CBCD Centre for Brain and Cognitive Development


# Regression (NT & NDDs), the importance of timing and of cross-syndrome comparisons

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# Outline

**NT: Examples of regression/loss of skills in neurotypical development**

**- Behavioural regression vs representational *pro*gression**

**- Balance – synapse strengthening vs pruning weak connections**

**NDD – Williams syndrome: lack of specialisation/localisation of neural function**

**possible lack of pruning?**

**NDD-ASD: Threshold too high – over-aggressive pruning**

**Regression due to pruning of strong connections,**

**Sequence of regressive behaviours hypothesized:**

**sensory -> motor -> language -> executive function**

**Early differences: ASD-sibs, controls and other NDDs**

# Behavioural regression vs representational progression in NT language

## Past tense/plural marking in early language development:

**T-1 Correct:** Papa went/Me caught ball/wet feet

**Isolated representations**

**T-2 Behavioural regression:** Papa goed/Me catched ball/wet foots

**T-2 Representational progression:** overgeneralisation of –ed past tense/-s plural patterns

**T-3 Correct as at T-1:** Papa went/Me caught ball/wet feet

**Representations have now become part of a system of morphological markers**

**Question we must ask of ASD regression:**
**Is behaviour *before* regression sustained by same mental reps as behaviour *after* the regression?**
**Is child *regaining* skills, or are the later underlying skills *different* even if overt behaviour seems the same?**

# NT loss of skills in infancy: face processing

**3-6 month olds:** discriminate own-race faces
discriminate other-race faces
discriminate other-species faces

**9-10 month-olds:** ability lost for other-race/other species due to pruning of lesser-used connections and strengthening of used ones

**12 months:** if experience given at 9 months with faces of other-race/other species, then ability = retained


Pascalis, Scott, Kelly, Shannon, Nicholson, Coleman & Nelson, 2005
Kelly, Quin, Slater, Lee, Ge & Pascalis 2007
Heron-Delaney, Wirth, & Pascalis, 2011

# NT loss of skills in infancy: speech processing

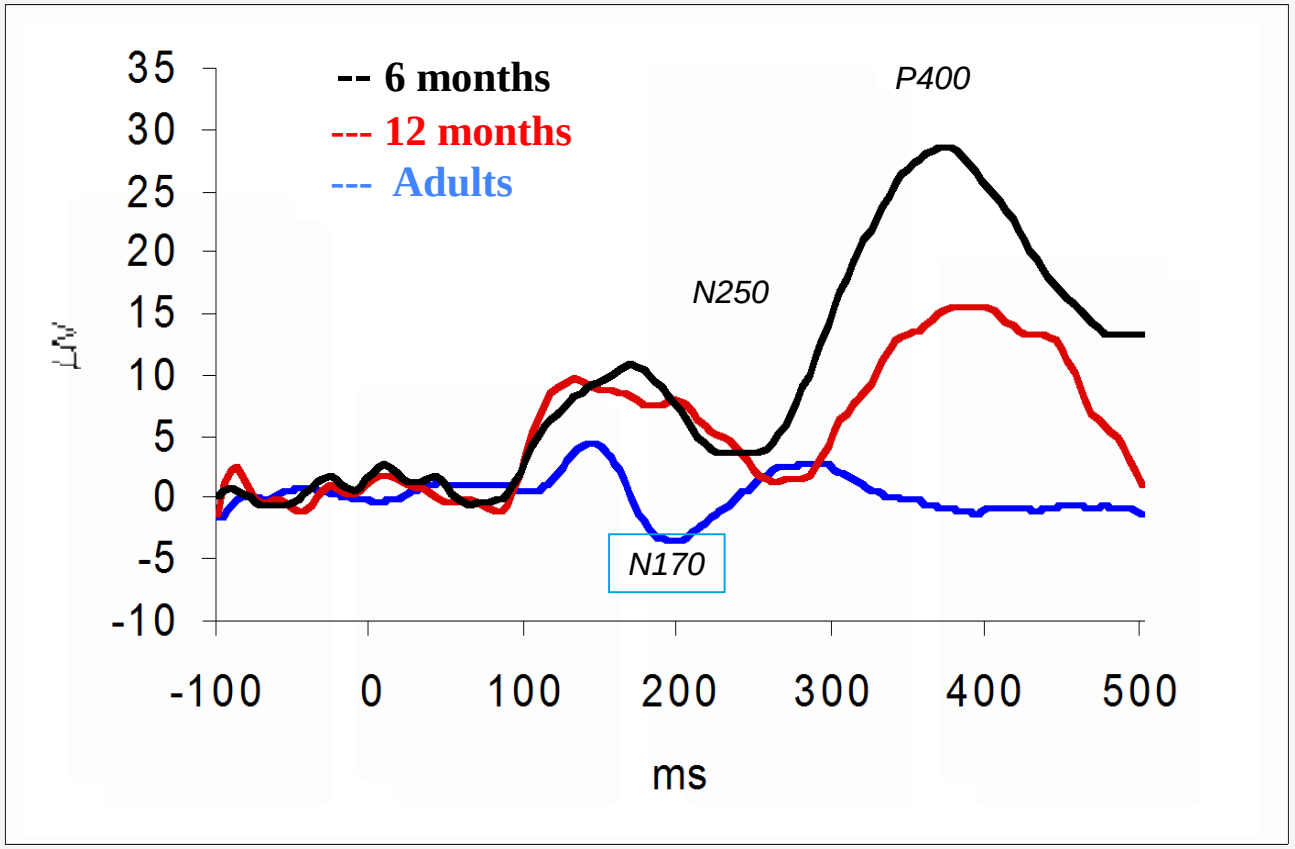
| | |
|---|---|
| 3-6 month olds: | discriminate phonemes in native language<br>discriminate phonemes in non-native languages<br>discriminate other-species' cries?? |
| 9-10 month-olds: | ability lost for non-native, due to pruning of lesser-used connections and strengthening of used ones |
| 12 months: | if experience given at 9 months with non-native phonemes, ability retained |

