UNIVERSITY OF BIRMINGHAM

The Cerebra Centre for Neurodevelopmental Disorders

Italy, 2012

Behaviour and cognition in Cornelia de Lange syndrome

Chris Oliver,
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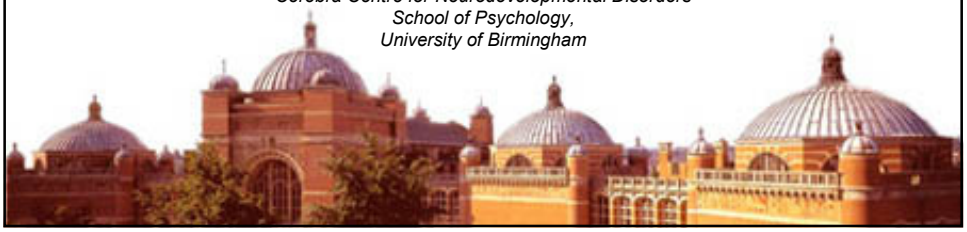
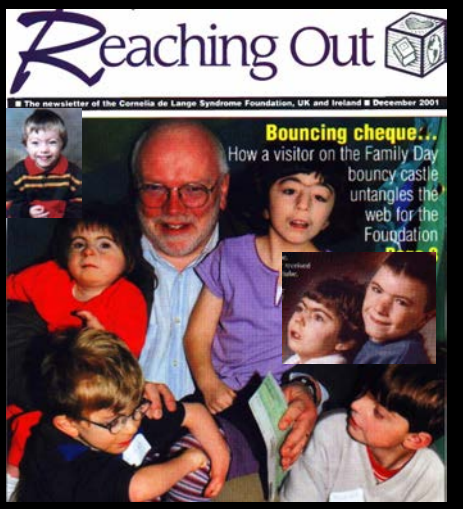
University of Birmingham



Our starting point

- In many, many ways children and adults with CdLS are just the same as everyone else and have the same needs, wants and rights as everyone else.
- Everyone is unique and each child and adult with CdLS is unique.
- In some ways children and adults with CdLS differ from people who do not have CdLS.
- We shall look at these differences but we will not forget the similarities or that everyone is unique.

- Prevalence: 1 in 40,000. (thought to be higher)
- Deletions on chromosomes 5, 10 and X
- Main features: mild\moderate to severe ID, small stature, upper limb abnormalities, distinctive facial features, gastroesophageal reflux, limited speech, hirsute, SIB.



de Lange, C. (1933). Sur un Type nouvea de degeneration (typus amstelodamensis) Arch.med. enf. 36. 713 - 719.

Brachmann,W. (1916). Ein Fall von symmetrischer Monodaktylie durch Ulnadefedkt, mit symmetrischer Flughautbildung in den Ellenbeugen, sowie anderen Abnormalitaten (Zwerghaftigkeit, Halsrippen, Behaarung). Jb. Kinderheilk., 84, 225-35.

Remember. CdLS is a syndrome. So there are a number of individual problems that need to be solved

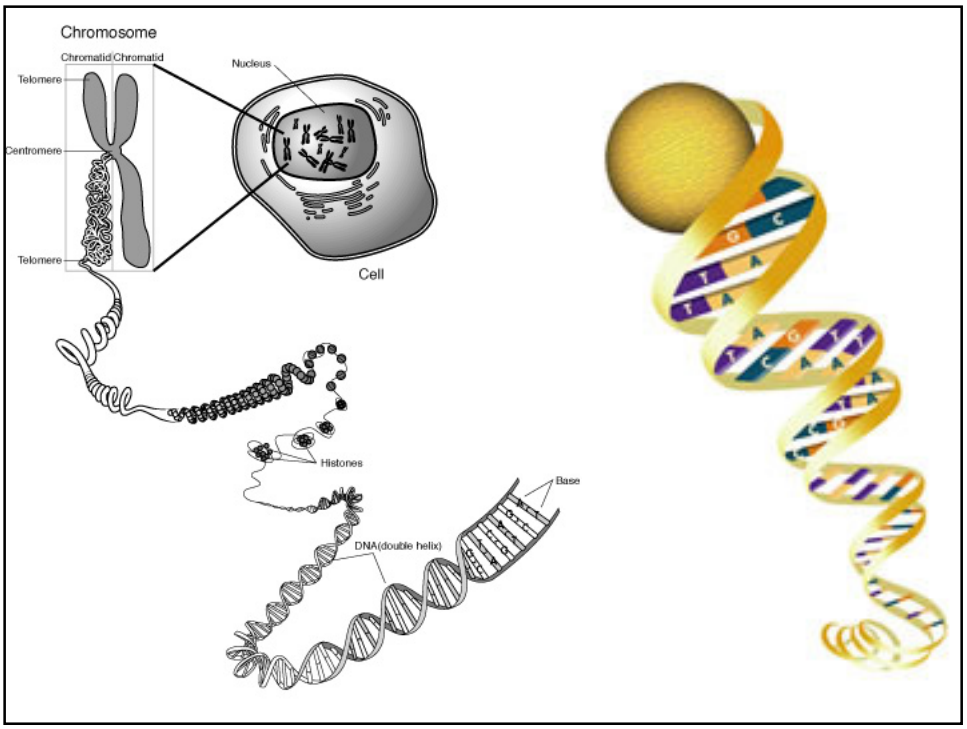
syn·drome (sĭn'drōm')

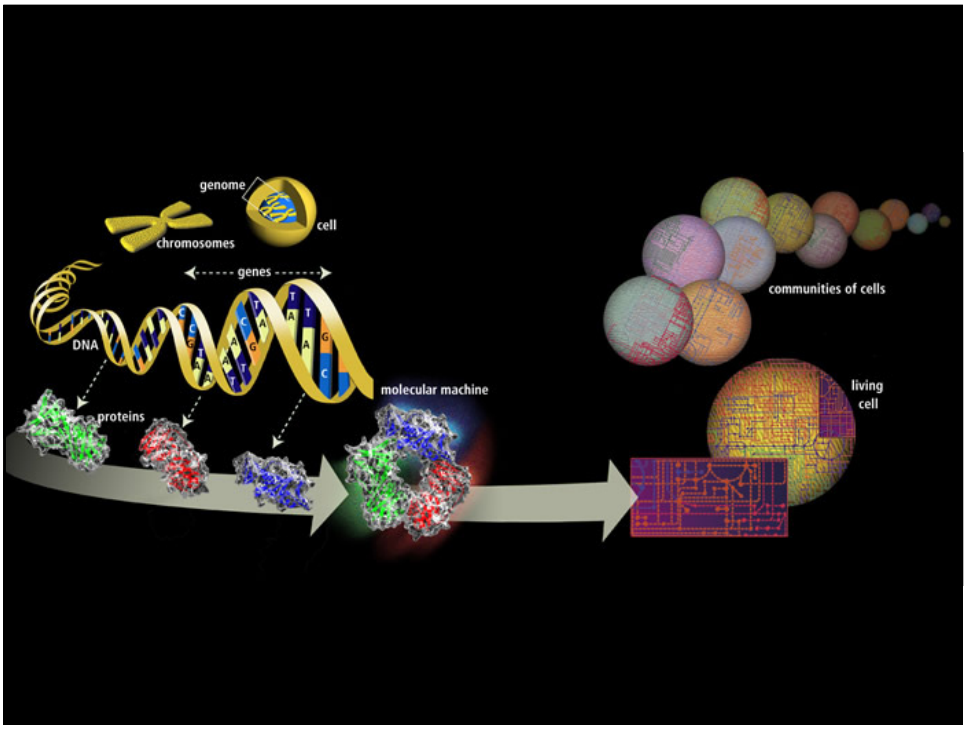
n.

1. A group of symptoms that collectively indicate or characterise a disease, psychological disorder, or other abnormal condition.

The key issues

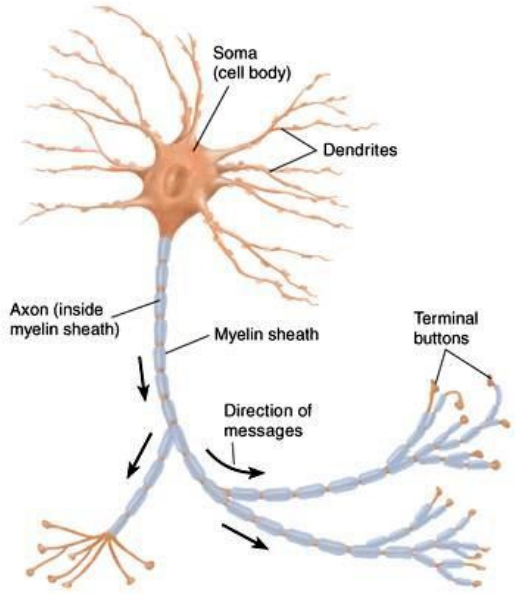
- Physical difference and disorder (health problems)
- Self-injury
- Poor expressive communication
- Autistic spectrum like behaviours
- Specific cognitive impairments
- Changes with age

