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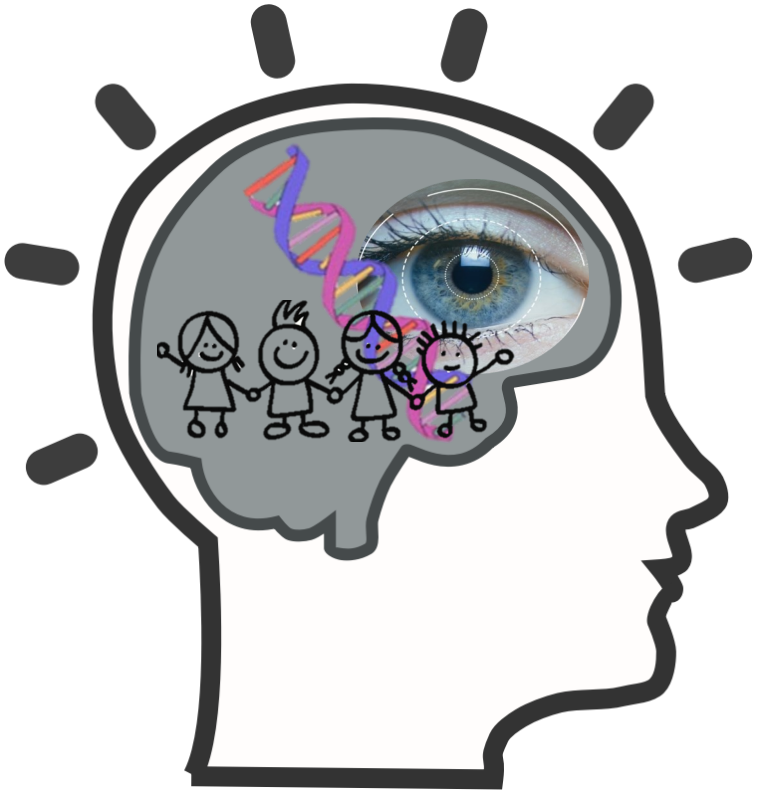
Neurodevelopmental Disorders Annual Seminar 2016



Workshop on "Overcoming and Considering the Difficulties of Research with Neurodevelopmental Disorders"

24th June 2016

Room 118, Chandler House
2 Wakefield Street,
London, WC1N 1PF

The Leverhulme Trust

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Workshop Schedule

Time	Event
9.00	Registration opens
9.20	Welcome: Emily Farran
9.30	The importance of understanding individual differences at genetic, neural, cognitive and environmental levels: the case of Down syndrome *Hana D'Souza*
10.30	Hacking a way through the garden of forking paths: A cause for poor reproducibility. Video* of Dorothy Bishop's presentation (with permission) from the Open Debate event: Replication and reproducibility in psychological science **If unavailable, we will use this slot to discuss reproducibility with reference to neurodevelopmental disorder populations*
11.00	Coffee Break: Room B02 Chandler House
11.30	Capturing and exploring rich data: Considerations for neurodevelopmental disorder research using behavioural, eye-tracking and EEG paradigms. *Megan Freeth*
12.30	Lunch: Room B02 Chandler House
1.30	Rare genotypes and small samples sizes: Discussing strategies. *Kate Baker and Gaia Scerif*
2.30	How to identify true stratification biomarkers for autism? Efforts adopted in the EU-AIMS Longitudinal European Autism Project (LEAP) to increase analysis transparency and reproducibility *Eva Loth*
3.30	*End of conference*

Workshop Abstracts

Hana D'Souza
Centre for Brain & Cognitive Development, Birkbeck, University of London

The importance of understanding individual differences at genetic, neural, cognitive and environmental levels: the case of Down syndrome

In this talk, we first introduce a summary of the general assumptions about Down syndrome (DS) still to be found in the literature. This neurodevelopmental syndrome is characterised by distinctive facial dysmorphology and an uneven cognitive phenotype including relative strengths and weaknesses. However, the phenotype of individuals with DS is far from homogeneous, and a wide range of individual differences is present at every level of description. On the genetic level, the trisomy can occur through different mechanisms at distinct developmental time points, and the expression of trisomy 21 may be modulated by different genes across individuals. On the level of the brain, individual differences in brain structure and/or function correlate with variation in cognition and behaviour, including communication skills. Large individual differences can also be observed on the cognitive level. For example, while some toddlers with DS are nonverbal, others reach expressive vocabulary levels close to those of typically developing children. Furthermore, individual differences on the environmental level, such as parent-child interaction, need to be considered. A wide range of individual differences has also been reported in other areas, including the motor domain, sleep, and medical and psychiatric comorbidities.