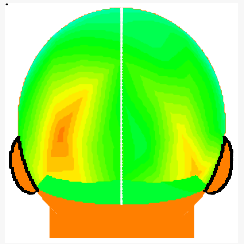
Different groups for face/speech. Single *domain-general* mechanism?
Need to research faces/speech tasks in *same* infants

Face and speech processing undergo perceptual narrowing in NT
Balance: strengthening of used connections + pruning of unused connections
*Progressive* specialisation and localisation of neural function

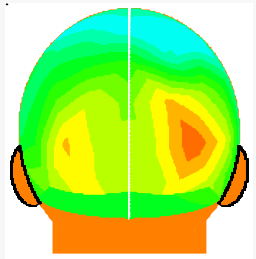
Tees & Werker, 1984
Nazzi, Jusczyk, & Johnson, 2000
Maye, Werker & Gerken, 2002
Best & McRoberts, 2003

# Specialization and localisation of brain function are *progressive*

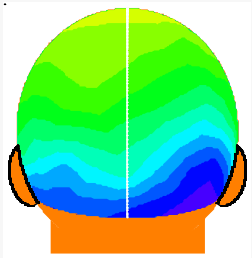


6 months



12 months

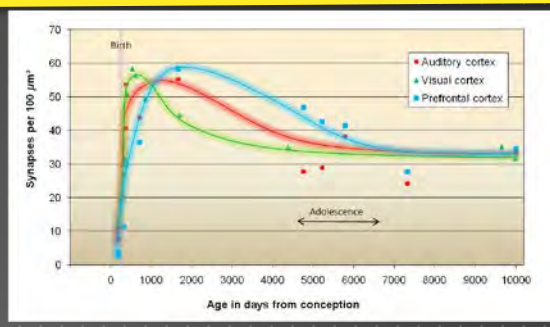


Adults

From de Haan, Pascalis & Johnson, 2002; Halit, de Haan & Johnson, 2005

See, also, Pascalis, deHaan & Nelson, 2002

# Hypotheses re NDDs: differences in pruning thresholds and specialisation/localisation of neural function?




**NT – Normal pruning threshold**
**Balance: strengthening/pruning**
**Different timing across neural regions**
**Specialisation = experience-dependent, progressive**

**WS? Under-pruning – imbalance stengthening/pruning?**
**Lack of neural specialisation despite behavioural mastery**

**ASD? Over-pruning – much higher pruning threshold than NT**
**Regression seen if development underway, camouflaged if development sl**
**Different timing of pruning across neural regions:**
**regression: sensori->motor->language->executive function**