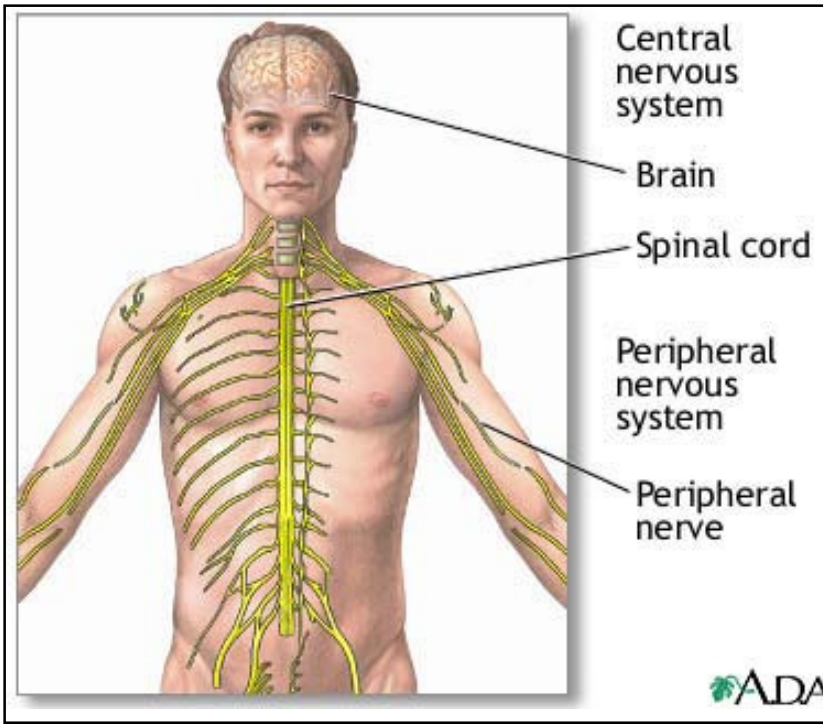


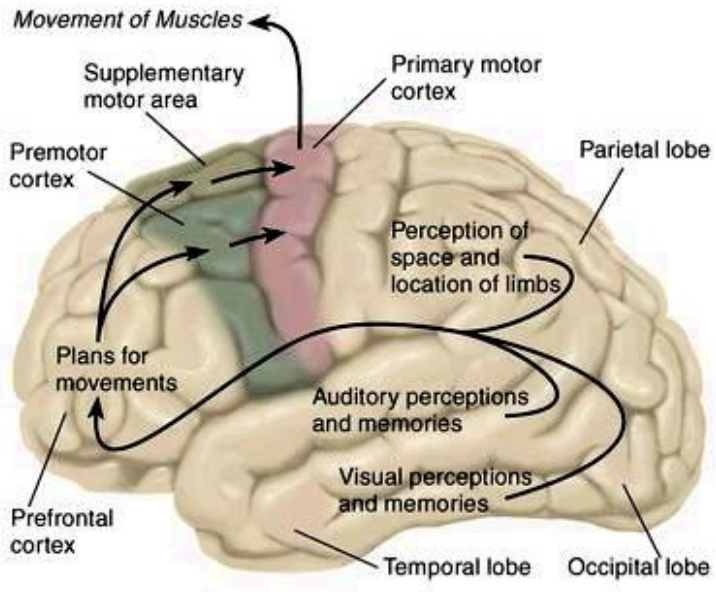

genome
cell
chromosomes
genes
DNA
proteins
molecular machine
communities of cells
living cell

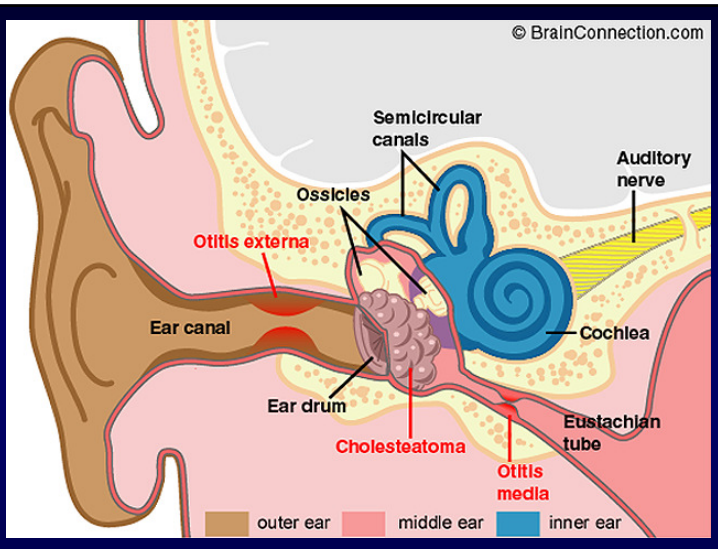

THE BEAUTIFUL FACES OF
Cornelia de Lange
TRIUMPHS
COURAGE
LOVE
PERSEVERANCE
"Strength does not come from physical capacity. It comes from indomitable will."

► **Multipolar Neuron**





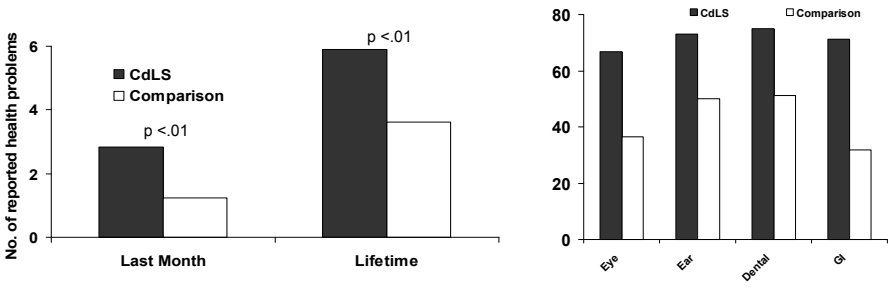




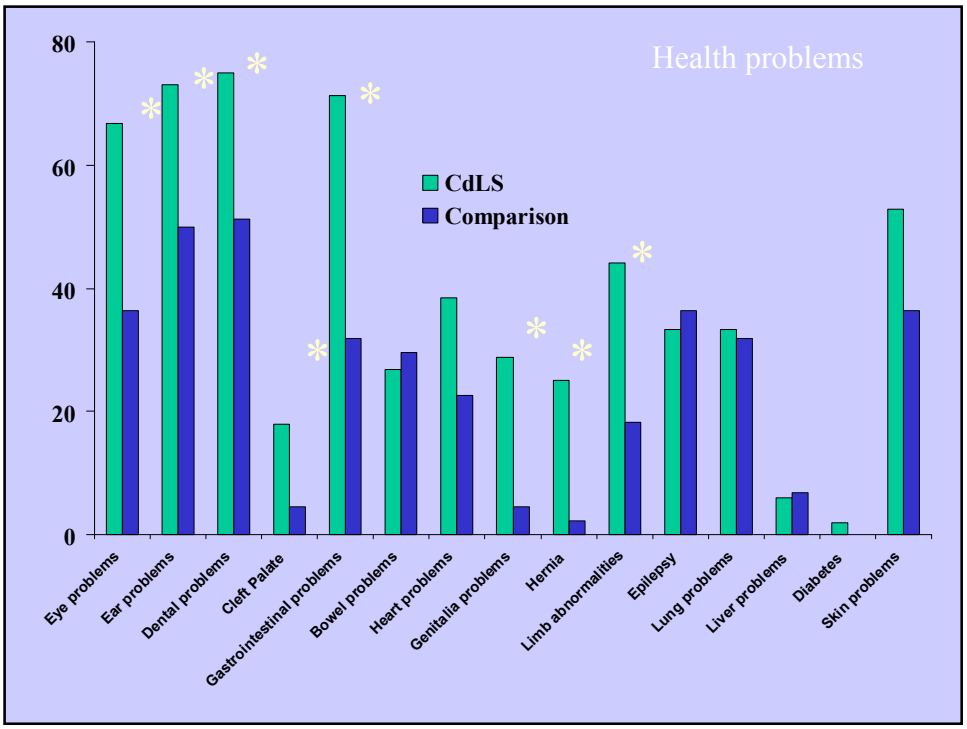
The ear canal is very narrow and the nerves in the ear may not form correctly. This effects hearing and, in turn, speech

Table 1 Percentage of individuals with Cornelia de Lange Syndrome (CdLS) showing specific health problems in published studies

		% of individuals experiencing health problems											
CdLS Studies	*n*	Limb abnormalities	Gastrointestinal	Heart	Dental	Genitalia	Genito-urinary	Eye	Ear	Respiratory	Epilepsy	Skin	Cleft palate
Hawley *et al.* 1985	64	33	71	28	93	94 (males)	–	–	–	–	14	–	–
Gualtieri 1990	138	–	41	15	–	–	8	–	–	18	25	–	–
Sataloff *et al.* 1990	45	–	–	–	–	–	–	–	–	–	–	–	59
Ireland *et al.* 1993	20	80	10	15	–	–	–	–	–	–	5	–	10
Jackson *et al.* 1993	310	–	48	25	–	73 (males)	12	50	60	25	23	16	–
Sommer, 1993	17	–	76	–	–	–	–	–	–	–	–	–	–
Kousseff *et al.* 1994	37	56	49	14	–	–	33	38	–	–	38	–	21
Berney *et al.* 1999	49	–	67	–	–	–	–	–	–	–	29	–	–
Tsukahara *et al.* 1998	50	–	–	26	–	–	–	–	–	–	–	–	–
Luzzani *et al.* 2003	43	–	65	–	–	–	–	–	–	–	–	–	–



Hall, S., Arron, K., Sloneem, J. and Oliver, C. (2008). Health and sleep problems in Cornelia de Lange Syndrome: A case control study. *Journal of Intellectual Disability Research,* **52**, 458-468.



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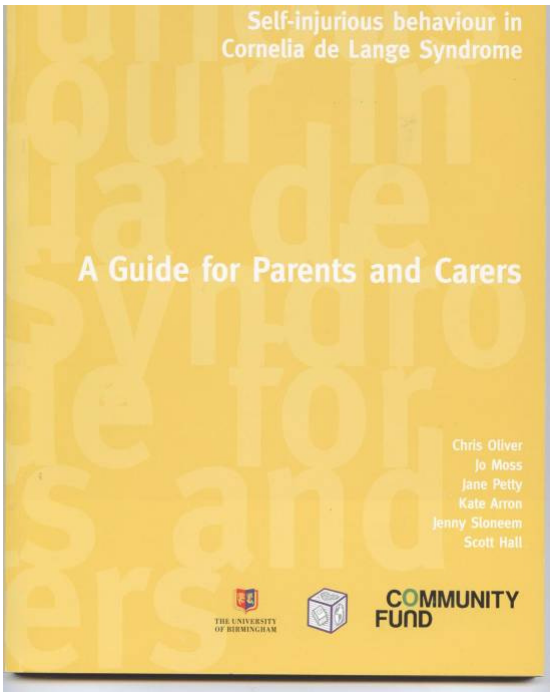

