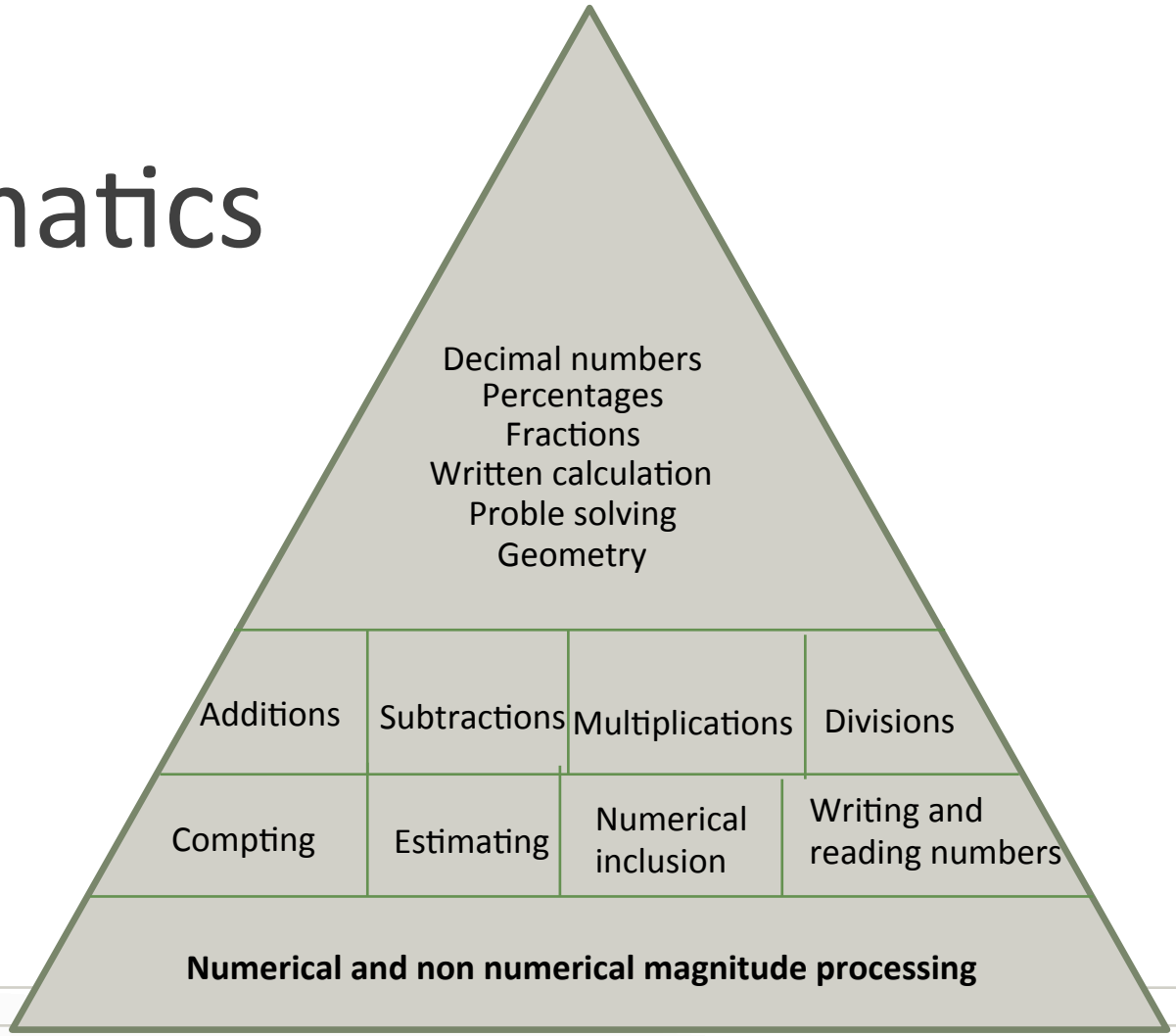
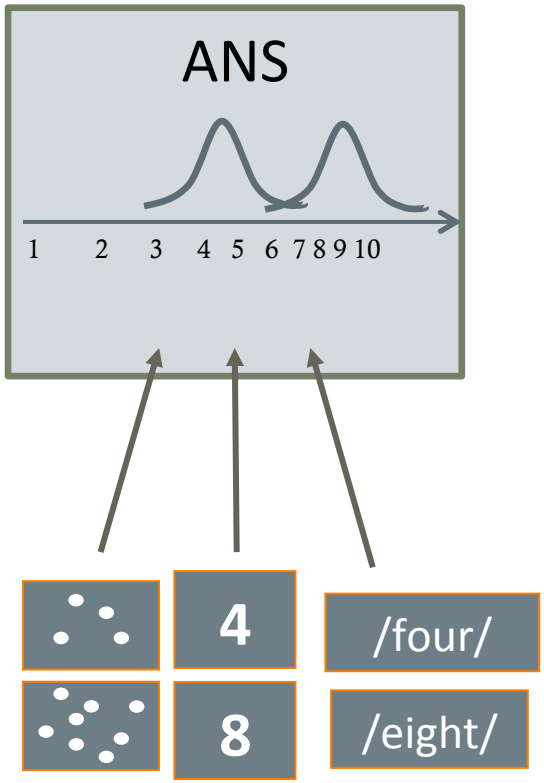
Basic numerical processing in genetic syndromes: The role of visuo-spatial processing and working memory.

