



# BRAINTRAIN NEWSLETTER 1

*BRAINTRAIN has started in November 2013 and is coordinated by Cardiff University (Professor David Linden, Wales, UK). Our consortium brings together 10 complementary partners, including 7 academic research institutions, one small medium sized enterprise, a larger industrial partner and a technology transfer/management company.*

*To achieve our objectives, BRAINTRAIN program comprises 6 complementary workpackages. WP1: Coordination and management of the consortium, has strong links to all other WPs as its objective is to ensure good management and timely implementation of the BRAINTRAIN workprogramme, communication between the different WPs via regular meetings and reports. So far, we have met twice, in Cardiff for the Kick-off meeting and in November in Maastricht for the annual meeting. In between, we have had five ExCom meetings, where WP leaders meet and discuss the strategic point of the project. You can find in the Braintrain secure intranet the main information related the contractual aspects and the meetings.*

*Each team has now been working on its work packages for one year and the next pages provide an overview of what we have been doing so far and a focus on some important developments.*

BRAINTRAIN will focus on 4 objectives

Objective 1

Develop new or optimize existing imaging technologies

Objective 2

Validate their application to mental disorders by integrating imaging data with complementary knowledge resulting from bioinformatics and clinical data.

Objective 3

Allow the diagnosis of mental disorders at the pre-symptomatic stage or early during development.

Objective 4

Better measure disease progression.

Scientific Coordinator  
Professor David Linden  
Cardiff University  
Institute of Psychological Medicine and Clinical  
Neurosciences  
School of Medicine  
Hadyn Ellis Bldg, Maindy Road  
Cardiff CF24 4HQ United Kingdom  
E-mail: LindenD@cardiff.ac.uk

Project manager  
Delphine Smagghe  
Inserm Transfert  
7 Rue Watt  
75013 Paris FRANCE  
E-mail: delphine.smagghe@inserm-  
transfert.fr

## *WP2: Methods development (RTD)*

Dr. Steffen Volz, MR physicist with experience in MRI sequence development and image processing started his work at the Wellcome Trust Centre for Neuroimaging (WTCN/UCL) in spring 2014. He is developing a toolbox for optimizing fMRI sequences with respect to BOLD sensitivity in user specified brain areas. The toolbox will be available for the whole SPM community when finished.

Steffen Volz and Nikolaus Weiskopf were faculty on the annual MR Physics for SPM Users course in October 2014. The course helps disseminating best practice in anatomical and functional MRI in the research community. Daniela Jardim Pereira, a member of the Braintrain team at University of Coimbra is visiting WTCN/UCL, London, for discussions about collaborations and training in the latest technical developments.

Nikolaus Weiskopf started the project "Non-Invasive In-Vivo Histology in Health and Disease Using Magnetic Resonance Imaging (MRI)" funded by an ERC Consolidator grant. Results from this project may help to better and more efficiently identify specific brain regions that are targeted by real-time fMRI neurofeedback. He is also active in the organizing committee of the conference on Real-time Functional Imaging and Neurofeedback rtFIN in Gainesville, Florida on February 12-13, 2015.

Three postdoctoral researchers, Judith Eck, Quentin Noirhomme and Florian Krause, with experience in fMRI and EEG research, started

working at Brain Innovation in spring 2014. Together with the two PhD students, Caroline Benjamins and Sascha Brunheim, who are experienced in psychological research and MR sequence development, respectively, the team will investigate the methodological and experimental parameters for improving realtime-fMRI neurofeedback and the possibilities for a translation to EEG paradigms. The software developer Samuel de Santis will create new tools to further investigate these paradigms with the use of EEG.

Work has started on first pilot projects on (1) the impact of different feedback displays on self-regulation performance, and (2) the potential benefits of using functional connectivity measures as neural targets. A research assistant, Mona Rosenke, will support data acquisition and analysis for these ongoing projects.

Furthermore the team is looking more into possible improvements running a real-time fMRI and neurofeedback study. Hereby they investigate the whole procedure before, during and after running the experiment e.g. related to data acquisition, real-time processing and neurofeedback presentation, subject/patient instruction, data storage and analysis. These results will be transferred to MR systems from different manufacturers and even to other modalities like EEG, as part of the standardisation of experimental realtime-fMRI neurofeedback procedures.