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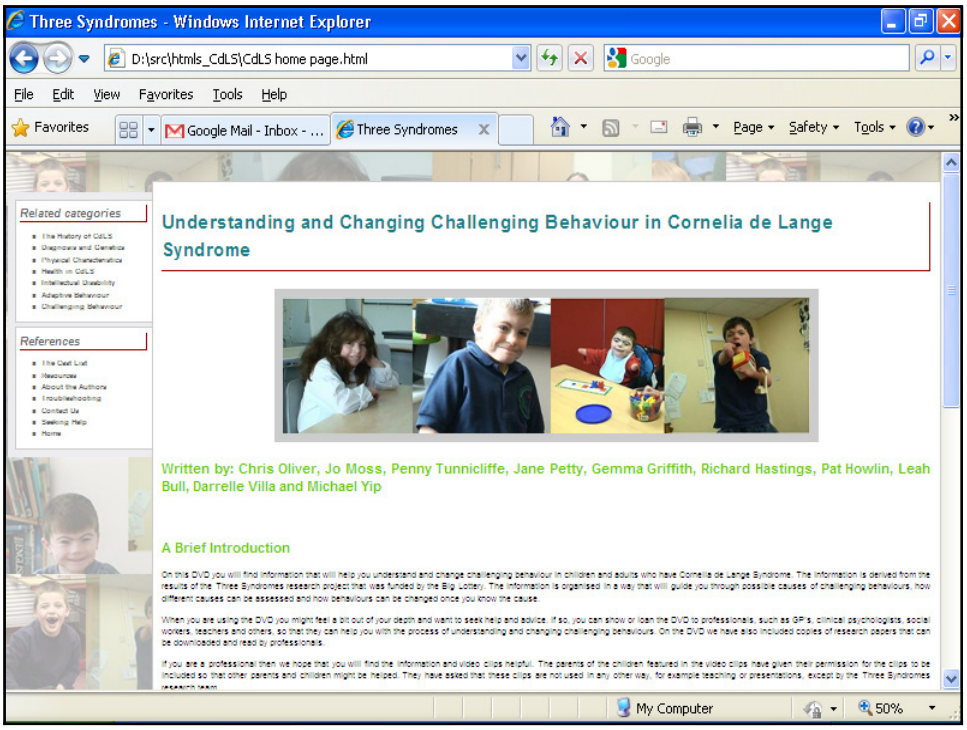
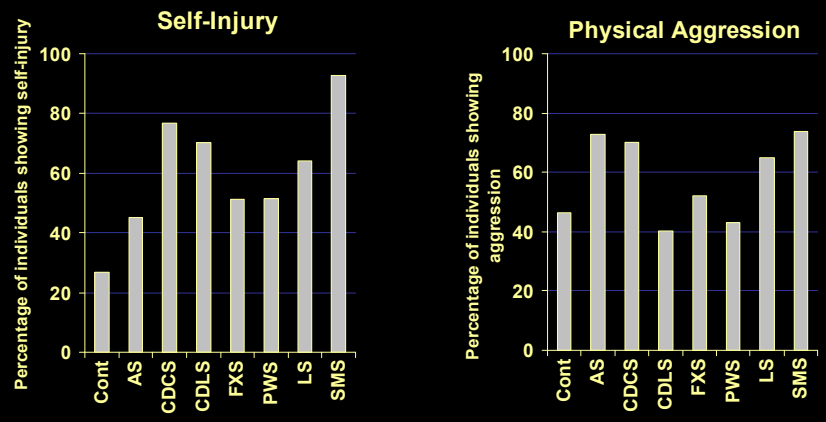
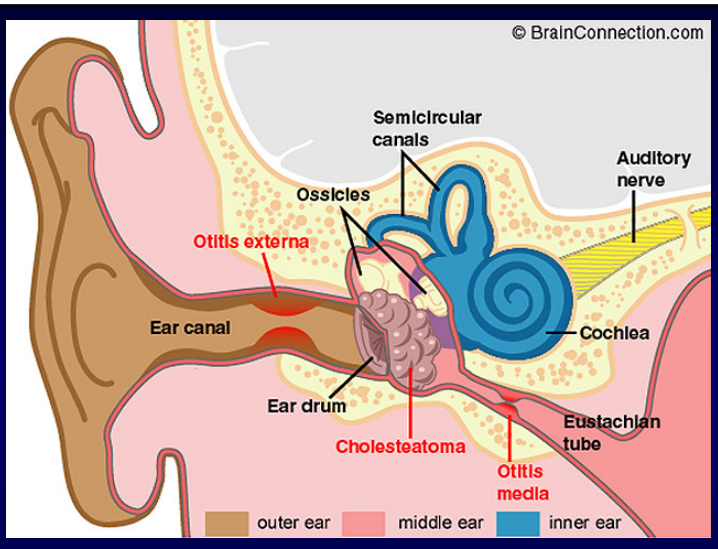
Understanding and Changing Challenging Behaviour in Cornelia de Lange Syndrome
Chris Oliver, Jo Moss, Jane Petty, Penny Tunnicliffe, Richard Hastings, Pat Howlin, Gemma Griffith, Leah Bull, Darrelle Villa and Michael Yip
LOTTERY FUNDED
KING'S College LONDON
BANGOR
Understanding and Changing Challenging Behaviour in Cornelia de Lange Syndrome


Three Syndromes - Windows Internet Explorer
D:\src\htmls_CdLS\CdLS home page.html
Google
File Edit View Favorites Tools Help
Favorites
Google Mail - Inbox - ...
Three Syndromes
Page Safety Tools
Related categories
References
Understanding and Changing Challenging Behaviour in Cornelia de Lange Syndrome
Written by: Chris Oliver, Jo Moss, Penny Tunnicliffe, Jane Petty, Gemma Griffith, Richard Hastings, Pat Howlin, Leah Bull, Darrelle Villa and Michael Yip
A Brief Introduction
My Computer
50%

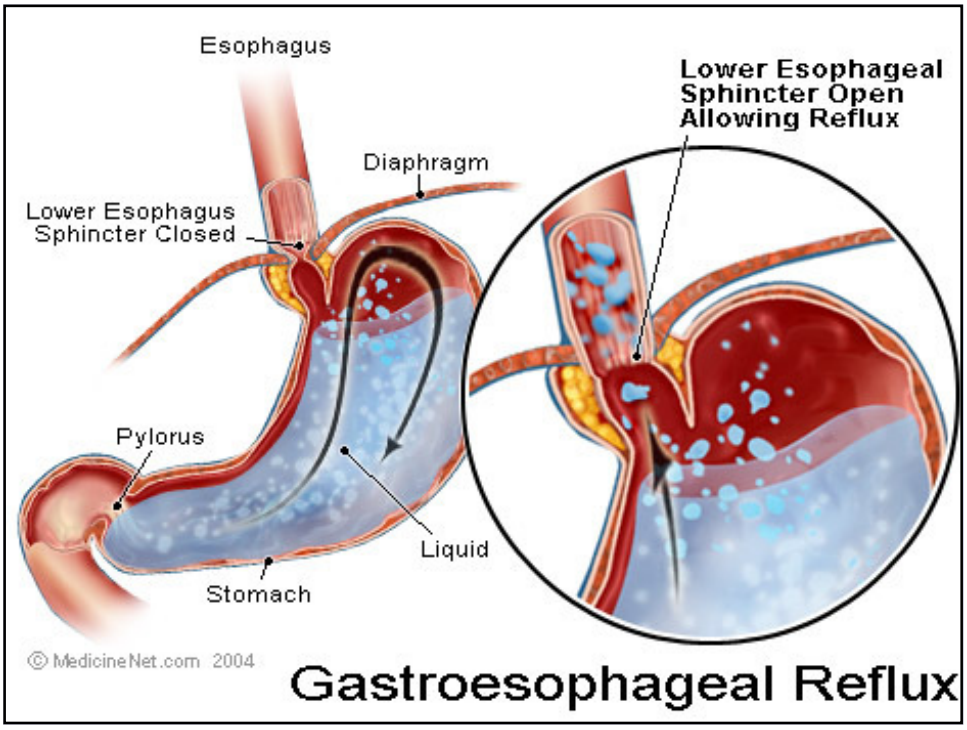
Prevalence of Self-Injury and Physical Aggression in Syndromes





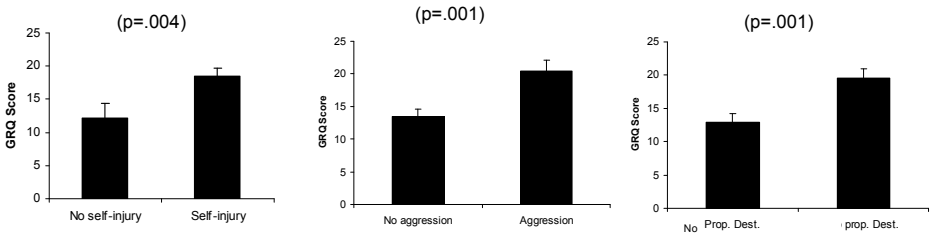
15% of <u>all</u> children bang their head between the ages of 1 and 4.

50% of these children have a middle ear infection.



Arch his/her back
Lie over object on stomach
Salivate excessively
Fidget/wriggle
Fingers in mouth
Chew clothes
Grind teeth
Scratch/rub chest/throat
Drink excessively

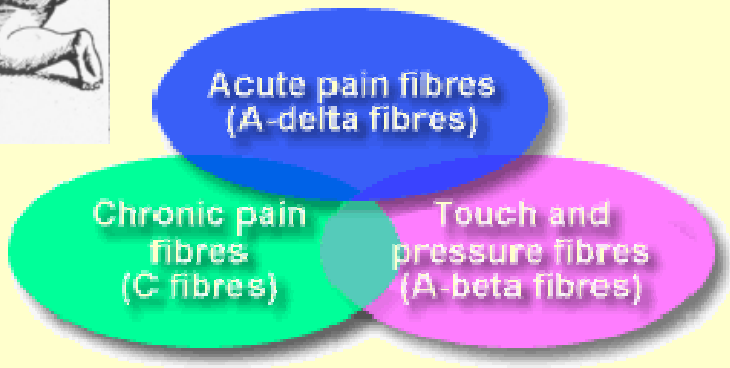
Cough/gag/regurgitate
Discomfort
Refuse food
Indecisive about food
Wake during the night
Sleep sitting or propped up
Bad Breath
Respiratory tract infections

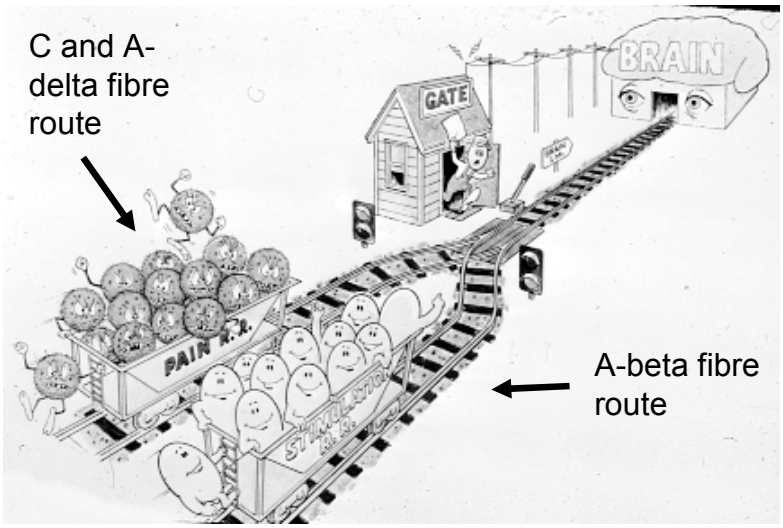


Pain gate theory

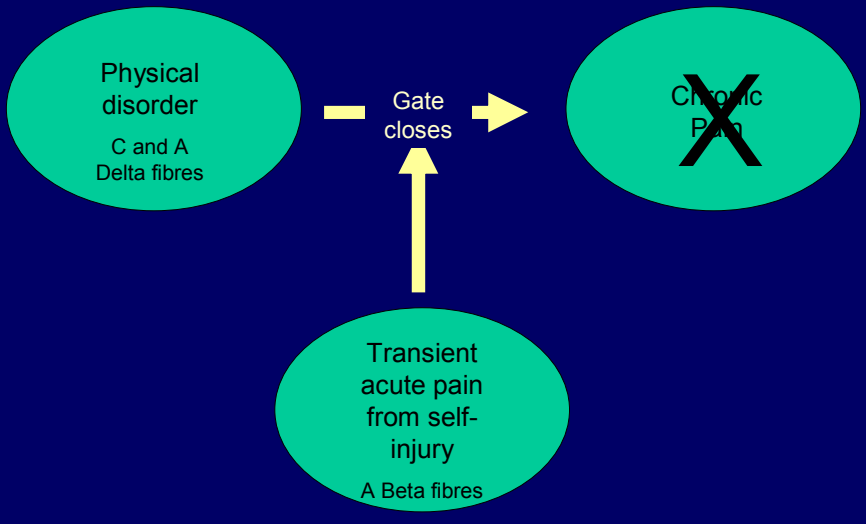
The experience of pain is influenced by many factors and there is no simple pathway from sensation to experience.

