33rd Meeting of the Australian Neuroscience Society: Program, Abstracts & List of Registrants (p. 61). Australia: ANS.

ORAL-17-05

DEFINING MECHANICAL STATES OF PERISTALSIS USING COMBINED IMPEDANCE/MANOMETRY INTRALUMINAL RECORDING

Dinning P.G.[1], Omari T.[2], Wiklendt L.[3], Spencer N.J.[1] and Costa M.[1]
[1]Human Physiology, Flinders University, South Australia. [2]Gastroenterology Unit, Child, Youth & Women's Health Service, South Australia. [3]Department of Medicine, University of New South Wales, NSW.

Purpose: Utilising measures of gut diameter (video) and intraluminal pressure (manometry) we have defined the mechanical states of the intestinal muscle during neurogenic and myogenic motor activity. Similar analysis of the gut mechanical states *in vivo* is not feasible, as video imaging of the gut cannot be performed. Intraluminal impedance has been used to assess the cross sectional area of the lumen (internal diameter) in human clinical research studies. Therefore, we used a combined manometry/impedance catheter to examine whether impedance could accurately measure changes in diameter, and then when combined with manometry recordings, identify the mechanical states of the muscle. **Methods:** Motor activity of isolated rabbit distal colon were studied in a bath of oxygenated Krebs solution at 37°C. Spatio-temporal maps of changes in diameter were constructed from video recordings and spatio-temporal maps of pressure and impedance were constructed from the measures recorded by a high-resolution impedance/manometry catheter. We developed combined maps of: i) diameter & pressure (DPMaps); ii) diameter & impedance (DImaps); iii) pressure & impedance (PImaps). Correlation between changes in diameter and impedance were assessed with Pearson cross correlation. The calculated mechanical states of the muscle were compared between DPmaps & PImaps. **Results** showed excellent correlation between changes in impedance and diameter ($r = 0.85$). States of active and passive neurogenic activity could be identified and matched to those defined between pressure and diameter. **Conclusion:** These results support the potential application of combined manometry and impedance to measure in humans the mechanical state of gut during normal and abnormal gut motility.

ORAL-17-06

DEVELOPMENT OF VIRAL VECTOR-MEDIATED PHARMACOGENETIC TOOLS TO FACILITATE *IN VIVO* INVESTIGATION OF NUCLEUS INCERTUS / RELAXIN-3 NEURAL NETWORKS

Hawkes D., Ong-Pålsson E.K.E., Smith C.M., Ma, S., White, M.D., Bathgate, R.A.D. and Gundlach A.L.
The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, VIC 3010, Australia.

Purpose: The complex heterogeneity of brain neurons/networks has fostered the use of viral vector-based techniques to facilitate modification and characterisation of specific neuron populations. 'Designer Receptors Exclusively Activated by Designer Drugs' (DREADDs) are modified muscarinic GPCRs that when expressed in neurons can induce either depolarization or hyperpolarization upon activation by the synthetic ligand, clozapine-N-oxide. The nucleus incertus (NI) in the midline tegmentum is a distinct GABAergic nucleus that expresses high levels of the neuropeptide relaxin-3 and is particularly amenable to viral-based manipulations (e.g. Callander GE *et al.*, PLoS One 7, e42300, 2012). Therefore, we are currently developing relaxin-3- and relaxin-3 receptor (RXFP3)- promoter-based viral vectors to drive expression of DREADDs in the NI and populations of its target neurons. **Methods**: The relaxin-3 and RXFP3 promoters have been cloned using the Invitrogen Gateway cloning system. High-titre viral preparations have been produced and are being validated *in vitro* and *in vivo*. **Results**: In studies so far, we have utilised small-scale, viral vector production to demonstrate the viability of *in vitro* transduction and protein expression driven by the relaxin-3 promoter. In future studies, we will express DREADDs in relaxin-3-expressing NI neurons or in RXFP3 receptor-positive neurons present in regions such as the amygdala or medial septum. **Conclusion**: These 'DREADD viral vectors' will allow us to better investigate the role of the ascending NI neural network and RXFP3-targeted neuron populations in the control of arousal/behavioural activation and cognition in response to mild and strong neurogenic stressors such as anxiety and fear conditioning.

ORAL-17-07

TOWARDS DEVELOPMENT OF AAV VECTORS FOR TREATMENT OF LEUKODYSTROPIES

von Jonquieres G., Klugmann C., Harasta A. and Klugmann M.
Translational Neuroscience Facility & Department of Physiology, School of Medical Sciences, University of New South Wales, Australia.