Laurence Rousselle
Lucie Attout
Line Vossius
Marie-Pascale Noël

Mathematics



Basic numerical processing



1. Approximate Number System

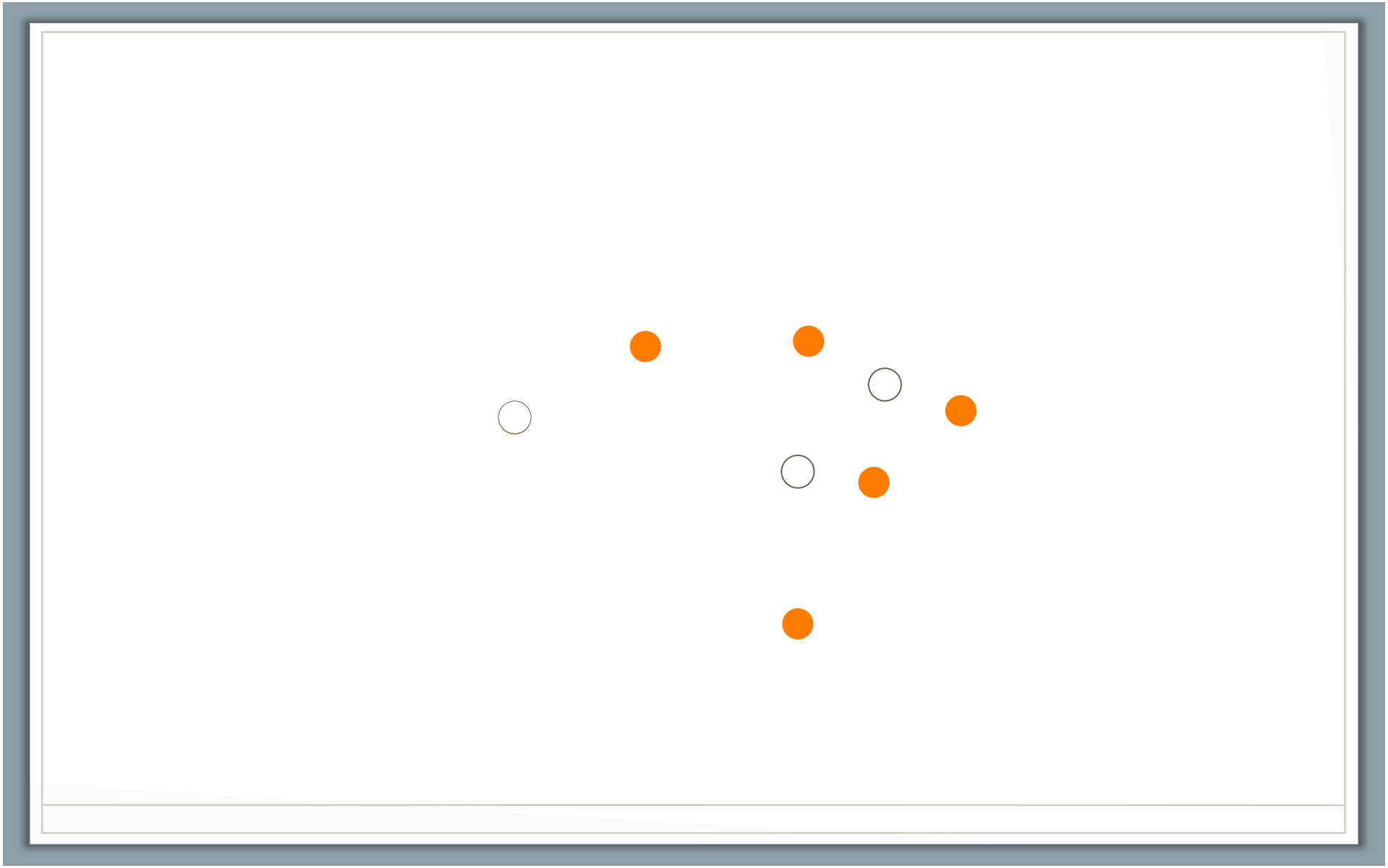
≅ Early sensitivity to numerosities

- Approximate : increasing imprecision with numerosity
- Innate/precocious : Independent of learning : babies could discriminate numerosities
- Basis of subsequent learning :
  - Connection with verbal number words
  - Connection with arabic numbers

Basic numerical processing

2. Object-file mecanism : pre-attentional process for keeping track of the location of about 4 stimuli in parallel, without serial displacement of attention

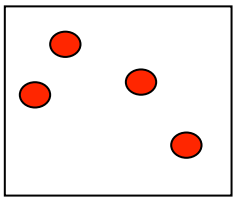
- Subitizing



Basic numerical processing