Three types of nerve fibres are important



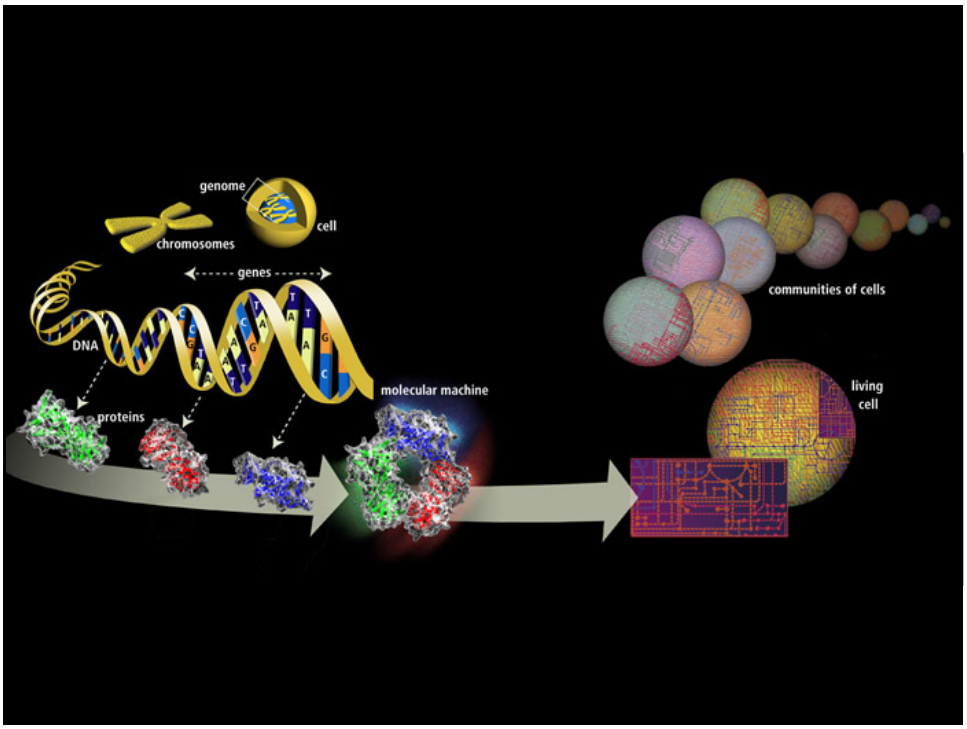


Chronic and sharp pain travel along the C fibres and A-delta fibres respectively. Messages from the fibres to the brain can be blocked by by stimulating A-beta fibres. (Rub it better!)

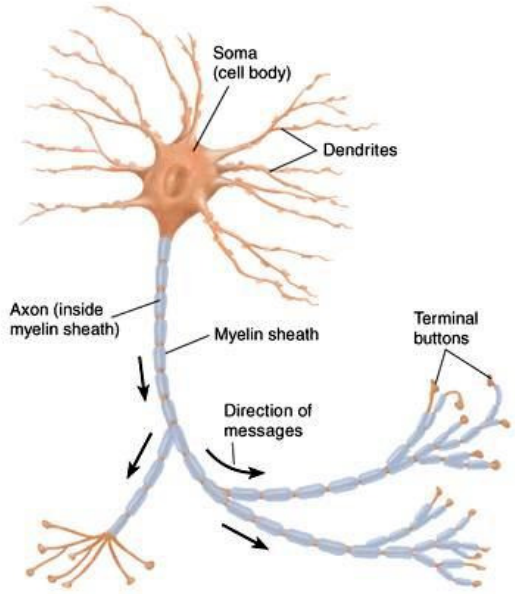


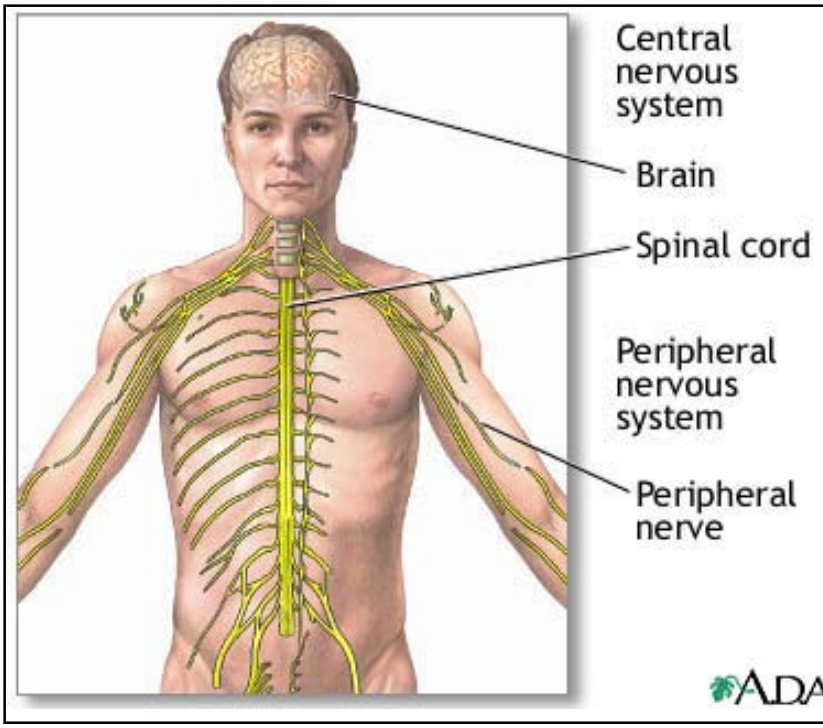
Pain gate theory and learning to self-injure

Disordered pain perception

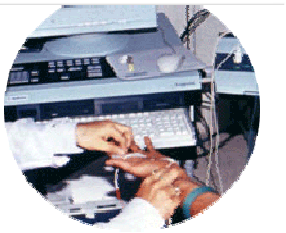


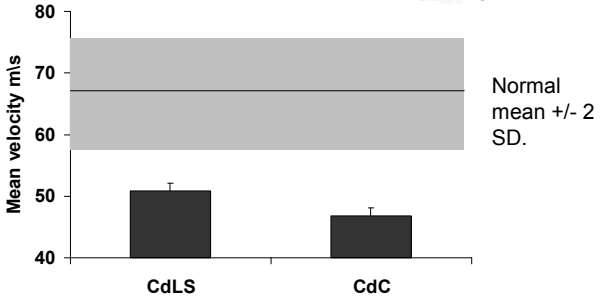
► **Multipolar Neuron**





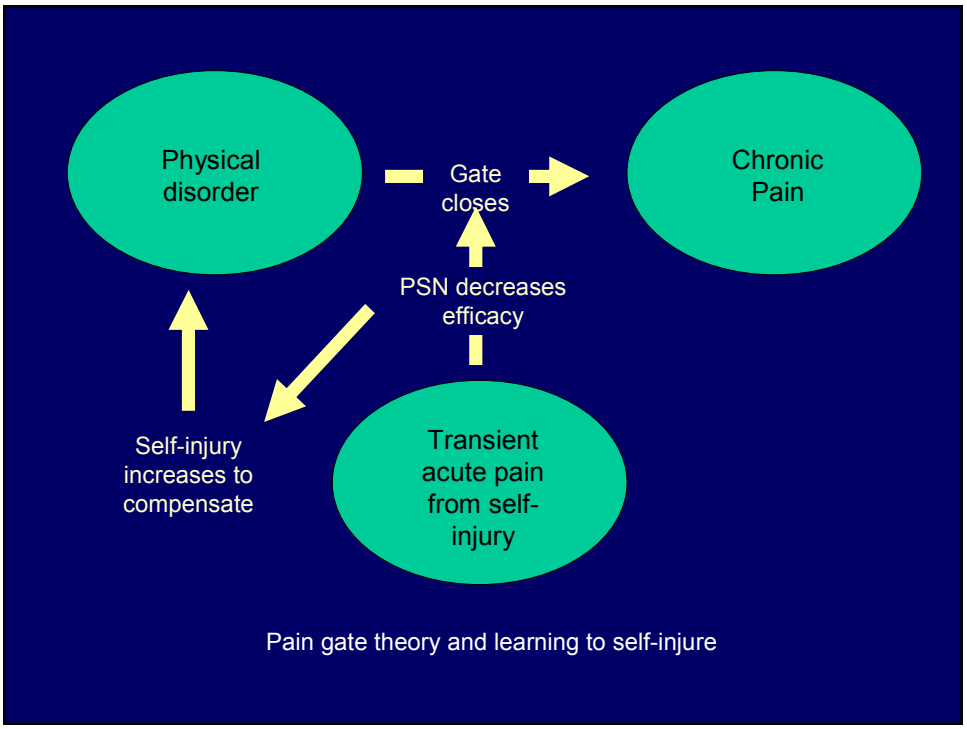
- Electrode stimulates the nerve with mild electrical impulse. Stimulus duration 0.1ms, frequency around 1Hz.
- Latency is time from the stimulus to the first positive peak of sensory nerve action potential (SNAP).
- Median (arm), medial plantar and sural (leg) nerves.
- Stable velocity at about 5 years old; median nerve mean = 67.5 m\s (SD 4.4)





Normal mean +/- 2 SD.

Wilkie, L., Oliver, C., Seri, S., Freiss, S. & Moss, J. (2005). The Role of Nerve Function in Cornelia de Lange and Cri du Chat Syndrome *Proceedings of the Greenwood Genetic Center*, **24**, 182.



