Improving the outcomes of hemispherectomy in children with intractable epilepsy: a novel approach based on movement analysis

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Hypothesis: Kinematic and muscle activity analysis of movement can improve the outcomes of hemispherectomy by (i) providing an accurate index of upper limb function, and the reorganization of hand motor control in candidates for hemispherectomy; (ii) determining how the system mobilizes plastic changes to compensate for lost functions of hand and arm movements as a result of the epilepsy and/or surgery; and finally (iii) contributing a comprehensive and accurate preoperative assessment of upper limb movement function in candidates for hemispherectomy in order to provide reliable prognostic indicators of post operative outcome and to guide therapeutic interventions designed to enhance recovery of upper limb function.

Aims and methods:

Background: Hemispherectomy, the removal/disconnection of an entire cerebral hemisphere, is an effective method of arresting intractable epilepsy in children. It is, however, a radical disruption to a brain in a critical phase of development, and as such raises major questions: (a) What are the risks of inflicting or exacerbating an existing unilateral paralysis that will show little recovery? (b) What are the likely outcomes for hand function, particularly when the removal entails switching of hand dominance, and what implications does this reorganization have on other aspects of sensorimotor and cognitive functions? (c) What should be the guiding principles of a therapeutic programme designed to maximise favourable outcome?

Aims: We aim to assess the degree of organisation and plasticity of the motor system by analysing movement performance during unimanual and bimanual tasks using motion capture and EMG techniques. We will then relate these objective measures of movement performance to sites of brain activation during manual tasks performed in the functional magnetic resonance imaging environment, thereby providing three-way convergent information about the relationship between brain and motor behaviour. The outcome of this research will have practice-changing implications for the delivery of physical therapies and interventions for children undergoing brain surgery.

Methods: To achieve better motor outcomes we need to more objectively assess movement function pre-and post-hemispherectomy and to assess the networks involved in voluntary movement production pre- and post-hemispherectomy.

First, we will seek to assess the degree of organisation and plasticity of the motor system by analysing movement performance during standardised tasks using state of the art methodologies from motor neuroscience: Neurophysiology, magnetic resonance imaging, and mathematical modelling. Specifically, we will investigate children who are candidates for hemispherectomy/lesionectomy before and after surgery using kinematics and electromyography of ipsilesional and contralesional upper limbs. Second, we will seek to develop new markers of upper limb function such that therapy goals will depend not only on residual function but also on an understanding of what has been compromised and what can be improved. Finally, we will relate the findings to functional magnetic resonance indices of brain activation to examine the neural substrates of both compromised (contralateral) and non-compromised (ipsilateral) limb movements.

References:

1. Vargha-Khadem F, Isaacs E, Papaleloudi H, Polkey C, Wilson J. Development of language in six hemispherectomized patients. Brain 1991 114:463-495.
2. Braddick O, Atkinson J, Hood B, Harkness W, Jackson G, Vargha-Khadem F. Possible blindsight in infants lacking one cerebral hemisphere. Nature 1992 360:461-463.
3. Vargha-Khadem F, Carr LJ, Isaacs E, Brett E, Adams C, Mishkin M. Onset of speech after left hemispherectomy in a nine-year-old boy. Brain 1997 120:159-182.
4. Holloway V, Gadian DG, Vargha-Khadem F, Porter DA, Boyd SG, Connelly A. The reorganisation of sensorimotor function in children after hemispherectomy: A functional MRI and somatosensory evoked potential study. Brain 2000 123:2432-2444.
5. Devlin AM, Cross JH, Harkness W, Harding B, Vargha-Khadem F, Neville B. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain 2003 126(3):556-566.
6. Dijkerman, HC, Vargha-Khadem, F, Polkey CE, & Weiskrantz, L. Ipsilateral and contralateral sensorimotor function after hemispherectomy: differences between distal and proximal function. Neuropsychologia, 2008. 46 (3), 886-901.

1) **FORMATTING INSTRUCTIONS AND APPLICATION PROCEDURE**

2) **FREQUENTLY ASKED QUESTIONS**

3) **PROJECT DESCRIPTIONS:**

- **Clinical and Population Health**
- **Genetics and Gene Therapy**
- **Infection and Immunity**
- **Neurosciences and Mental Health**
- **Stem Cells, Development and Disease**

1) Formatting instructions/email application procedure:

(a) Email applications should have "PhD Studentship Application" in the subject field, and should comprise:

- **a covering letter**
- **CV**
- **a summary/abstract of any research project already undertaken (which should be no more than one side of A4)**
- **the names and addresses of two referees.**

(b) Save your application as a single Word document attachment. Name your Word document using your surname first and then your first name, eg Smith John.doc

(c) Please indicate in your covering letter where you saw the advertisement and also where else you have looked for studentships.

(d) Please state your nationality and how you will fund international fees if applicable.

(e) Applications should be sent direct to the Research Degrees Administration Office (ICH.Chratapps@ucl.ac.uk).

(f) SEPARATELY, you should arrange for your two referees to provide a reference once you have submitted your application. Please ask your referees to use the Reference Form provided (see main advertisement) and to send the reference by email to ICH.Chratapps@ucl.ac.uk no later than 2nd January 2012.

Overseas applicants should also see FAQ1 below BEFORE submitting an application.

Please note that if you apply without following the guidelines given above, your application may not be considered.

2) Frequently Asked Questions

Q1. Can students from outside the UK apply?

A. Yes, overseas students have previously been accepted into the programme. The PhD Programme in Child Health Research will fully fund UK/EU students. Non-UK/EU students receive the normal stipend, and the UK/EU component of their fees is paid, but they must pay the extra overseas fees themselves (the current difference for 2011/12 is £14,400 per year and there is normally a 4 percent increase on fees each year). Furthermore, all candidates who are selected for the Programme must be interviewed, and we unfortunately have no money to pay for overseas students to come to interview.

Q2. Can I come to visit the Institute before the interviews?

A. Yes, there is an Open Day at ICH on Wednesday 16 November 2011 from 2.00pm onwards when prospective applicants will meet the Postgraduate Tutors, existing PhD students, and have the opportunity to take up tours of the facilities.

Q3. I have a lower second degree but I am now doing an MSc. Is this equivalent to an upper second?

A. Assuming you passed your MSc, you could be eligible to hold a PhD studentship. Please note, however, that in the previous year's applications nobody with such a background was successful.

Q4. Does my age matter?

A. No.

Q5. I will be away at the time of the interviews (Monday 30th and Tuesday 31st January 2012).

A. Contact us: we may be able to interview early.

Q6. Do I need to have chosen my project from the portfolio, prior to interview?

A. No. The best candidates will be selected and offered studentships and we will then arrange for you to come back to ICH and visit potential supervisors/labs before you make a final decision. However, if only one or two projects would be of interest to you because of your specialist background, please say so in your covering letter.

Q7. I have another PhD offer, which needs a decision before you decide on your studentships.

A. Ask them to wait (they usually will); if not, contact us.