**Huttenlocher & Dabholkar, 1997; Huttenlocher, 2002**
**Thomas, Knowland, & Karmiloff-Smith, 2011**

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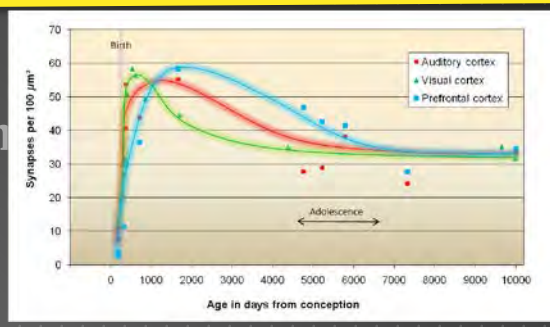


NT – Normal pruning heshold
Onset of pruning = timing maturatioanlly constrain
(individual differences?)
Different timing across neural regions
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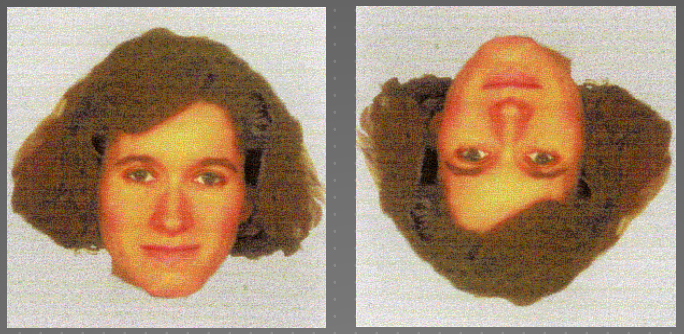
# WS face processing:
## behavioural scores "in the normal range"

Different teams worldwide:
WS face processing: *'in the normal range'*
on standarised tasks (Benton, Rivermead)



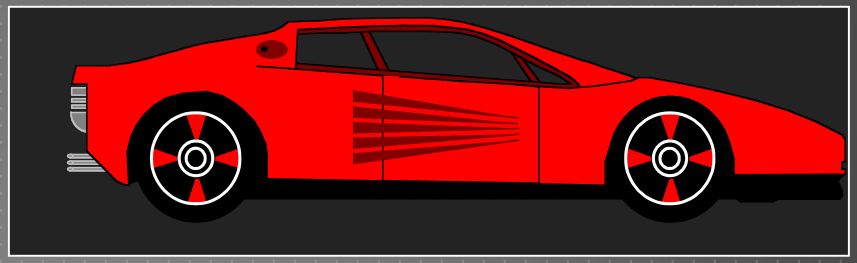
BUT inversion effect (hallmark of *configural* processing)
doesn't emerge developmentally at any age in WS

