Differences in the Neurophysiology of Infants with Down Syndrome May Predict Protective/Risk Markers for Subsequent Alzheimer's Disease.

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Background

- Most individuals with DS: AD brain pathology by middle age but not all get dementia
- Amyloid precursor protein (APP) gene on Hsa21 over-expressed ***from infancy onwards***
- Signs of amyloid plaque build-up already present in some infants at 20 months (Gyure et al., 2011).
- Still not understood why some do/don't go on to develop AD dementia
- **Only way to fully understand phenotypic endpoint at neural, cognitive or behavioural levels: trace it back to its *developmental origins* (Karmiloff-Smith 1998)**

Aims

- **Understand early *individual differences* in memory abilities of infants with DS that may be predictive of subsequent cognitive phenotypes of AD**
- Trace phenotypic outcome back to origins in early development
- Elucidate individual differences in DS infants associated with specific neurocognitive phenotypes of AD
- Focus on outliers as *meaningful* source of variation
- Identify protective vs risk markers for AD
- **Can we identify, already in *infancy* (in this very high-risk population) risk/protective factors for later AD?**
- Target early intervention for those likely to develop AD
- Link our findings with other LonDownS studies: adults with DS & AD, mouse models, genetic and cellular profiles of those with/without AD dementia

Participants

	DS	NT
N	54	26
Range (months)	6-63	4-52
Mean (months)	27.25	24.34
SD (months)	13.9	13.7

Memory Measures

- We ran an **Object memory task** using the Tobii TX300 eye-tracker to observe looking patterns during object recognition
- We also ran an **ERP old-new memory task.**

Object memory task (eye-tracking)

Why object memory?

- Memory decline, preceding AD diagnosis and continuing to decline thereafter.
- Memory measures are sensitive: can measure memory subtleties in DS and AD (adult stream).

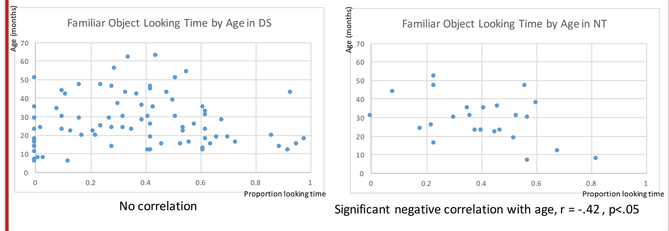
Procedure

- Infants given repeated exposure to 4 images and, during test, one of the images is replaced with a novel image
- Measure: looking time, to ascertain whether infants are sensitive to the change

Study trials x 3 *Test trial*

Behavioural Results

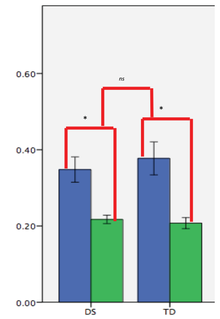
Age and Object Memory in DS



No correlation

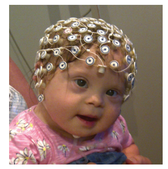
Significant negative correlation with age, r = -.42 , p<.05

- NT infants: spend less time spent looking at the familiar object as they increase in age.
- This is expected; as infants grow older they tend to explore novelty more.
- This is not true for the DS group in the current study – possibly stimuli was not encoded fully?
- Sample sizes are smaller in NT (but the study is still well-powered, Power = 0.7).



- *Both groups look significantly longer to novel object (F(1,125) = 15.84, p <.001).*
- *No significant difference between groups RMANOVA, F(2,125) = 1.29, p = n.s.).*

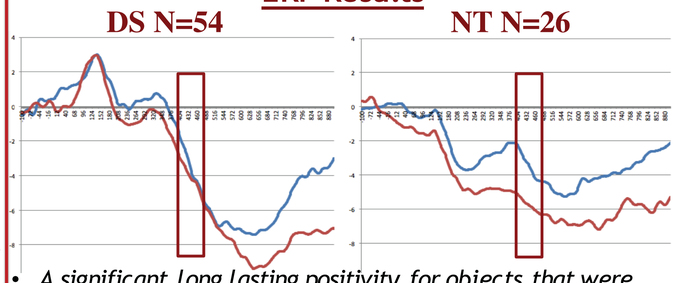
Electroencephalography



Old-New Memory ERP task

- Participants play with 15 toys pictured during a 7.5 minute interactive session with the researcher, prior to the EEG.
- During the EEG they are presented with pictures of toys they have played with ('old' pictures) as well as 15 'new' pictures.
- Pictures were equated for color, complexity and attractiveness between conditions.
- Draws on familiarity/recollection and the episodic memory system (Duzel, 1997; Rugg & Curran, 2007)
- The passive variant of the task is non-verbal so can be used ***early*** with infants

ERP Results



- *A significant long lasting positivity for objects that were old versus novel was observed for the NT group (F(1,25) = 4.16, p< .05) at Fronto-parital scalp locations.*
- *The effect was marginal in DS (F(1,53) = 3.5, p = .06).*
- *There was a group interaction effect.* From 400 – 500 ms, 500-600 ms, 600-700 ms, 700-800 ms and 800-900 ms there was a Group by Old-New ((F1,75) = 8.69, p < .005), F(1, 75) = 5.67, p <.05, F(1, 75) = 8.61, p <.005, F(1, 75) = 6.05, p <.025 and F(1, 75) = 4.65, p <.05 respectively) where the Old-New amplitude differences were significantly smaller in DS compared to the NT group.

Summary

- Age modulated looking time behaviours for NT individuals only. This finding is what we would expect given previous studies of NT developing individuals (Weizmann et al., 1971).
- There was an old-new effect by group interaction. The old-new significantly smaller in DS during the 400-900 ms time window.
- This time window falls within the time window of the parietal old-new effect (Curran et al., 2007), which is modulated by episodic memory tasks.
- More work is needed to understand how the effect is modulated in DS, but a promising start.
- Memory decline is a common in Alzheimer's Dementia. This task is being conducted with older adults with DS, some of whom are developing AD symptoms.

TAKE HOME MESSAGE

- Old-new effect is attenuated in DS from 400 – 900 ms.
- Individual differences in neurophysiology may be a meaningful source of variation and could predict onset of AD in DS
- Our previous data already highlight considerable individual variation in memory ability of infants with DS.
- At the *behavioural* level, Infants with DS may not differ group-wide from neurotypically developing infants, but they do at the neural level
- EEG/ERP reveal differences in neurophysiology and can be used to investigate if similar behavioural scores are underpinned by *different neural processes in DS.*

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