Studying cognitive development in babies with Williams syndrome compared to other neuro-developmental disorders

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Why study babies?

Only way to fully understand phenotypic endpoint at neural, cognitive or behavioural levels:
Trace it back to its *developmental origins*  
(Karmiloff-Smith, *Trends in Cognitive Sciences*, 1998)

Infant brain = highly plastic / less specialised

Brain and cognition undergo many changes during infancy; more inter-region interaction

Early deficit in one domain can have cascading effects on other emerging domains over developmental time

Cross-modality effect

- Delayed verbal language
- Atypical triadic interaction
- Atypical eye gaze following
- Low-level visual deficit in saccadic eye mvt planning
Cross-syndrome comparisons

Examples from *infancy*:
- WS & Fragile X syndromes: attention
- WS & Down syndrome: number
- WS & Down syndrome: face processing
- WS, DS, FXS & autism sibs: speech processing
Examples from *infancy*:
Attention
Number
Face processing
Speech processing
Predictive cues/inhibition: WS/FXS

MA controls learn to inhibit looks to predictive cues

Both FXS & WS fail task, but for different reasons:
- Infants/toddlers with FXS fail to inhibit looks
- Infants/toddlers with WS fixate centre throughout

Scerif, Karmiloff-Smith et al., 2005, J Cog Neuro
Cornish, Scerif, & Karmiloff-Smith, 2008, Cortex
Examples from *infancy*:
- Attention
- Number
- Face processing
- Speech processing
Behavourial tasks
Now + eye-tracking

Eye-tracking *patterns* (not simply total looking time)

Often total looking time = same
but scanning pattern = different

Tobii TX300 calibration
Where do number difficulties originate?

Are they the same across syndromes: WS and DS?
Small number discrimination in WS & DS infants

Exact small number (2 vs 3):
NT infants OK @ 3-4 months
WS/DS tested @ 10-39 months

WS=NT  DS=no significant difference

Replicated with 2nd set of infants with dot arrays

WS=NT > DS

Paterson et al., 1999
Paterson, Girelli, Butterworth & Karmiloff-Smith, 2003
Van Herwegen, Ansari, Xu & Karmiloff-Smith, 2008
Large number discrimination in WS & DS infants

Approximate large number (magnitude)
NT infants OK @ 6-7 months  ratio 1:2

WS & DS tested @ 9-40 months  8 vs 16  (ratio 1:2)

DS=NT   WS=no significant difference

DS=NT > WS

Karmiloff-Smith, d'Souza, Dekker, van Herwegen, Radic, Xu & Ansari, 2012
Maybe DS/WS differences in number = not specific to number but due to more general differences in visual attention/visual scanning patterns

Several experiments on visual saccade planning/attention

- **WS** = very impaired saccades + serious visual disengagement problems
- **DS** = proficient saccades, but serious sustained attention problems
How do WS/DS infants scan numerical arrays?

Hypothesis:

Maybe DS/WS differences in number = not specific to number but due to more general differences in visual attention/visual scanning patterns

Several experiments on visual saccade planning/attention
  WS = very impaired saccades, plus serious visual disengagement problems
  DS = proficient saccades, but serious sustained attention problems

Scanning large arrays--> need to rapidly move eyes across global quantities => DS good
Scanning small arrays--> need to sustain attention on individual objects => WS good
DS infant: focus on global quantities

WS infant: focus on individual objects
Examples from **infancy:**
- Attention
- Number
- Face processing
- Speech processing
Why High Density EEG/ERP?
(128-channel Geodesic Sensor Net)

Very easy to administer to babies
Fine temporal patterns of brain activity
Scalp maps of approximate brain location

Important: often *behavioural* scores similar but *different neural processes*
Example of how neural measures can reveal what behavioural measures miss

Williams syndrome face processing: *in normal range* on standardized tasks
(Rivermead and Benton)

Intact face processing in WS?
Temporal signatures for face and car processing in Williams syndrome

WS adolescent in Geodesic HD net
Behavioural scores in normal range... but different neural processes

Healthy controls:
Progressive processing restriction of input type

WS: failure to specialise

WS: failure to localise
Healthy controls:
Progressive restriction of brain circuits

Featural processing
Where do the face processing differences in WS originate?
Longer looking to featural vs configural change

Featural processing

D’Souza et al., 2015
Examples from *infancy*:
- Attention
- Number
- Face processing
- Speech processing
Why is WS language delayed when later so proficient?

- delayed in onset of babbling
- delayed in segmenting speech stream
- lack of hemispheric lateralisation
- rely more on perceptual cues than linguistic labels
- comprehension/production not normal relationship
- don’t use or follow eye gaze for referential communication,
  despite fascination with faces (dyadic but not triadic attention)
- production often precedes pointing
- don’t understand referential function of pointing

But, new study-→
Cross-syndrome comparison
WS/DS: both language delayed

- 70% standards: /u/ low pitch
- 15% speech deviants: /i/ low pitch
- 15% pitch deviants: /u/ high pitch

WS and DS matched on Mullen scores
Cross-syndrome neural differences: P3a (250-350ms-attentive orientation) to pitch/speech

Brain reveals different developmental trajectories

D’Souza & Karmiloff-Smith, 2015
Implications for intervention

- Should be *syndrome-specific* from basic research

- Should start in *early infancy*
  
  WS: *before* e.g. number, face or speech processing strategies emerge

- Not necessarily in domain of deficit
  e.g. *don’t train number*: WS infants: train saccadic eye mvts
  DS infants: train sustained attention

Potential cascading effects *over developmental time* on *several* different cognitive domains