2. Object-file mecanism : pre-attentional process for keeping track of the location of about 4 stimuli in parallel, without serial displacement of attention

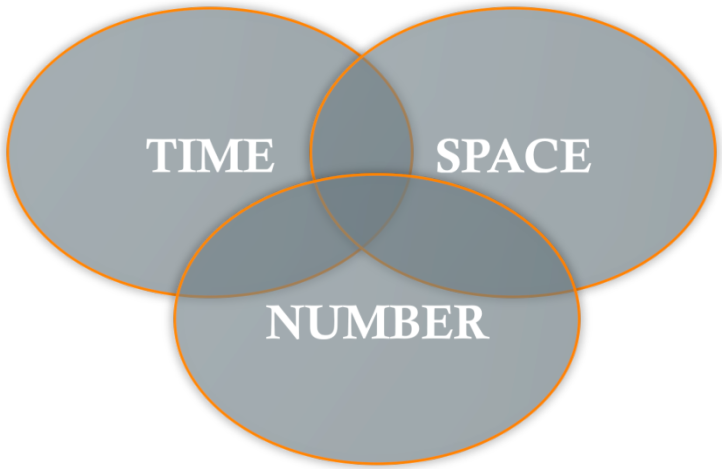
- Subitizing
- Fast and precise
- Innate/precocious : Independent of learning
- Basis of the learning of number word cardinal meaning in young children



[four]

A central magnitude system

Walsh (2003) :



Simon (2008, 22q11 deletion syndrome) : Spatiotemporal processing form the basis of numerical and mathematical competence: Spatiotemporal processing deficit create "*suboptimal foundation for the subsequent development of numerical and mathematical competence, thereby ''cascading'' impairments into those more academic domains*"