Pain gate theory and learning to self-injure

The pain cycle and sel

1. Chronic or sharp pain is cau… …on or trauma
2. The child blocks the … …ing or hitting.
3. The fibres c… …al work very slowly so the ch… …s more and harder.
4. The … …s and hitting leads to tissue … …harp pain.
5. …

Early intervention and aggressive treatment

Development and Learning

- Once a behaviour has occurred a number of times it can acquire a function
- The function can be to gain pleasant sensory stimulation (spinning) or to stop unpleasant sensory stimulation (scratch-itch)
- The function can become social or communicative. The behaviour can function to 'say':
  - "Come here and pay attention to me"
  - "Give me…..! I want…!"
  - "Stop! No! I don't like that!"
- When behaviour has a social or communicative function it can get worse over time

The key issues

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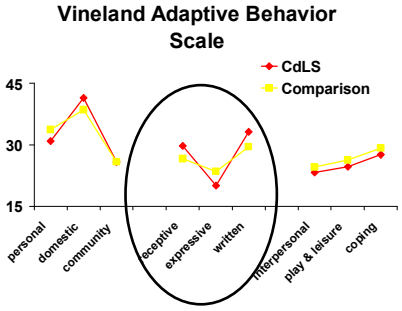
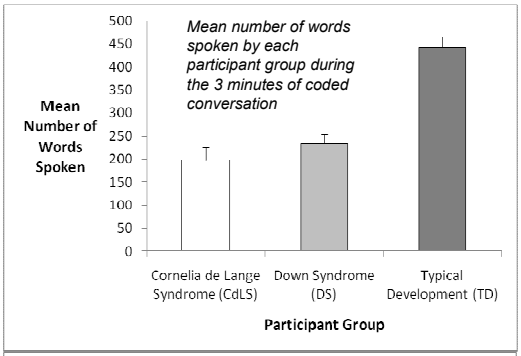
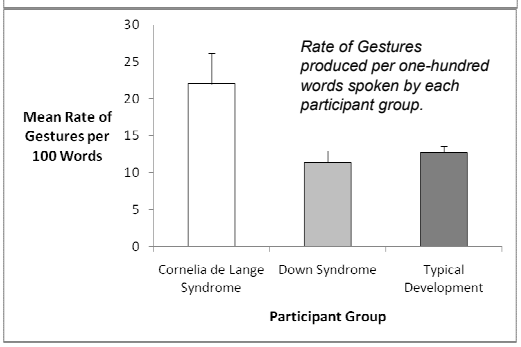
- Self-injury
- Poor expressive communication
- Autistic spectrum like behaviours
- Specific cognitive impairments
- Changes with age







Sotaro Kita and Eva Nielsen

The key issues

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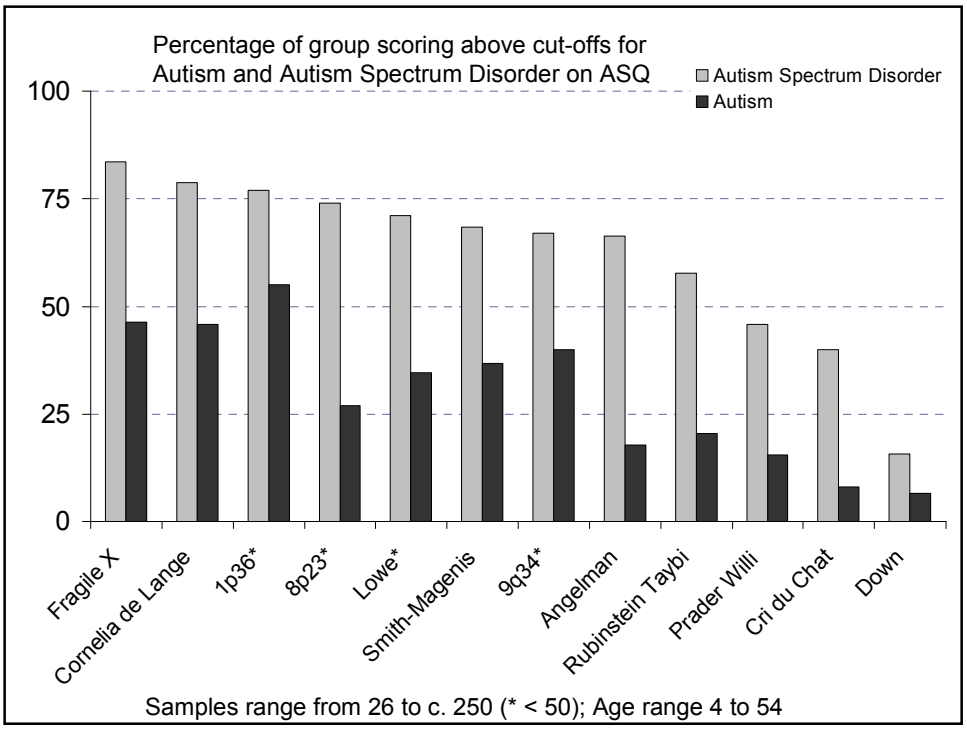
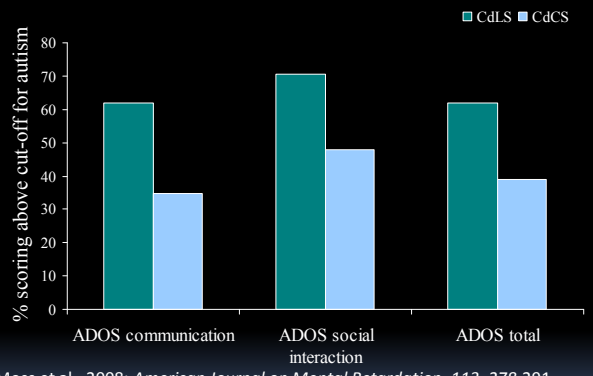


ASD in CdLS



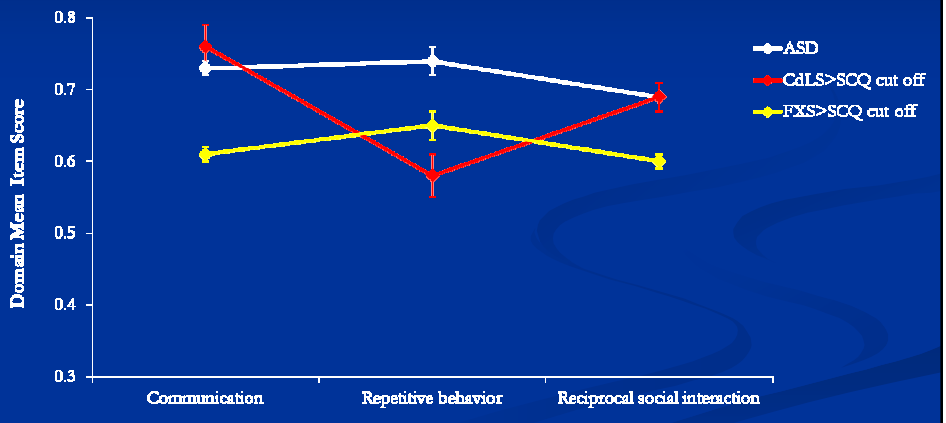
Comparative studies show that the heightened prevalence in CdLS is not solely accounted for by degree of intellectual disability .

Moss et al., 2008; *American Journal on Mental Retardation, 113, 278*-291

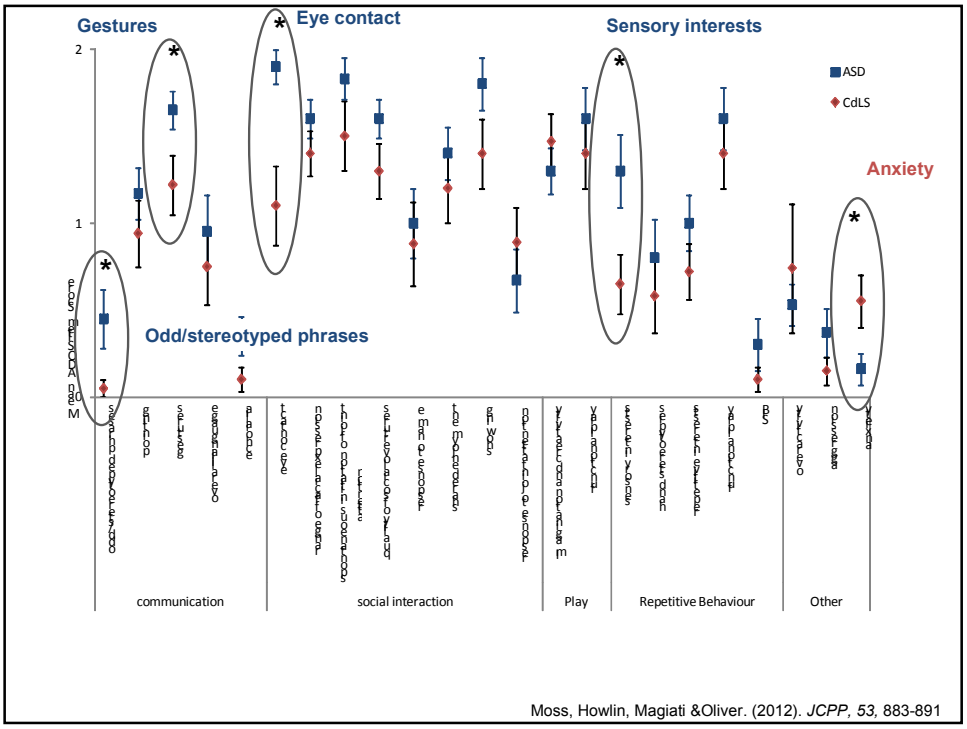
Table 3 Percentage of participants in each category of autism (as defined by the Childhood Autism Rating Scale) broken down by group

Group	Non-autistic	Mild to moderate autism	Severe autism	χ^2	*P*
Cornelia de Lange syndrome group	52.8	15.1	32.1	8.77	0.012
Comparison group	71.4	21.4	7.1		

Presentation of ASD characteristics in CdLS



Moss, Oliver, Nelson, Richards & Hall. (In press). *AJIDD*



Moss, Howlin, Magiati &Oliver. (2012). *JCPP, 53,* 883-891

Social anxiety in CdLS

- High levels of anxiety associated with social situations, particularly with unfamiliar people and unfamiliar situations.
- Motivation for social contact appears to be intact.
- Strong preference to observe rather than participate.
- Increased withdrawal when social demands become heightened.

"He can hold conversations but he is quieter when it comes to strangers".

"He is content to just sit there until he's asked a question".

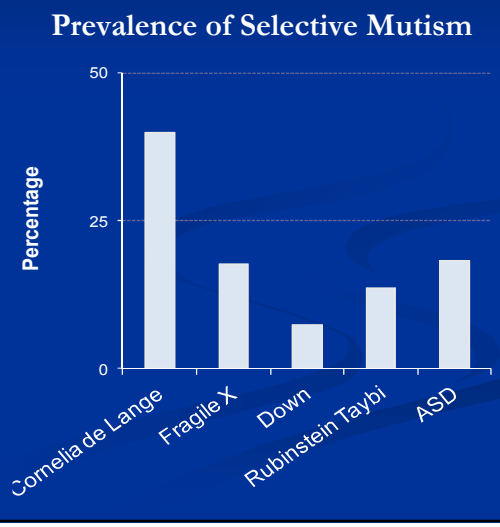
"He tells you he has no friends…it will put him in a mood for about an hour".