**WS brain signature?**

**Karmiloff-Smith et al., 2004**

# Temporal neural signatures for face and car processing in WS

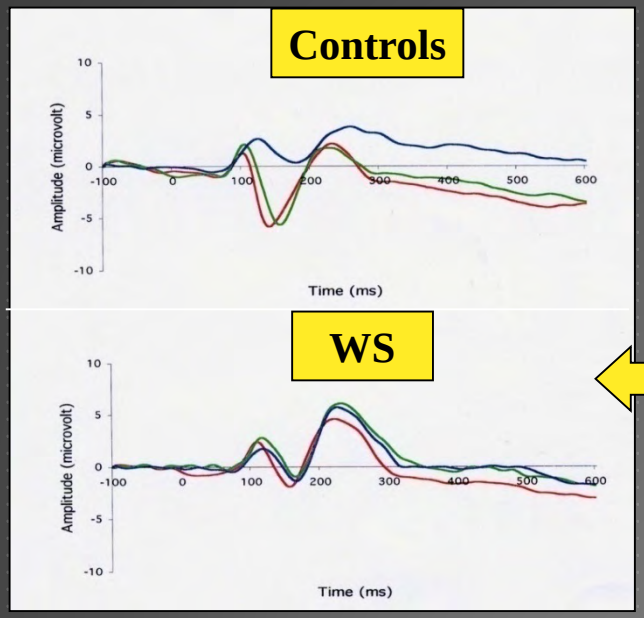
WS adolescent in
Geodesic HD-ERP net



All Ss in “normal range” on standardised face processing tasks

Grice, deHaan, Halit, Johnson, Csibra, & Karmiloff-Smith, 2003

# *Behavioural* scores in normal range… but different *neural* processes

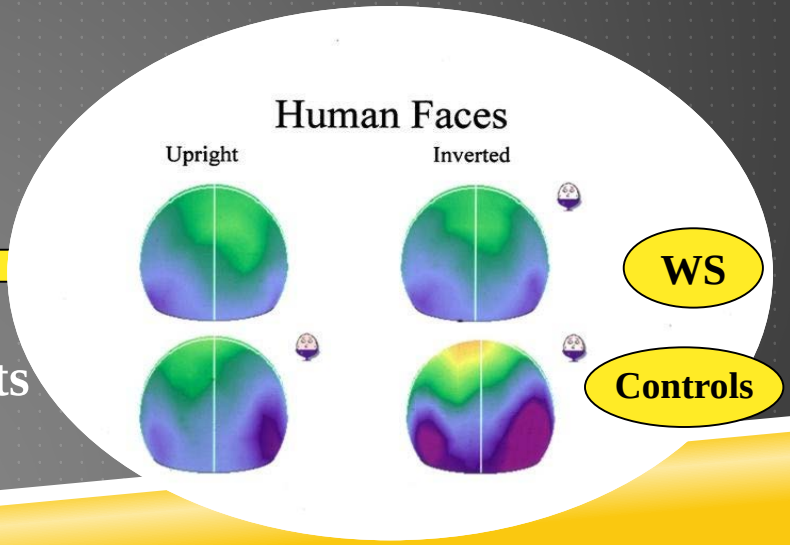



**Healthy controls:**
**Progressive processing restriction of input type**

**WS: failure to specialise**

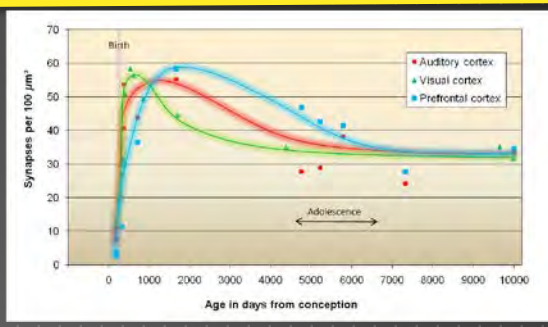
**WS: failure to localise**

**Healthy controls:**
**Progressive restriction of brain circuits**




**Featural processing**

# Hypotheses re NDDs: differences in pruning thresholds and specialisation/localisation of neural function?

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Regression seen if development underway, camouflaged if development slow
Different timing of pruning across neural regions:
hypothesis-regression: sensori->motor->language->executive function

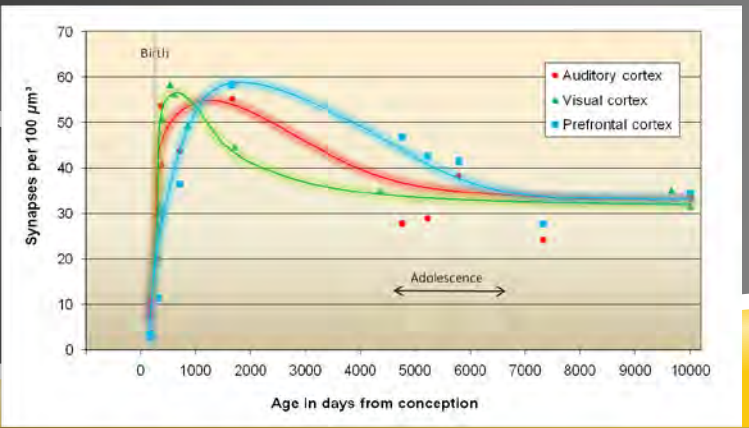
Huttenlocher & Dabholkar, 1997; Huttenlocher, 2002
Thomas, Knowland, & Karmiloff-Smith, 2011

# Over-pruning hypothesis – ASD?

**Not necessarily rare gene mutation but allelic difference in common gene(s) affecting pruning threshold -> exaggeration of normal developmental pruning process - ASD very high pruning threshold means not not only weak unused connections are pruned, but also stronger ones -> regression**

**Pruning occurs at different times in different brain areas (Huttenlocher & Dabholkar, 1997)**
**- Predicts -> first few months, prior to pruning = normal, followed by behavioural symptoms: 1. sensori-motor 2. social/language 3. executive function**