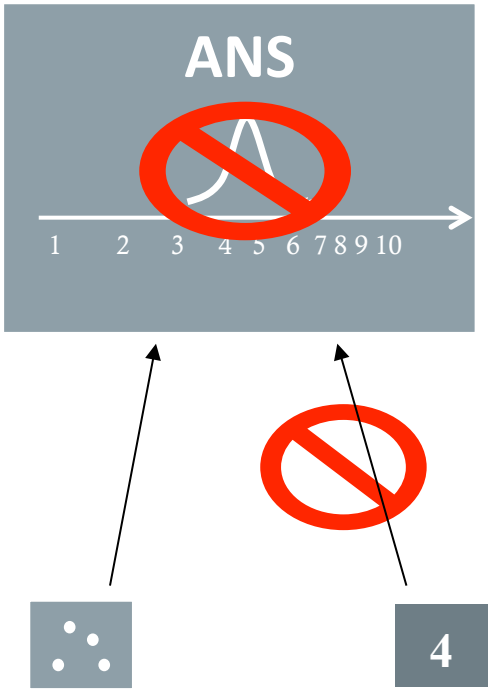
Mathematic learning disabilities

- Specific developmental disorder occuring in children with IQ in the normal range
- Difficulty in
  - learning or comprehending arithmetic
  - in understanding and manipulating numbers
  - and learning arithmetic facts (3x4, 2+3)
- Frequent co-morbidities with reading learning disorders and ADHD
- Multi-determined learning disorder

Mathematic learning disabilities

Functional origins of MLD?

- Non numerical factors:
  - working memory (calculation and arithmetic fact)
  - sensitivity to interference (arithmetic fact)
  - finger agnosia (calculation and learning arithmetic fact)
- Numerical factors:
  - Basic inability to represent quantities (number sense)
  - Basic impairment of the ability to connect symbolic numbers to their meaning



Genetic influences

- Familly studies (including 1 child with poor math competence) : Higher prevalence of poor math competence in father, mother and siblings (Shalev et al., 2001)

- Twin studies : Concordance rate of math learning disability reach 58% in monozygotic twins and 39% in dizygotic twins (Light & Defries, 1995)

- Higher prevalence of MLD in patients with Turner, X-Fragile, Williams or 22Q11 deletion syndrome.

Ex : 42-79 % prevalence of MLD in girls with Turner

➡ **interindividual ≠ in math partially accounted for by the genotype**

Mathematical development in genetic syndromes

- Genetic syndromes ….Why?
  - Better understand genotype-phenotype relationships
  - Opportunity to track early the origin of their math learning disorders
  - ➡ Model of Mathematics learning difficulties (MLD):
    - Distinguishing different trajectories leading to MLD
    - Examing how their particular cognitive profile can contribute to number processing difficulties (working memory impairment, visuo-spatial disorders)

Cross syndrome studies

- Three genetic syndromes
  - ➡ Turner, 22q11.2 and Williams
- Associated with MLD
- Divergent IQ
- Similar cognitive profile

Overall description

Turner	22q11.2	Williams
Deletion of one of the two X chromosome X : Complete (45X0), Partial (45X∧), Mosaïc (45X0/46XX)	Deletion of 30 à 40 genes on the long arm (q) of the chromosome 22, region 11.2	Deletion of 20 à 30 genes on the long arm (q) of the chromosome 7, region 11.23
1 : 1900 à 4500	1 : 4000 à 6000	1 : 7500
IQ : in the average range	IQ~70:[average IQ-moderate intellectual disability]	QI~60:[limited to severe intellectual disability
	➥ most: IQ limited to –mild intellectual disability	➥ Most: mild intellectual disability
Verbal IQ > non verbal IQ	Verbal IQ > non verbal IQ	Verbal IQ > non verbal IQ

Cognitive phenotype

Turner	22q11.2	Williams
➡ visuo-spatial impairments	➡ visuo-spatial impairments	➡ visuo-spatial impairments
➡ Working memory : ▪ Verbal component OK ▪ VSSP component : inconsistent ▪ Executive component : KO	➡ Working memory : ▪ Verbal component OK ▪ VSSP component : KO ▪ Executive component : KO	➡ Working memory : ▪ Verbal component relatively preserved ▪ VSSP component : KO ▪ Executive component : KO
➡ Executive control impairment : inhibition, switching, planification	➡ Executive control restriction: inhibition and switching	➡ Executive control impairment