"When you ask him a question….it takes a bit to register….and you have got to give him time to answer ".

Moss et al., 2008. *AJMR 113,* 278-291;
Collis et al., In preparation;
Reid, Nelson , Moss & Oliver, In preparation

Signs of social anxiety in Cornelia de Lange Syndrome

- Skin picking
- Fidgeting during interaction
- Asking repetitive questions
- Avoidance/delay behaviours
- Challenging behaviours
- Selective mutism



Moss et al., 2008. *AJMR 113*, 278-291;
Collis et al., In preparation;
Reid, Nelson , Moss & Oliver, In preparation

Problems with expressive communication and anxiety (especially social anxiety)

The key issues

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- Self-injury
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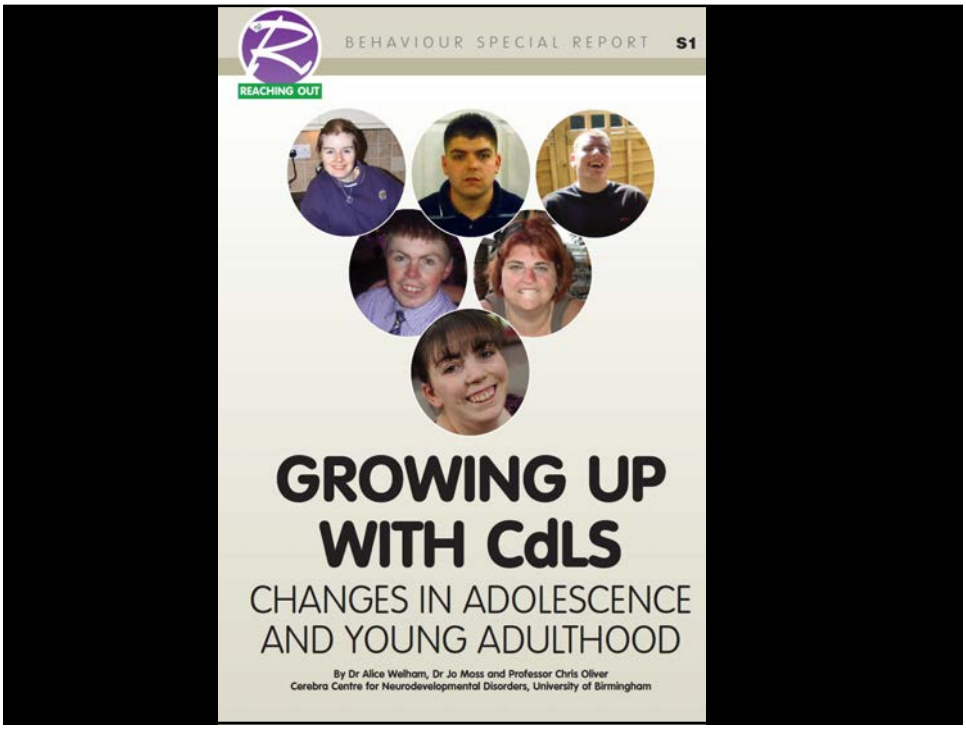
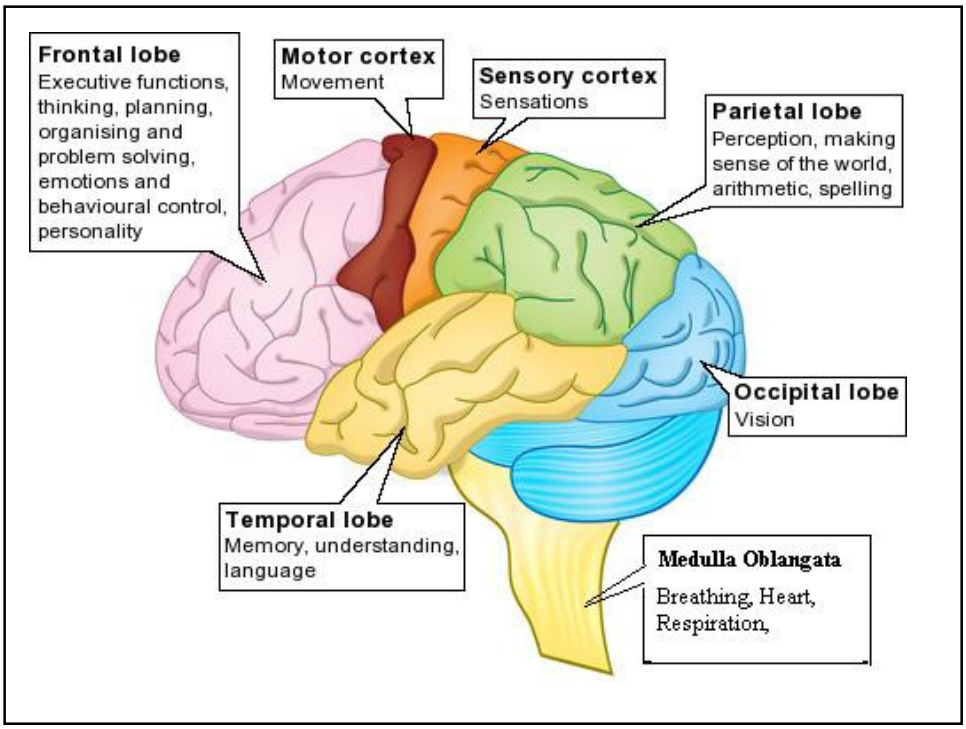
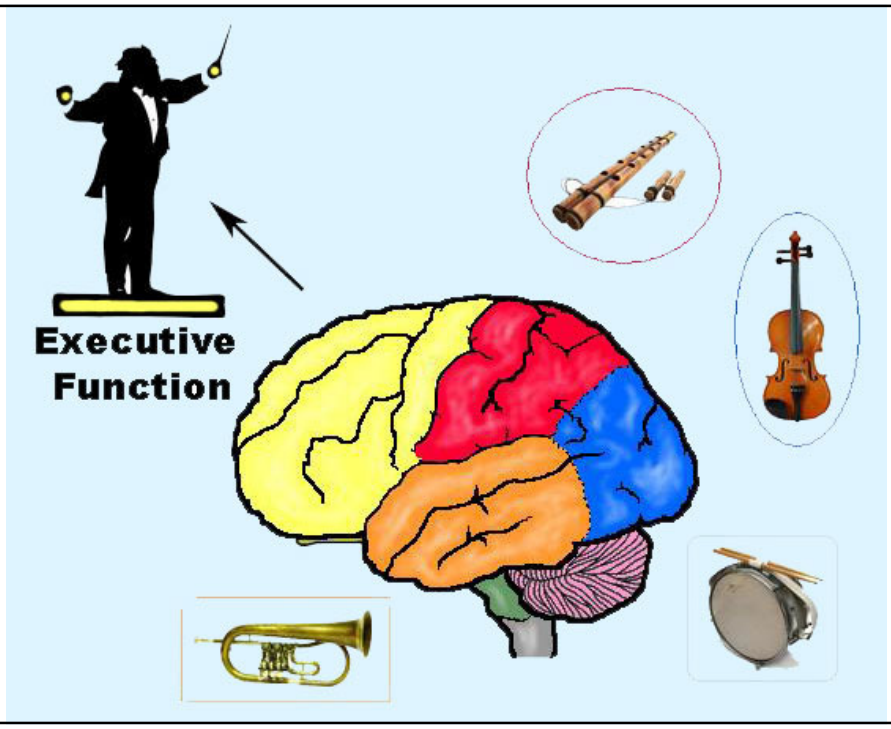
- Autistic spectrum like behaviours
- Specific cognitive impairments
- Changes with age


BEHAVIOUR SPECIAL REPORT S1
REACHING OUT
GROWING UP WITH CdLS
CHANGES IN ADOLESCENCE AND YOUNG ADULTHOOD
By Dr Alice Welham, Dr Jo Moss and Professor Chris Oliver
Cerebra Centre for Neurodevelopmental Disorders, University of Birmingham

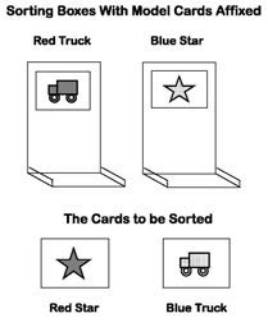

Frontal lobe
Executive functions, thinking, planning, organising and problem solving, emotions and behavioural control, personality
Motor cortex
Movement
Sensory cortex
Sensations
Parietal lobe
Perception, making sense of the world, arithmetic, spelling
Occipital lobe
Vision
Temporal lobe
Memory, understanding, language
Medulla Oblangata
Breathing, Heart, Respiration,

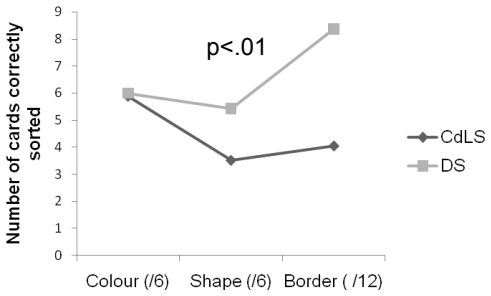


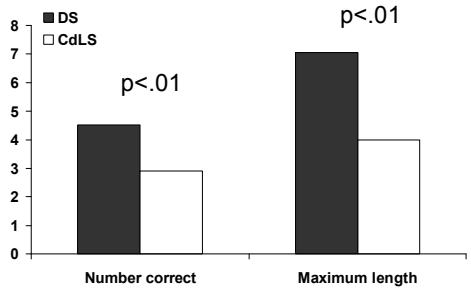
Some important differences in how the mind works

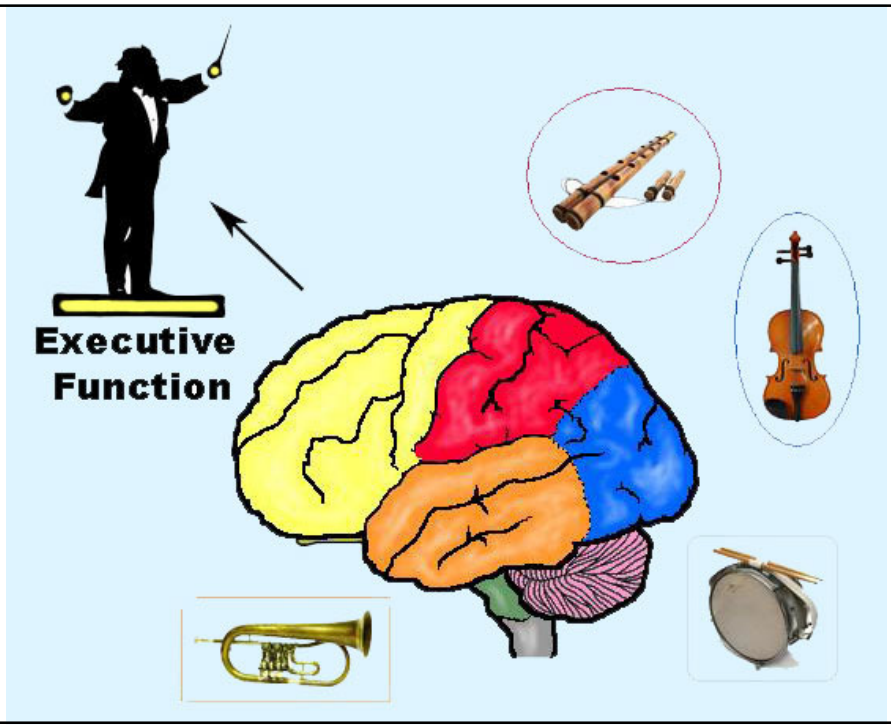
- Executive function (the manager of the mind)
  - Working memory (remember and use)
  - Inhibiting (don't do that!)
  - Shifting (attending to one thing and then moving to another)

Are there specific cognitive impairments in CdLS?







