Season’s Greetings!

This has been an eventful year for our research. Many of you have volunteered for the longitudinal study led by a group from Pittsburgh in the USA. This study’s aim is to bring together information from many participants with Down’s syndrome to understand the critical changes that happen in the brain, as people with Down’s syndrome grow older. Liz Jones, Conchy Padilla and Anna Bickerton have been working very hard making the necessary arrangements so that you can take part. Shahid Zaman leads this study and is responsible for liaising with the USA grant holders. Isabel Clare oversees the detailed psychological testing and the staff from the Wolfson Brain Imaging Centre (WIBC) undertake the scans - it is very much a team effort.

In addition, in 2017, Sally Jennings was awarded her PhD and is now working on the scientific papers. Many congratulations to Sally for this achievement and for all her work. She has identified changes in the way the brain responds that may be an important indicator of the future risk of Alzheimer's disease. This observation together with the findings from the eye study by Maddie Walpert, are important developments in trials of treatments to prevent dementia. We will need these markers to help us understand whether the treatments are working. Maddie is close to completing her PhD and will be examined early in 2018. With the help of many of you she was also able to complete an additional study called, DARC. This study uses a new technique for detecting dying cells in the retina (the back of the eye). What is happening to them may tell us something about what is happening in the brain.

Ruma Raha-Chowdhury has worked closely with us for some years and has recently had two further papers published in the scientific literature, one particular paper challenging some of the conventional wisdom about Alzheimer's disease. These and other papers are listed in this newsletter and if you would like a copy of these papers do let Agnes know (her details are on the back page). Elijah Mak is working with Conchy Padilla using the most up-to-date techniques to undertake further analysis of the brain scans from our previous MRC funded study.

I visited New Delhi earlier in the year as a guest of the DS Federation of India to talk about ageing. It was an exhilarating meeting. I am now working with an international group under the leadership of DS International to develop international guidelines on the diagnosis and treatment of dementia in people with Down’s syndrome.

So where does this all take us? It is a slow journey but our aim is to have a trial of some of the new medications that are being developed to see if it is possible to delay or prevent Alzheimer's disease in people with Down’s syndrome. With this in mind Carol Routledge, Research Director of AR-UK, attended one of our recent review meetings. Thank you again for your support and dedication to the research. I have said it many times but it is always worth repeating - it is a team effort and we couldn't do it without you.

Professor Tony Holland
A Call for Participants

We are so grateful to our participants whose involvement allows us to carry out our work. However, we are always looking for more! If you know anyone aged 25-35 with Down’s syndrome who might be interested in taking part in the MRI/PET scanning study, we would be extremely grateful if you could let our NiAD team know by contacting ej268@medschl.cam.ac.uk or ajb333@medschl.cam.ac.uk. Tel: 01223 465268.

Ruma’s Findings!

Activation of innate immunity and inflammation are early events in Down’s syndrome (DS). Triggering receptors expressed on myeloid cells 2 (TREM2), an innate immune gene plays a critical role in inflammation and is essential for neuroplasticity and myelination in Alzheimer’s disease (AD) brain (Raha et al, 2016).

Using human brain sections from DS, we discovered impairment of TREM2 trafficking to the erythrocyte plasma membrane that could influence the amyloid clearance mechanism thought to be important in AD pathogenesis (Raha-Chowdhury et al, 2018).

Down’s syndrome brain section stained with amyloid-b antibody (b-Amyloid-42, green), recognised Senile plaques and TREM2 (red) visible around the plaques.

Trem2 is essential in neuronal plasticity. In embryonic stem (ES) cells TREM2 protein (green) was visible in the proliferative cell and BlIIT an exonal marker (red) co-localised with TREM2 in exons.

Study Updates

Many of you have now visited Cambridge to take part in our newest study – the NiAD study. Liz, Anna and Conchy are all working with participants to monitor the progression of Alzheimer’s disease in people with Down’s syndrome (DS).

To do this we are measuring amounts of Amyloid and Tau, which are proteins found in the brain associated with the disease. Certain types of Amyloid clump together and become toxic causing brain cells to die. This leads to symptoms of Alzheimer’s such as memory loss. As chromosome 21 contains the gene to the precursor of Amyloid, an extra copy of this chromosome, the cause of DS, increases the risk of developing Alzheimer’s.

To measure the amount of these proteins in the brain we use PET imaging. This involves using a dye which binds to the different proteins. The participant waits a bit once the dye is used, then they go in the scanner and an image of the brain is taken with the dye highlighting the Amyloid and Tau. So far our scans have been very successful! We’ve had 15 participants who have been scanned and all of them have been excellent. Some participants have found it hard to stay still in the scanner, but they have all left feeling proud for taking part!

Maddie is writing up the results of her eye study for her PhD thesis, to submit in time for Christmas. The next step is to use similar technologies to look at different aspects of the eye in a study based at Addenbrooke’s hospital which is in collaboration with a national Alzheimer’s study. Maddie will start working on this project in March 2018.