**Other individual difference factors interact with pruning threshold to create risk, leading to differences in ASD trajectories**




**Need to consider balance of specialisation vs pruning?**
**?NT tasks with at risk ASD infants?**


**Huttenlocher & Dabholkar, 1997; Huttenlocher, 2002**
**Thomas, Knowland, & Karmiloff-Smith, 2011**
**Rogers, 2009; Staples & Reid, 2010**
**Estes, Zwaigenbaum…IBIS group, 2015**

# Differences in early development
# ASD sibs, controls, other NDDs? What is ASD-specific?

- Atypical saccadic eye movements (WS also)
- Shorter fixation times to social and non-social scenes (Wass et al., 2015) (DS also)
- Attention to eyes declines between 2-6 months (Jones & Klin, 2013) (Rett/FXS?)
- Atypical face processing in infants/adults (featural vs configural) (D'Souza et al. 2015) (WS also)
- Follow head shift but not eye gaze shift (Thorup et al., 2016) (WS also)
- Lack of triadic attention (WS also)
- ERPs to dynamic eye gaze differ (Elsabbaghet al., 2012) (NDDs unknown, being tested)
- EEG frontal-occipital hyperconnectivity (Orekhova et al., 2014) (NDDs unknown, being analysed)
- Disengagement problems (Sacrey, Bryson & Zwaigenbaum, 2013) (WS also)
- Lack of attn to/discrimination of speech/pitch stimuli (D'Souza,Karmiloff-Smith, 2016) (FXS also)
- Enhanced visual search (Kaldy, Kraoewr, Carter & Blaser, 2013; Gliga,et al., 2015) (unique)

**Similar cross-syndrome exercise re brain differences**

More subtle with cross-syndrome than with NT

# Concluding thoughts…

**NT:** initially surplus neurocomputational resources to retain flexible response to environment; then strengthening of used connections/pruning of weak connections to save metabolic

**NT:** skills not "regained"; change of underlying representations/change of function

**ASD?** Suffice to have a mutation on a common gene with risk allele regulating pruning threshold
More aggressive, so risk of pruning not only under-used connections but also good ones -> regression.

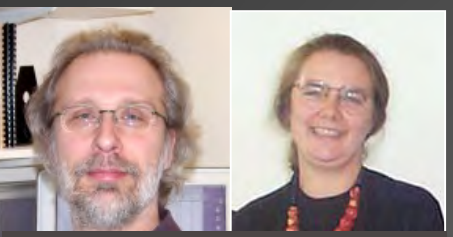
Regression: If behavioural development slow in ASD, then above could happen before behavioural skills emerge and therefore camouflage regression

Regression should first occur in sensori-motor patterns:
Parents likely to notice language loss, but loss of reaching/pincer grip?

If pruning too rapid/aggressive -> lack of flexible response to environment -> Rigidity/repetitive behaviours?

Need to focus on individual differences and subtle cross-syndrome comparisons rather than group data compared to NT controls