### **WP3:**

#### ***Functional network mapping and development of specific neurofeedback probes (RTD)***

***From WP3 team***

Our first task in WP3 was the demarcation of specific emotion-related neural targets for fMRI neurofeedback. We decided to create an open internet database for functional localizers of affective processes, which can serve the entire relevant community. It proposes experimental paradigms, statistical fMRI maps, analysis software and documentation on affective processes related to four relevant domains: empathy, emotion regulation, motivation, and threat. We further saw the need in developing additional localizers for embodied-simulation and theory of mind processes, and for distraction and reappraisal techniques in the contexts of empathy and emotion regulation, respectively. Thus, we generated two new paradigms for these domains, and collected fMRI data on the emotion regulation task. Finally, we ran a neurofeedback experiment whose target was to train the subjects in modulating their ventral medial prefrontal activity using a game-like paradigm. We found that subjects who showed improvement in neurofeedback success from a first to a second run also demonstrated enhanced emotion regulation capabilities as measured by the implicit Etkin's adaptation test.

### **WP4:**

#### ***Clinical feasibility studies / trials (RTD)***



***From David Linden***

The preparation of the clinical trials of neurofeedback in alcohol dependence (Cardiff), autism (Coimbra), obesity (Tuebingen), post-traumatic stress disorder (Tel-Aviv) and childhood anxiety (King's College London) is well under way. WP4 had two very informative meetings at the South East Wales Trials Unit (SEWTU) in Cardiff, on 10/11 July and 22 September 2014. Rebecca Playle and Rachel McNamara gave presentations on trial design, methodology and governance and Gareth Watson introduce the principles behind the setup of a common database. Each group in WP4 identified a data manager, and these data managers have been working with Gareth's team on the metadata for the clinical, cognitive and personality measures that will be used as predictive and outcome measures in the trials. Although all trials will be designed as single-site studies, the nature of the consortium and the harmonisation of outcome measures (for example anxiety and depression scales) across trials will allow us to pool data across trials. This will be particularly interesting for the field of neurofeedback because some of its effects may not be confined to disease-specific measures but effect the overall experience of

self-efficacy and thus well-being, quite independent of the specific protocol employed.

In order to explore service user expectations from our research and ensure the practicability and relevance of our research design several partners conducted focus

groups with representatives of the target groups of their interventions. For example, the Cardiff group met with a group of users of an alcohol use disorder service in the South Wales Valleys. Miles Cox's reflections on this focus group can be found in this newsletter on page 6.

### *Clinical Trial database*

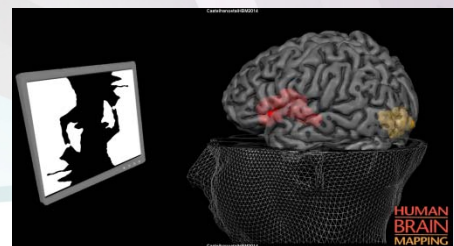
*Sam Clarkstone and Vincent Poile (pictured) are database developers working in the South East Wales Trials Unit (SEWTU) within Cardiff University. They have been developing the information system to support the clinical trials in WP4. This will bring together all data for the WP4 studies and allow for researchers to view, enter and edit data relating to their study. Gareth Watson, Head of Information Management for SEWTU, gave a demo of the work completed to date on the system in the annual meeting in Maastricht on 25th November.*



### *WP5: Real-life transfer protocols (RTD) From Miguel Castelo-Branco*

WP5 aims at assisting the translation of the clinical neurofeedback techniques through **real-life transfer protocols for neurofeedback**. We will develop transfer technologies by combining fMRI-NF with EEG and serious gaming, which is a completely novel approach to assistive technologies in mental health.

A paper from the group of Coimbra and within the scope of BRAINTRAIN was recently highlighted as the cover of the journal Human Brain Mapping (see image). In this article, the authors describe simultaneous EEG/fMRI experiments that allowed to dissect the neural correlates of face processing and decision. The identification of such circuits is important for the design of Neurofeedback probes. Miguel Castelo-Branco disseminated some of the key concepts and first results in a TEDx event in Matosinhos, Porto, Portugal, following an earlier dissemination event in the Portuguese Parliament.



## WP6: Dissemination and exploitation Plans (OTHER)

The objective of WP6 is to insure an effective dissemination using different tools. A brochure was already distributed to the partners, a logo for BRAINTRAIN was created and we have now a public website which is updated regularly. In parallel, partners are very active presenting neurofeedback research at national and international conferences and invited seminar talks. We can list the following presentations:

✚ **David Linden presented at the symposium “Non-EEG Neurofeedback: fMRI, NIRS”, organised by Rainer Goebel at the 2014 Meeting of the Society of Applied Neurosciences (SAN) and the Dutch National Initiative Brain and Cognition (NIHC) in Utrecht, and at the 22<sup>nd</sup> European Congress of Psychiatry in Munich. He also gave talks on “Brain Control” at the MRC Cognition and Brain Sciences Unit in Cambridge, the University of Birmingham, the Universities of Geneva and Amsterdam, and City University and the Institute of Psychiatry in London. David Linden also organised a symposium at the International Congress of the Royal College of Psychiatrists, where neurofeedback was embedded in the wider topic of invasive and non-invasive brain modulation approaches. Niklas Ihssen, also from the Cardiff group, gave a lecture on Neurofeedback and Brain Computer Interfaces at the Bristol MR summer school 2014.**