New Papers

⇒ Natalie Neale et al (in press), Neuroimaging and Other Modalities to Assess Alzheimer’s Disease in Down Syndrome, Neuroimage: Clinical.

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Catherine’s Charity Work

Anna and Tony recently visited Catherine in her home and asked her some questions about working in a charity shop and why she likes to take part in our research.

“I work Monday, Friday and Saturday so 3 days. It’s a mixture really, a mixed bag, you steam clothes, put sticker prices on so they can go on the shop and there’s bric a brac. I work for Age UK which helps supports older people like my grandma. “I love taking part in research especially for other people if they have Alzheimer’s disease and things — I have a good heart my mum and dad say and I would encourage others to do it.”

Caring Claire Shares her NiAD Experience

We asked Claire, a carer, how she feels about people with DS being part of our research:

“I support people with Down’s syndrome to take part in the research, as once they understand what it’s about and why they are needed, they want to help and make a difference. “I support them to do that and empower them to understand what a fantastic thing they are taking part in.”

What it’s Really Like to be a Research Participant

One of our participants, Hannah recently flew all the way from Glasgow to take part in the NiAD study. She completed some puzzles and quizzes and our research assistant, Anna, asked her some questions over tea and biscuits.

Hannah, it’s nice to meet you.
Nice to meet you too, Anastasia.
Haha, thank you! So where are you from?
I originally lived with my mum and then my sister took me in, in Glasgow.
Can you tell me a bit about why you are doing the study and what you know about it?
The reason I’m doing the study is to get the message across to other people who’ve got the same as me – Down’s syndrome and you’ll get a cure to make them feel better.
Yeah that’s really good! So do you know which disease we’re looking at?
Is it dementia? And they’ve also Alzheimer’s disease. I don’t have these ones – touch wood.
Touch wood indeed - so you’re doing this to help other people who might have it.
*Nods* I’m doing this to help other people who can come to the place to see what it’s all about and then you’ll get the cure for it.

And have you enjoyed your days with us?
I enjoyed my week! I don’t really want to go home!
Haha, really! Don’t tell your sister that!
I just did! *laughs*
And did you like doing the quizzes and the puzzles?
I liked doing the quizzes and I liked doing the... the blocks! And I liked doing the sentences as well.
Yeah you were really good at that! And how was the scanner?
It was okay. I couldn’t move, but it was okay!
Well you were brilliant - we got some really good images.

Thank you! Thank YOU!

Hannah (right) with her sister Janet outside Douglas House
**Celebrating Together**

On 29th September we held a day of events at Clare College, Cambridge, to mark the end of our 15 year partnership with the Health Foundation. Funding from the Health Foundation enabled us to establish the team here and we wanted a chance to present the results of our work to those of you who have worked as partners with us, supporting our research and taking part.

In the morning we held a series of academic workshops discussing the main themes of our research. This was followed in the afternoon by a more relaxed event including posters, presentations and the chance to ask questions and discuss how best to involve people with Down’s syndrome in research and the potential benefits. We were so pleased that many of you were able to attend and we look forward to continuing to work together with you in the future.

**Racing Ahead!**

In September Russell Ramsey ran the Chariots of Fire race for Alzheimer’s Research UK with Maddie, which is a 1.6 mile relay race through some of the famous colleges in Cambridge including King’s College.

Although the weather was a bit grey the atmosphere was lively with all the teams motivated to raise money for such a good cause. Russell was supported by his family and researchers from Douglas House and all of Russell’s hard work in training paid off when he completed the course in around 18 minutes.

Russell was extremely pleased when he had the opportunity to meet Harry Gardner, a singer from Britain’s Got Talent who was also at the event. Russell and Maddie were part of the ARUK “orange wig” team, and there was also another “orange tutu” ARUK team! Russell raised £485 for ARUK, more than his target, so a massive thank you to everyone to donated to his just giving page! The event raised £70,000 in total to support future research into Alzheimer’s disease.

**Meeting the Monitor**

Recently, we had a visitor from the US called Renarda to check that the NiAD work we do in the UK is up to scratch with the other sites in the US. It was her first time coming to the UK and she enjoyed it even if it was a bit colder than sunny California! We showed her the WBIC, the CRF, Douglas House and even managed to squeeze in a trip to King’s College. It was really nice to meet Renarda and hopefully some of you can meet her on her next annual visit!

**Thank you!**

Just to say thank you again to everyone that takes part in our studies. We absolutely love working with people with Down’s syndrome and truly believe in the importance of the work we achieve together! If you would like more information on anything in this newsletter or to be added to future mailing lists please contact our administrator, Agnes Hoctor, phone: 01223 465 216, email: ah937@medschl.cam.ac.uk, post: Department of Psychiatry, Douglas House, 18b Trumpington Road, Cambridge CB2 8AH.