# Joint work mentioned in talk with past and current Colleagues/Postdocs/Students



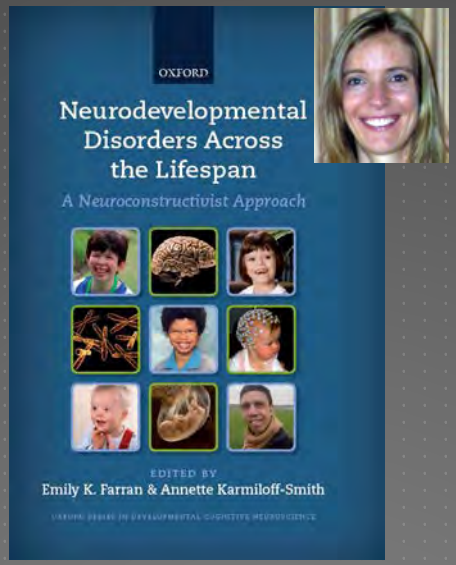
Mark Johnson



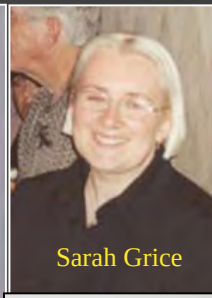
Sarah Jeeves

Gaia Scerif

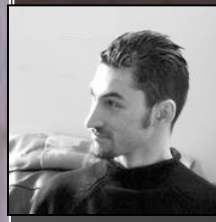
Michelle de Haan




Michael Thomas



Sarah Grice



Dean D'Souza

Victoria Knowland

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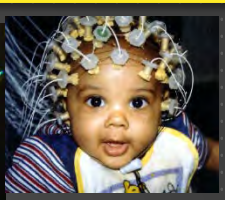
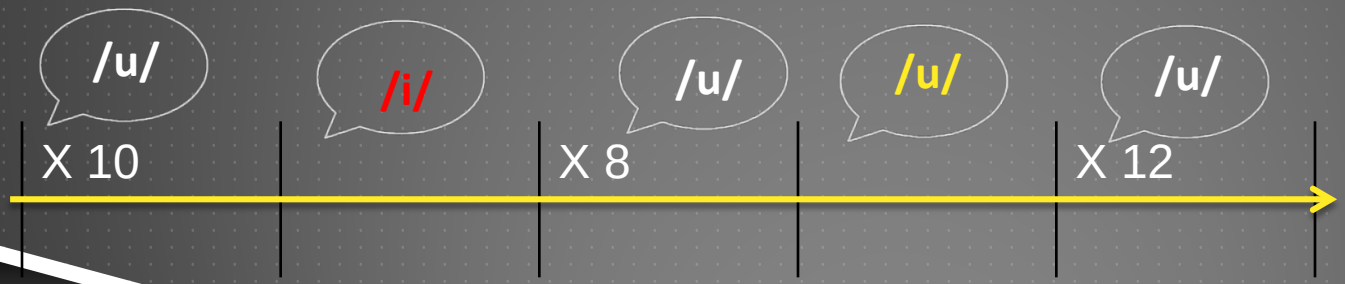
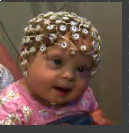
# Cross-syndrome comparison
# WS/DS/FXS/Sibs (MA-matched on Mullen)

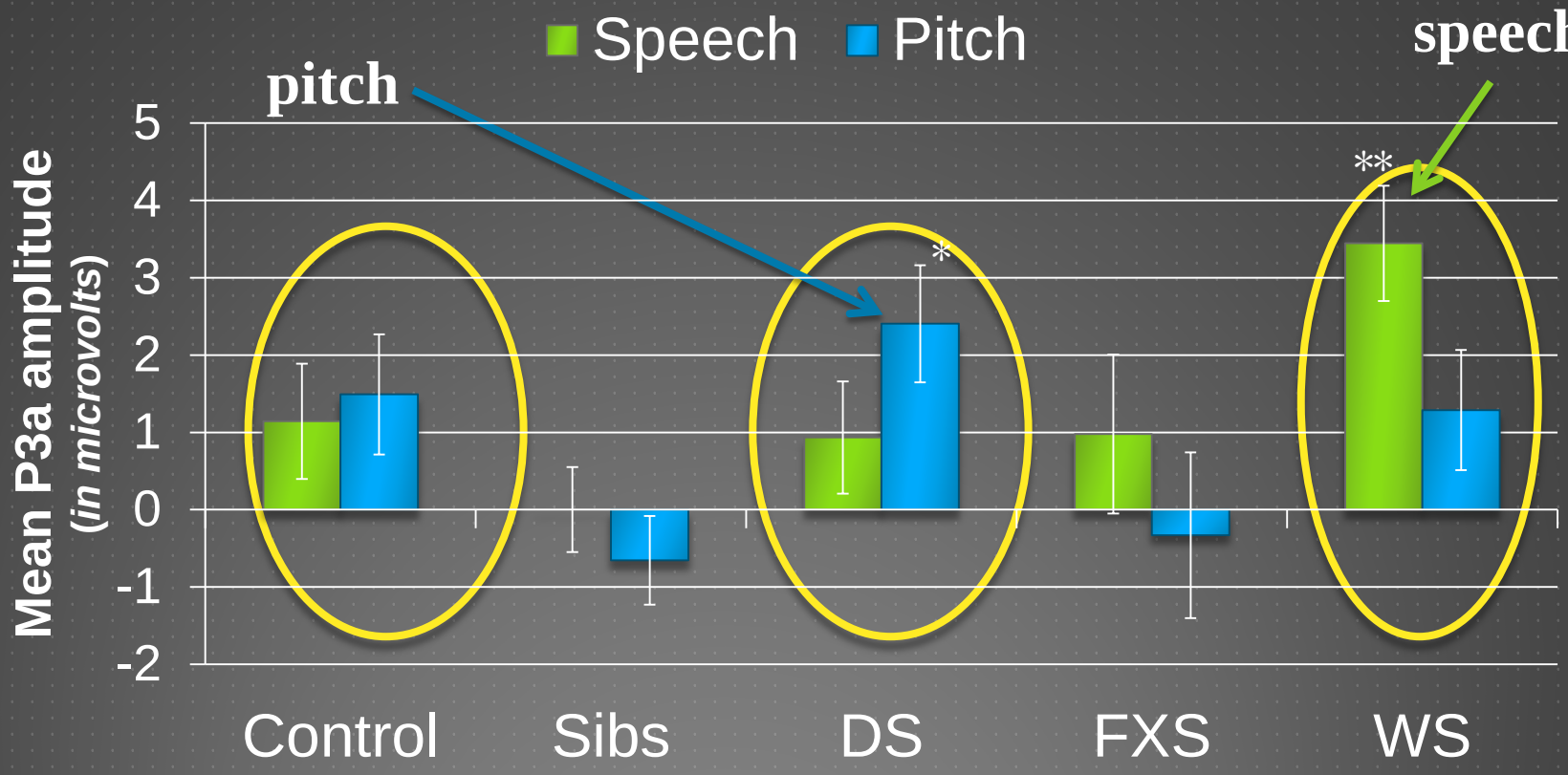
- 70% standards: /u/ low pitch
- 15% speech deviants: /i/ low pitch
- 15% pitch deviants: /u/ high pitch