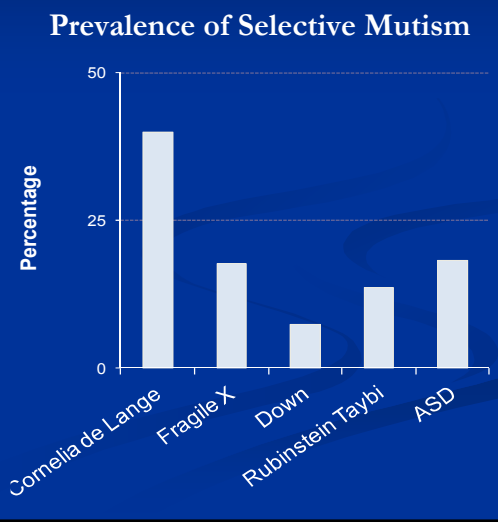


Some important differences in how the mind works

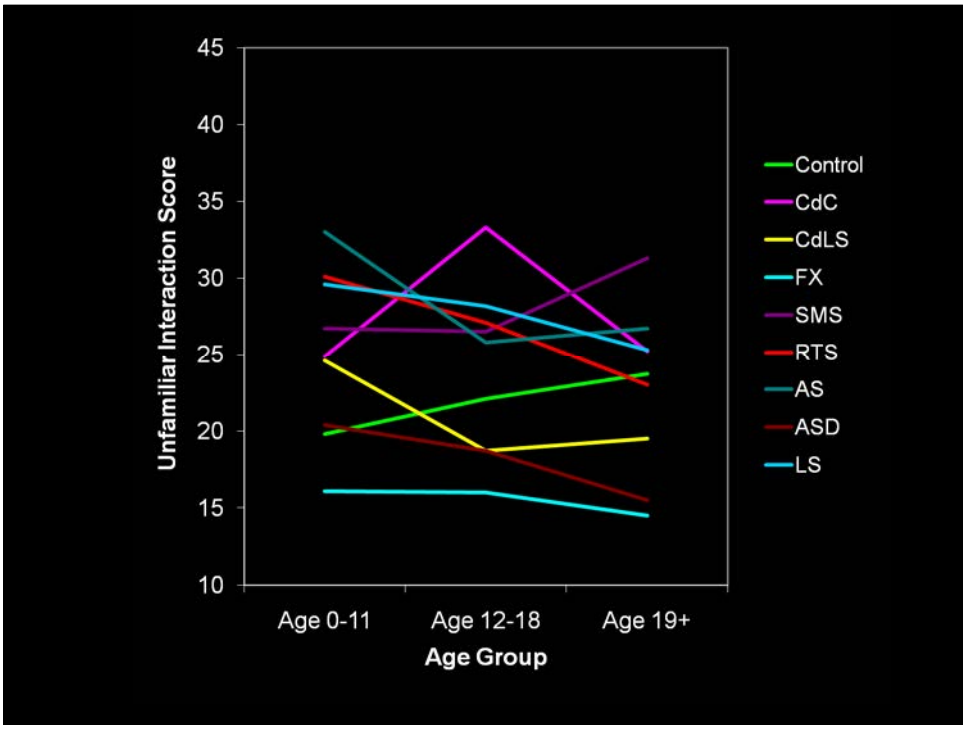
- Executive function (the manager of the mind)
  - Working memory (remember and use)
  - Inhibiting (don't do that!)
  - Shifting (attending to one thing and then moving to another)
- ..... is related to social anxiety\less speech in social interactions (see how you do when you talk to someone new!)

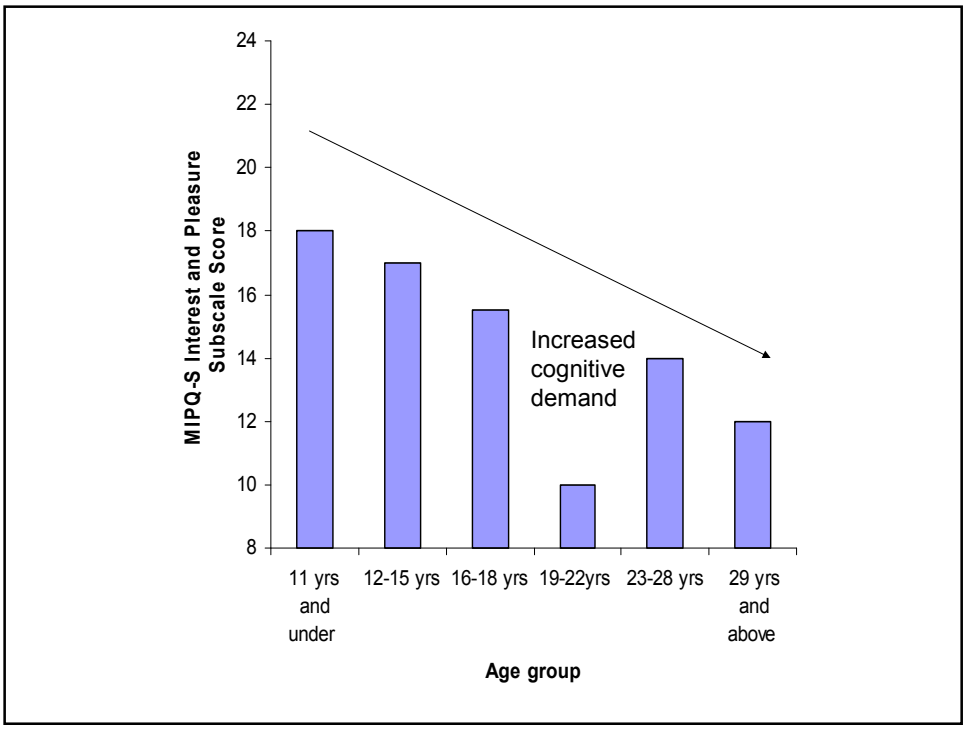
Signs of social anxiety in Cornelia de Lange Syndrome

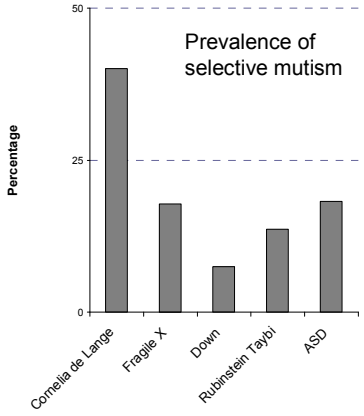
- Skin picking
- Fidgeting during interaction
- Asking repetitive questions
- Avoidance/delay behaviours
- Challenging behaviours
- Selective mutism

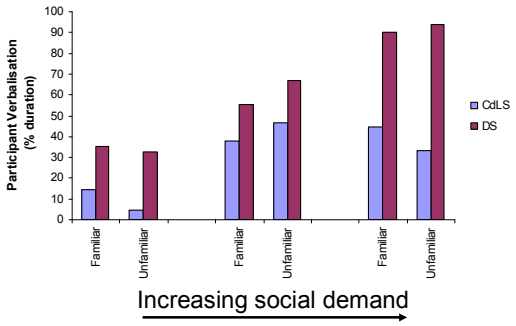


Moss et al., 2008. *AJMR 113*, 278-291;
Collis et al., In preparation;
Reid, Nelson , Moss & Oliver, In preparation


45
40
35
30
25
20
15
10
Unfamiliar Interaction Score
Age 0-11
Age 12-18
Age 19+
Age Group
Control
CdC
CdLS
FX
SMS
RTS
AS
ASD
LS


24
22
20
18
16
14
12
10
8
MIPQ-S Interest and Pleasure Subscale Score
Increased cognitive demand
11 yrs and under
12-15 yrs
16-18 yrs
19-22yrs
23-28 yrs
29 yrs and above
Age group



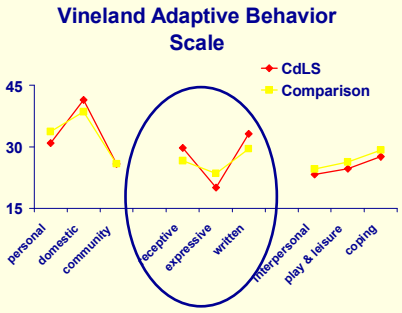


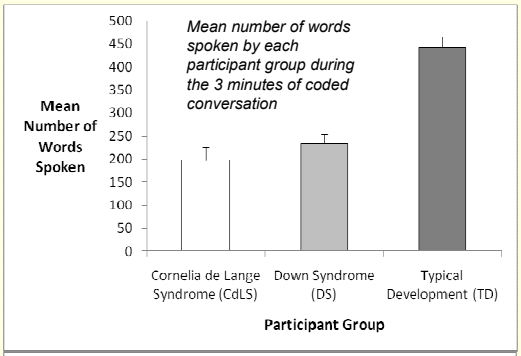
	Inhibit subscale	Shift subscale	Emotional control subscale	Working memory subscale	Plan/Organise subscale
Cornelia de Lange Syndrome	-.41*	-.26	-.31	-.57**	-.62**
Down syndrome	-.24	.07	-.12	.10	-.07

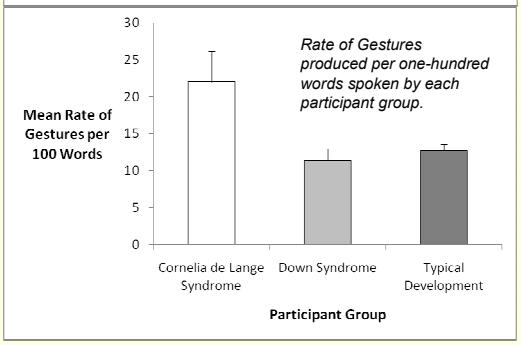
Correlations between participant speech and executive function

No problem with word finding, grammar, vocabulary, content of speech.