We argue that, in the context of significant increases in DS life expectancy, a focus on individual differences in trisomy 21 at all levels − genetic, cellular, neural, cognitive, behavioral, and environmental − constitutes one of the best approaches for understanding genotype/phenotype relations in DS and for exploring risk and protective factors for Alzheimer's disease in this high-risk population.

Megan Freeth
Psychology Department, University of Sheffield

Capturing and exploring rich data: Considerations for neurodevelopmental disorder research using behavioural, eye-tracking and EEG paradigms.

Research with individuals who have neurodevelopmental disorders can be difficult due to the low prevalence of these conditions and challenging practicalities. It is therefore extremely important that opportunities to work with individuals from such populations are optimised. In this talk I will discuss various examples of ways to collect and analyse rich data from these populations which can result in discoveries which may otherwise be overlooked. Approaches to be discussed are: Interpretative Phenomenological Analysis, a qualitative approach which can help researchers to understand the lived experience of individuals where the emphasis is on data quality not quantity; Eye-tracking, moving beyond analysis of total gaze duration and exploring modelling of eye movements to gain insights into visual attention and perception; EEG, using ICA to clean data and isolate components of interest thus using data collected from all electrodes rather than merely extracting data from a small subset of electrodes. I will explain how these approaches can enable researchers to gain new insights from their data and avoid overlooking a rich tapestry of evidence.

Kate Baker and Gaia Scerif
Experimental Psychology, University of Oxford

Rare genotypes and small samples sizes: Discussing strategies

One of the main challenges to understanding cognitive profiles that are specific to rare genotypes is that many of our current statistical tools are as yet not well suited to investigating individual differences, developmental trajectories and rich datasets in modest to very small sample sizes. In this talk we would like to raise discussion on a number of complementary and non-mutually exclusive strategies that might ameliorate this problem: 1) at the genetic / neurscience level, the idea that relatively rare genotypes can cluster into larger families of functional gene networks; 2) in terms of experimental / study design, longitudinal studies can help disentangle individual differences that make cross-sectional comparisons complicated; 3) in terms of analytical strategies, multi-level modelling approaches can help muster and model intra-individual as well as inter-individual variability. These three strategies have strengths, but also constraints and caveats – we hope to generate discussion and hopefully consensus on robust approaches to new study designs and analytical plans.

Eva Loth
Sackler Institute for Translational Neurodevelopment, Institute of Psychiatry, Psychology and Neuroscience, King's College London

How to identify true stratification biomarkers for autism? Efforts adopted in the EU-AIMS Longitudinal European Autism Project (LEAP) to increase analysis transparency and reproducibility

Autism Spectrum Disorder (ASD) is a clinically, etiologically and genetically heterogeneous life-long neurodevelopmental condition. This heterogeneity has been a major obstacle in developing and testing treatments/ interventions as many treatments may only be effective in particular persons with ASD. Therefore, we need biological risk markers to divide people with ASD into more homogenous subgroups. So far, stratification research in ASD is in its infancy. Most studies used case-control designs, which focus on between-group differences usually at the cost of examining and reporting within-group variability. Moreover, as in many areas of neuroscience, findings are often difficult to replicate. Small sample sizes, differences in methodologies, analyses approaches, and the prevailing 'positive' publication bias make it difficult to compare studies and differentiate candidate biomarkers from artefacts.

In this talk I will introduce the Longitudinal European Autism Project (LEAP), which includes over 400 individuals with ASD and 300 individuals with typical development or mild intellectual disability from 6-30 years. Each volunteer is comprehensively characterized in terms of clinical symptom and neurocognitive profile, brain structure and function, biochemical biomarkers and genomics. I will describe approaches used to identify and validate stratification biomarkers, and measures we adopt to increase data robustness and reproducibility. This includes registration of projects, standardized Quality Control and analyses techniques within each data modality, standardized format of reporting, and efforts to publish/ or make publicly available both positive and negative results. It also includes sharing our protocols and Standard Operation Procedures with other international groups to enable independent replication. We hope that the scale of the project and in-depth level of characterization will enable us to confirm, reject and refine existing hypotheses and to better understand how phenotypic and etiological may map onto one another.