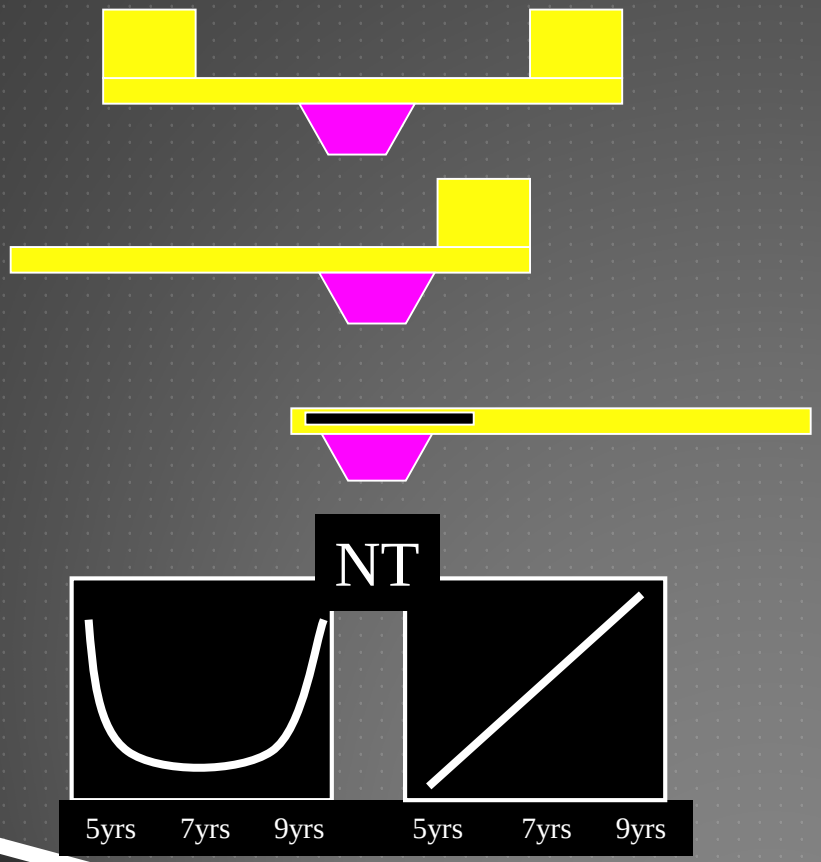
# Cross-syndrome neural differences:
## P3a (250-350ms-attentive orientation) to pitch/speech




D'Souza, Karmiloff-Smith et al., 2016

# Behavioural regression vs representational progression in NT vs Down syndrome

## 5 and 9 year olds




## 7 year olds