Background: Acute or chronic demyelination underlies the pathology of leukodystrophies, inherited myelin diseases typically caused by single gene mutations altering function or viability of oligodendroglial or astroglial cells. These disorders are incurable and associated with substantial morbidity and mortality. Recombinant adeno-associated virus (rAAV) vectors have proven to be a safe and versatile tool for gene transfer to the central nervous system. Despite its potential, lack of vectors with cell type selective, glial tropism has precluded gene therapy for leukodystrophies. **Purpose**: Design of rAAV vectors and treatment strategies for gene therapy of leukodystrophies. **Methods**: Examination of AAV vector tropism and spread of novel AAV serotypes expressing GFP controlled by promoters of genes encoding myelin basic protein (MBP), myelin associated glycoprotein (MAG), glial fibrillary acidic protein (GFAP) and chicken beta actin (CBA) in vivo. **Results**: Following intrastriatal injection of 2x109 vg, the novel serotypes AAVrh20, AAVrh39 and AAVcy5 showed significantly better vector spread than mosaic AAV1/2. Despite subtle, serotype specific differences targeting transgene expression to specific cell types depended on the promoter and developmental stage of the animal. In adult mice intrastriatal AAV-CBA-GFP injection resulted in robust neuronal GFP expression, AAV-GFAP-GFP conveyed transgene expression in astrocytes and injection of AAV-MBP-GFP or AAV-MAG-GFP restricted GFP expression to oligodendrocytes. While astrocyte specificity was maintained after neonatal AAV-GFAP-GFP delivery, oligodendrocyte specificity of AAV-MBP-GFP and AAV-MAG-GFP was not, but recurred in animals injected at postnatal day 10. **Conclusion**: In vivo targeted transgene expression depends on serotype, promoter and developmental status at intervention. All require consideration during development of gene therapies targeting leukodystrophies.

ORAL-17-08

MEASURING THE SPATIOTEMPORAL PROFILES OF NEURONAL ACTIVITY AND BOLD IN EARLY VISUAL CORTEX USING HIGH RESOLUTION FMRI

Schira M.M.[1, 2], Breakspear M.[3] and Aquino K.M.[4]
[1]Neurscience Research Australia, Randwick, Australia. [2]Sch. of Psychology, Univ. of Wollongong, Wollongong, Australia. [3]Queensland Inst. of Med. Res., Herston, Australia. [4]Sch. of Physics, Univ. of Sydney, Sydney, Australia.

Background: Crucial aspects of visual scene processing are enacted by neuronal interactions within visual cortex, including lateral interactions within areas and divergent connections along the visual stream. These processes are reflected by short and long range neuronal point spread. Whilst functional Magnetic Resonance Imaging (fMRI) provides, in principle, an ideal opportunity to assess this intra- and inter-areal connectivity, the spatial properties of the BOLD (Blood Oxygen Level Dependent) signal partly reflect neurovascular responses. This includes processes non-separable in space and time. **Methods:** Subjects (n=10) viewed an annular flickering (4Hz) boom-gate stimulus (3.5 degree ecc.) one pixel wide (0.03 degree vis. ang.). Three different moderate contrasts (16% gray, 25% gray 35% M-L isoluminant) on a mid gray (16 candela/m^2) background were used. fMRI was recorded at high resolution (1.5mm) and super high resolution (0.8mm) using 3T MRI system. A detailed spatiotemporal hemodynamic response function (Aquino et al., PLoS Comp. Biol. 2012) allowed us to disambiguate vascular and neuronal contributions to the spatial profile of the BOLD signal. **Results:** We find point spread parallel but not orthogonal to the cortical surface. This spread amounts to 7.5+-0.6 mm in V1, extending to 12 +- 0.8 mm in V2 and 14 +-1.2 mm in V3. A small negative BOLD response occurred 13-20 mm from the primary response unilaterally towards the periphery, exclusively in V1, reflecting inhibitory surround processing in primary visual cortex. These responses were invariant to the use of isochromatic versus isoluminant contrast stimuli (Wade & Rowland, JNsc 2010). Hemodynamic deconvolution reveals the spatial profile of neuronal responses underlying these changes in the BOLD signal, allowing unique insight into the profile of synaptic connectivity within V1 and quantitative estimates of divergence along the visual stream.