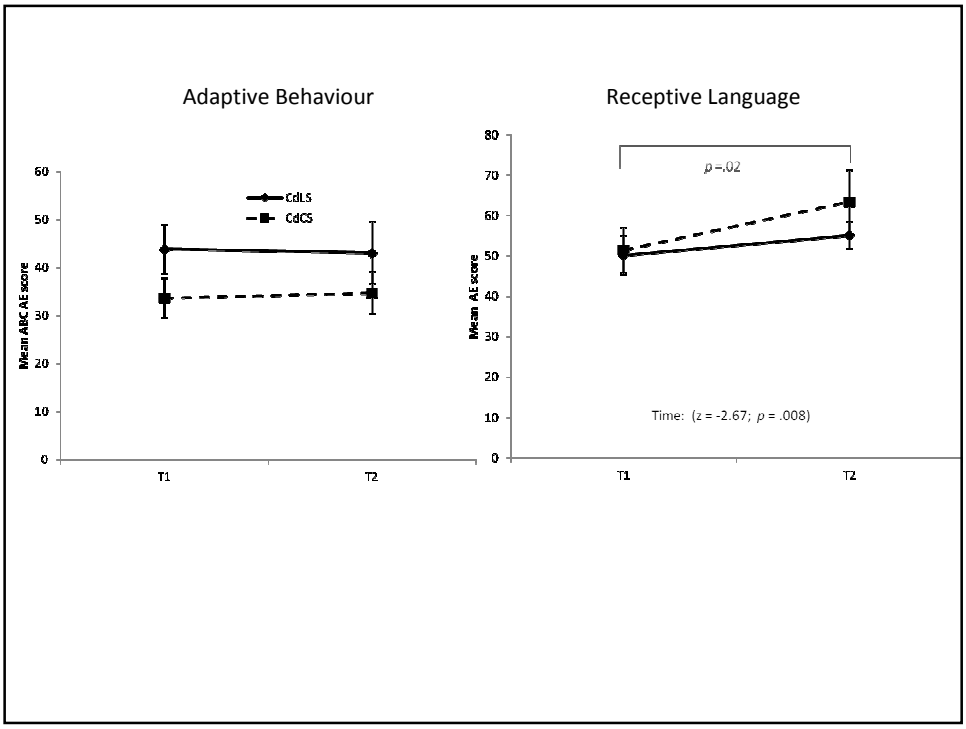
Significantly more pauses and blocks

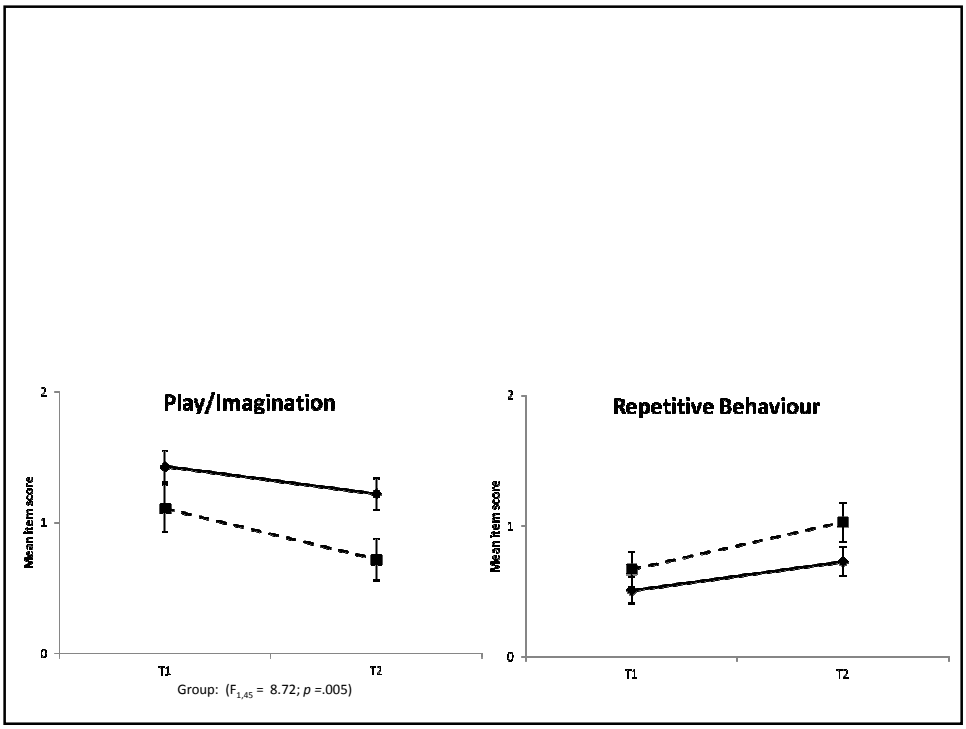


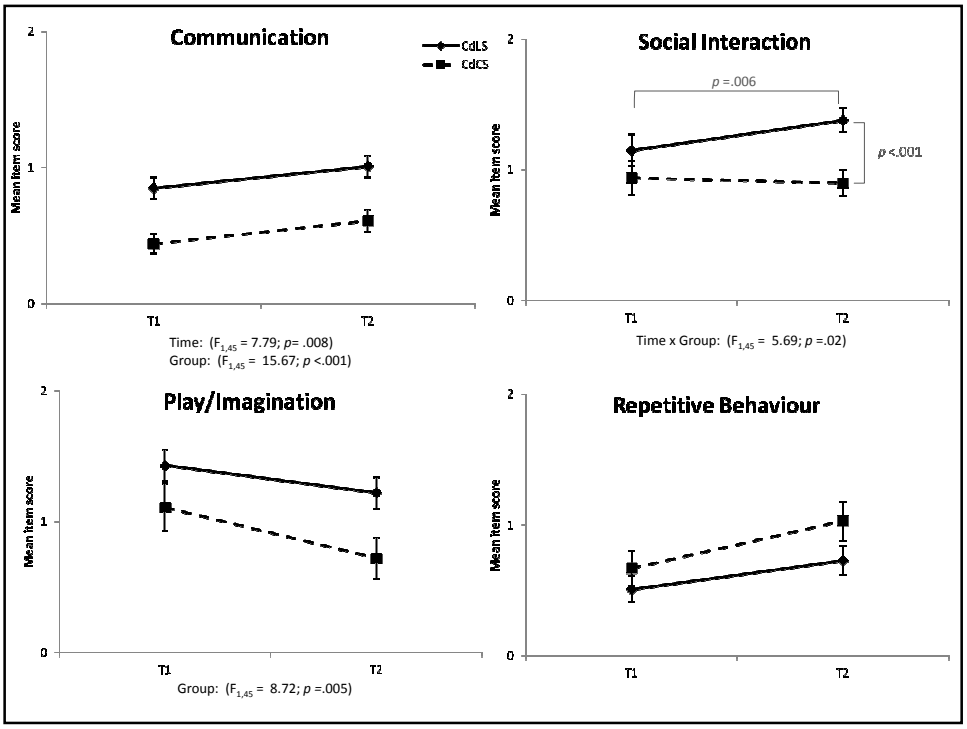




Sotaro Kita and Eva Nielsen


Adaptive Behaviour
Receptive Language
CdLS
CdCS
Mean ABC AE score
Mean AE score
p =.02
Time: (z = -2.67; p = .008)
T1
T2


Play/Imagination
Repetitive Behaviour
Mean item score
T1
T2
Group: ($F_{1,45}$ = 8.72; p =.005)



The take home messages

- Health and pain
  - Know
  - Act
  - Advocate
- Early hearing problems and speech
- Autism Spectrum Disorder
  - Does the diagnosis help me and my child
- Thinking differently
  - Predictability and routine (softly, softly)
  - Imbalance in ability
  - Support for what if's
- The future
  - Planning for change

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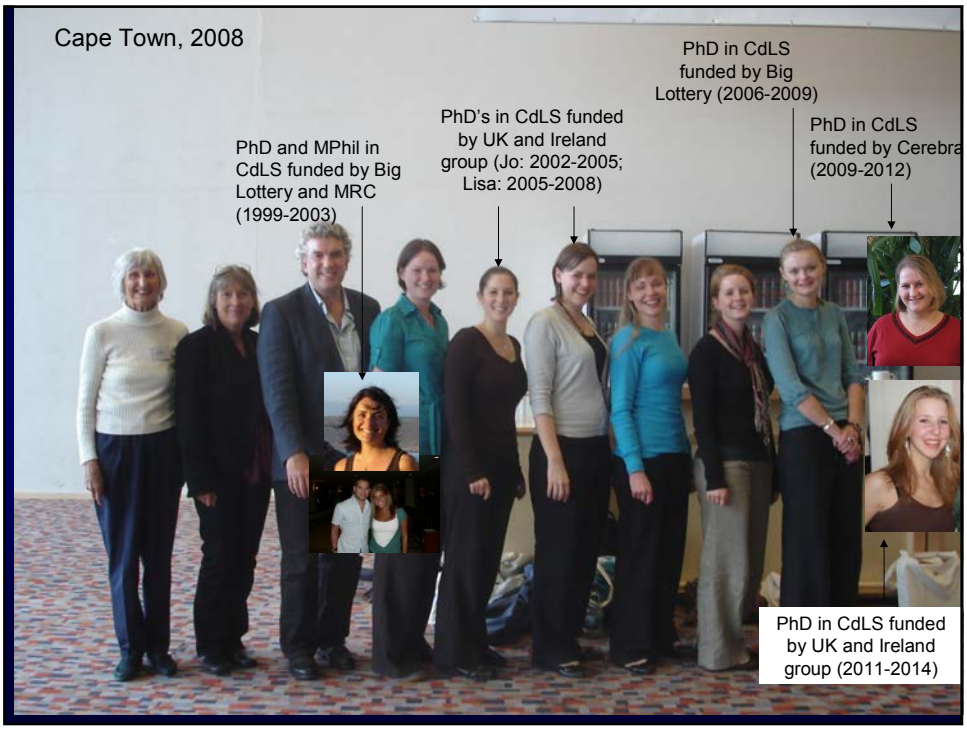

The Cerebra Centre for Neurodevelopmental Disorders

Cerebra
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Core Funding

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Birmingham Children's Hospital
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Newlife
National Autistic Society
ESRC
Tuberous Sclerosis Alliance

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