

REPORT FOR THE CASTANG FOUNDATION

Early Intervention: Preventing and Reducing the Impact of Developmental Disorders

Edinburgh, Royal College of Physicians, 13 & 14 March 2014

Dear Castang Foundation Trustees and Scientific Committee

I am pleased to offer this report on this very successful meeting that we held in Edinburgh on your behalf and hope that we are able to assure you that it was of benefit in furthering the missions of the Castang Foundation. I enclose a copy of the programme which lists the invited participants and you can see that we had an international flavour with our researchers and a wide and ambitious programme.

Already a number of initiatives have been taken forward by diverse researchers who have benefited from hearing about each other's work. Here are some examples:-

- Taking forward harnessing the epidemiology of national cohorts. Dr Rachael Woods and Albert King have informed us that they are now developing data linkage further to answer questions which were raised by Prof Jane Norman when examining mothers and babies at risk of a poor outcome and Prof Phil Wilson's research on population-wide assessments of neurodevelopmental/neuropsychiatric problems. What was intriguing with the latter presentation was that it illustrated that even though children can be identified in preschool years with additional needs in their communication and developmental behaviour, this is not reflected in the standard data captured when they enter school. It emerges in data capture by mid-primary school and this may possibly be linked to the emergence of difficulties in literacy, maths and academic attainment. However, we know that preschool children who have predisposing difficulty in areas such as language and attention are at high risk of going on to experience these types of academic failure. Therefore Phil, Rachael, Albert and Jane's work coalesces and in particular, Rachael and Albert are going to look at whether we can improve on the situation and understand why this early identification is not passed through at an early stage at school entry.
- Dr James Boardman talked about neonatal neuroimaging and its relationship with neurodevelopmental outcome. He discussed his research that shows diffuse white matter injury in the brain along with changes in the globus thalamus that could be considered the 'signature' of preterm birthing injury. He subsequently linked with our developmental psychologists contributing to the conference, Dr Sue Fletcher-Watson and Dr Bonnie Auyeung, and is proposing research linking the long term neuropsychological outcome for the children with imaging biomarkers in order to understand the progression of their early medical features into long standing developmental perturbations. This research also referred to genetic variation in vulnerability and thus linked with the address by Dr Mandy Drake on transgenerational stress, as well as touching on nutrition which we expanded further towards the end of the conference with Prof Charlotte Wright's address on feeding the disabled child.
- We had a fantastic contribution on molecular genetics and mechanisms from Prof Peter Kind, Sir Adrian Bird and Dr Dianne Newbury and this allowed the researchers to think about possible contributions of animal models eg with the 'knockout' mouse model and recent advances in the more rat rodent model and brain imaging potential. There was cross-fertilisation of ideas around how these models can inform

understanding and mechanisms of injury to the developing brain and Sir Adrian Bird and Prof Anne O'Hare discussed recent work on adolescent onset cognitive regression and neuropsychiatric symptoms associated with the A140V MECP2 mutation. This is a variant of the Rett syndrome and stimulated thinking about what this presentation might look like between the human and the animal model. In understanding the human, most of the symptomatology did not start until secondary school and continues to feed into the understanding of the molecular basis of Rett syndrome and Sir Adrian Bird's work which has shown reversibility of what was previously thought to be a permanent neurological deficit in the animal mouse model.

- Dr Richard Bowman talked about the cascading impacts of cerebral visual impairment which led to a lot of discussion along with Dr Karrie Gillespie-Smith into employing novel technologies like eye tracking methodology to measure early disturbances in social functioning in infancy and visual attention. Discussion then ensued about whether this technology could be harnessed to measure visual acuity in very young infants which has not been done to date and needs to be developed further. Prof O'Hare has taken this forward from discussion with Dr Bowman for further discussion with a research physicist in Child Life & Health in the University of Edinburgh, to see if such a system was technically feasible.
- The second day of the conference built forward from Dr Karine Pelc's address on early intervention to optimise motor development and had a rousing start with Sir Harry Burns rallying the researchers to use their understanding of the biology of adversity to think about 'creating wellness'. This resonated with the earlier work, such as that by Dr Mandy Drake and was further exploring the effects of stress, emotional abuse and neglect on children's development. The latter was expanded on by Dr Minnis and a good deal of discussion developed around Dr Julia Jakel's address on neonatal risk and protective factors. This was so pertinent as it showed how sophisticated we need to be in understanding how best to facilitate resilience and plasticity and recovery by showing that certain preterm survivors are more responsive to certain styles of facilitated parenting. There was a good discussion of the different tools that can be used to measure characteristics of parental facilitatory skills such as telephone interview techniques which have been discussed further by a number of researchers attending the meeting.
- Prof Hans Forssberg enhanced this by discussing the biochemical map of synapse development and the modulation of the dopaminergic system changing properties of the neurones and synapses and thus illustrating with emerging technologies the plasticity of the central nervous system. This resonated very well with Dr Fletcher Watson's work explaining how competent the very young and disabled autistic child can be in mastering new technology with iPad apps such that there was discussion around how all these new technologies might be fed into future research.
- These inspiring talks on the science of the child's central nervous system potential for recovery, plasticity and resilience culminated with Dr McLellan's work on the outcomes for children with very severe childhood epilepsy who had undergone surgery. This led to consideration of how one might capture the breadth of developmental outcomes for the children as well as a reduction in their seizures.

We are continuing to build links between the researchers and develop grant applications and learn from each other's work and methodologies. We would like to thank the Castang Foundation for so generously supporting this exciting meeting which we are confident will take forward the agenda of improving the outcome and quality of life for children and young people affected with disabilities.

Yours sincerely

Prof Anne O'Hare and Dr Paul Eunson