✚ **Rainer Goebel gave a talk at the 20th Annual Conference of the Human Brain Mapping Organization in Hamburg (June 8-12, 2014) in the symposium “Brain Machine Interfaces: Foundations and Perspectives” on “Real-Time fMRI Brain Computer Interfaces at 3 and 7 Tesla: From Basic Research to Clinical Applications”. He gave a TEDx talk in Amsterdam, which can be watched at: <http://www.tedxamsterdam.com/2014/11/rainer-goebel-real-time-brainscanning-new-therapy/>**

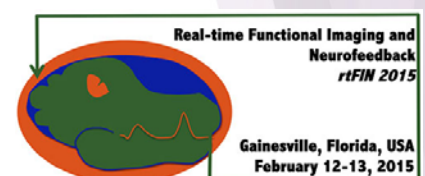
✚ **Talma Hendler gave a lecture on “Neural traces of stress effects: from markers to modulation” at the F C Donders Center Summer School at Nijmegen University in August 2014 and presented a poster at the Annual Conference of the Society for Biological Psychiatry in New York City.**

✚ **Nikolaus Weiskopf is on the organising committee for the 2015 International Neurofeedback Conference in Gainesville, Florida, USA (<http://reg.conferences.dce.ufl.edu/rtFIN>):**

✓ **The BRAINTRAIN website is available at the address: [www.braintrainproject.eu](http://www.braintrainproject.eu)**

✓ **The extranet where you can find all the important documents regarding the agreement, the meetings and the dissemination is available at this address: <https://extranet-braintrain.atreal.fr/>**

✓ **The Next Annual meeting will be held in Israel in November 2015**



## *Focus Group Conducted With Substance–Abuse Service Users*

*March 2014*



*From Miles Cox*

In March 2014, three members of the Cardiff University Research Group (Miles Cox, Niklas Ihssen, and Raman Sakhuja) led a focus group with substance–abuse service users in Pontypridd, Wales (near Cardiff). The purpose of the meeting was (a) to inform service users about the research being conducted at Cardiff University and (b) to solicit their views about it and how it might be adapted to best meet service users’ needs. The objective of the research is to use functional magnetic resonance imaging (fMRI) to provide participants with feedback about their brain activation when they view alcohol-related pictures and alternative goal-related pictures in the scanner and to train them to down-regulate the former and to up-regulate the latter. Ultimately, the researchers aim to determine whether these changes in brain activation will result in reductions in alcohol consumption.

Members of the group asked general questions about the nature of addiction, such as: “Does it run in families?”; “Is it genetic?”; and “If it is genetic, why am I the only one in my family with a problem?” The group felt that exposure to images of alcohol in the scanner would not be a problem for them (e.g. would not cause undue craving). After all, they said, they are confronted with images like these in everyday life. They seemed pleased that they would be paid a modest fee for participating; it seemed that the payment would help to motivate them. They would prefer to be paid cash rather than with a voucher. They should be trusted, one person said, not to buy alcohol with the money.

The group made a number of excellent and insightful suggestions about the alcohol such as:

1. Photos of scenes involving alcohol would be more potent than simply a glass filled with an alcoholic drink.
2. The odour of an alcoholic drink would be more potent than a visual stimulus. The research group, however, later concluded that using odours in the scanner would be impractical to implement.
3. Brand names (e.g., *white lightning* [a brand of hard cider]) would remind them more of alcohol than would a glass filled with the drink.

4. When asked which drink(s) would most remind them of alcohol, some answered *cider*: (Cider is often preferred because it is inexpensive and readily available.)

5. They thought that, prior to the study proper, it would be good to have a group of pilot participants evaluate a bank of potential

stimuli for their potency. They also felt that this would help them to get involved in the research, which they would like.

6. Then, in the actual study, each participant could choose stimuli from a stimulus bank that most reminded that person of alcohol.

In summary, the members of the focus group seemed to understand the research quite well, and they made excellent suggestions about the stimuli. It was very encouraging to see how positive and enthusiastic they were about it.

**List of recent publications from BRAINTRAIN:**

Sokunbi MO, Linden DE, Habes I, Johnston S, Ihssen N. Real-time fMRI brain-computer interface: development of a "motivational feedback" subsystem for the regulation of visual cue reactivity. *Front Behav Neurosci.* 2014 Nov 25;8:392. doi: 10.3389/fnbeh.2014.00392.

Esmail S, Linden DE. Neural Networks and Neurofeedback in Parkinson's Disease. *Neuroregulation* 2014. <http://www.neuroregulation.org/article/view/144255>