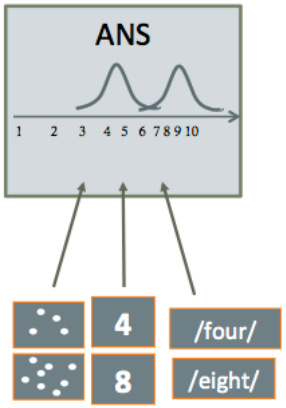
Mathematics

Turner	22q11.2	Williams
Calculation procedures **KO**	Calculation procedures **KO**	Restriction +++ of math learning
Arithmetic facts quite preserved	Arithmetic facts OK	Calculation procedure **KO**
		some arithmetic facts could be stored in memory
Number processing OK	Number processing OK	Number processing: Reading single digit OK but two digits KO < S. Down
Symbolic number magnitude (digit comparison) : inconsistent results	Symbolic number magnitude **KO** (digit comparison)	Symbolic number magnitude **KO** (digit comparison)

What about the origins?

- Up to now : Information about the *nature* of the difficulties experienced quite late in the development
- But no information about the *origins* of these difficulties, about basic numerical processing (= foundation of math competence)

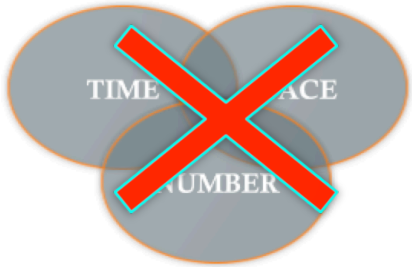
Magnitude representation
Subitizing



Basic numerical processing

	Turner	22q11.2	Williams
Non numerical magnitudes	KO (no control for IQ)	KO (no control for IQ)	No data
Non symbolic number magnitudes	No data	No data	KO
Quantités numériques symboliques	Contradictory results	KO	KO
Subitizing	KO (no control for IQ)	OK	OK

Hypothesis : Basic deficit of magnitude representation



Basic numerical processing in genetic syndromes

Premature conclusion…

→ Only tested with visual stimuli, some of them requiring to process their spatial position

But, all have visuo-spatial processing impairment

- How do they process numerical and non numerical magnitudes in tasks with no visuo-spatial processing requirement?
- What is the impact of their cognitive profile (visuo-spatial and working memory deficit) on their ability to process magnitude?

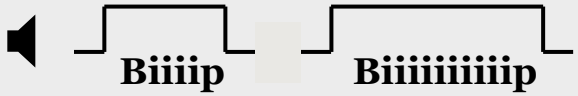
Participants

Turner	22q11.2	Williams
• 20 patients with TS (mean CA: 18 [7-33 y-o])	• 27 patients with 22q11DS (mean CA : 10;7 [5-23 y-o])	• 21 patients with WS (mean CA : 22;1 [5-52 y-o])
• 20 typically developping children and adults matched on chronological age (mean CA : 18 [7-34 y-o])	• 27 typically developping children matched on verbal mental age (mean CA: 7;10 [3-13 y-o])	• 21 typically developping children matched on verbal mental age (mean CA: 7;6 [4-11 y-o])
	• 27 typically developping children matched on visuo-spatial abilities (mean CA: 7;2 [3-12 y-o])	• 21 typically developping children matched on visuo-spatial abilities (mean CA: 6;1 [3-10 y-o])

Tasks

Contrasting magnitude comparison tasks with different visuo-spatial and working memory processing requirements

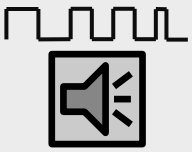
Non numerical magnitudes

Visual	Auditive
« the longest stick ?»	« the longest sounds ?»
	

Tasks

Contrasting magnitude comparison tasks with different visuo-spatial and working memory processing requirements

Numerical magnitudes

Visuo-Spatial ++	Visuo-spatial - -	Auditive
« who has more pieces of puzzle?»	«Who flashed more »	« Who buzzed more ?»
		

Stimuli

Table 1. Pairs of Magnitudes Presented in the Numerical and Non-Numerical Comparison Tasks.

	Ratios					
	1/2	**2/3**	**3/4**	**5/6**	**7/8**	**8/9**
Numerosities	7–14	6–9	6–8	5–6	7–8	8–9
	8–16	10–15	12–16	10–12	14–16	16–18
Lengths[a]	70–140	60–90	60–80	50–60	70–80	80–90
	80–160	100–150	120–160	100–120	140–160	160–180
Durations[b]	525–1050	450–675	450–600	375–450	525–600	600–675
	600–1200	750–1125	900–1200	750–900	1050–1200	1200–1350

Weber fraction :

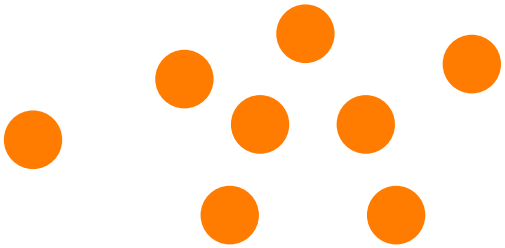
- Measure < from psychophysics to determine the smallest perceptual difference that could be perceived > acuity
- index of **numerical acuity**

Tasks

Contrasting magnitude comparison tasks with different visuo-spatial and working memory processing requirements

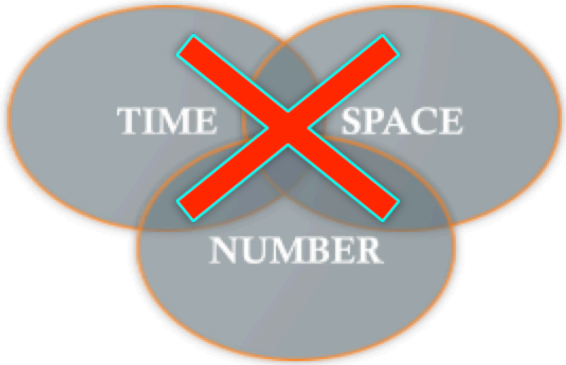
Subitizing task

200 ms



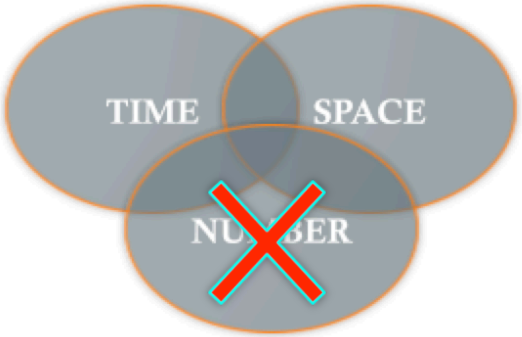
Predictions :
Global magnitude deficit

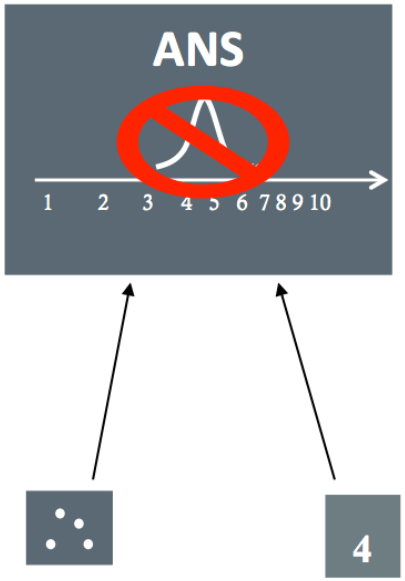
- All tasks impaired except subitizing
  - Length
  - Duration
  - Collection
  - Sequences of dots and sounds



Predictions:
Approximate Number System

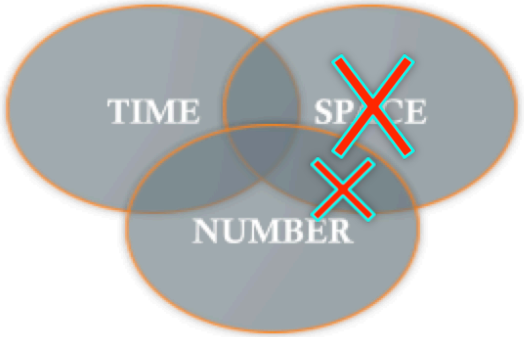
- Deficit in non symbolic numerical comparison tasks
  - Collection
  - Sequence of dots
  - Sequence of sounds





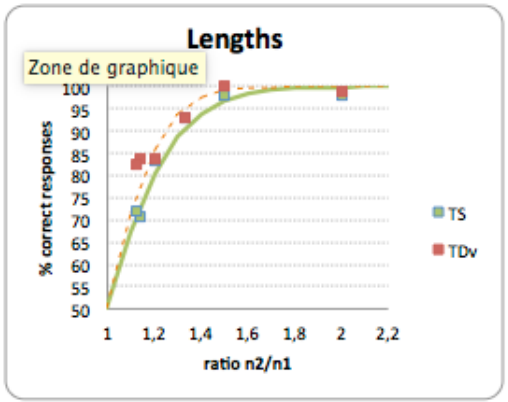
Predictions:
Non numerical factors

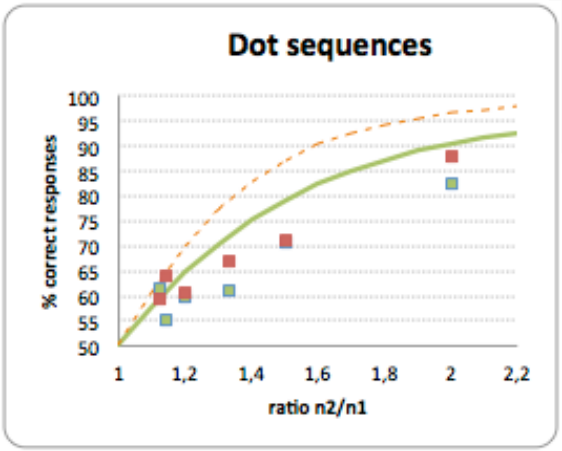
- Impact of visuo-spatial deficit
  - Lengths
  - Collections

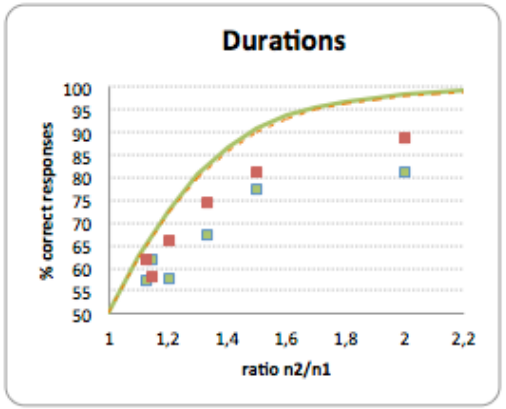


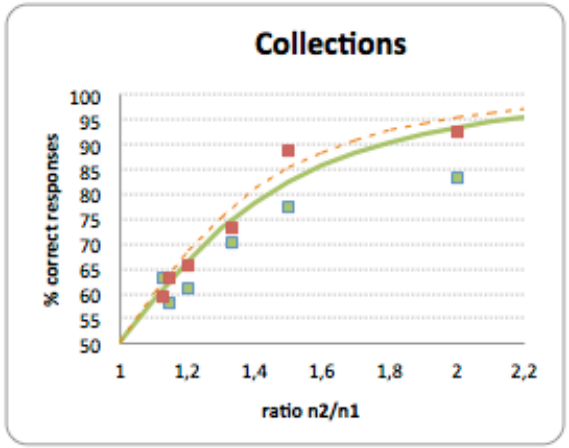
- Impact of working memory impairment
  - Sequence of dots
  - Sequence of sounds

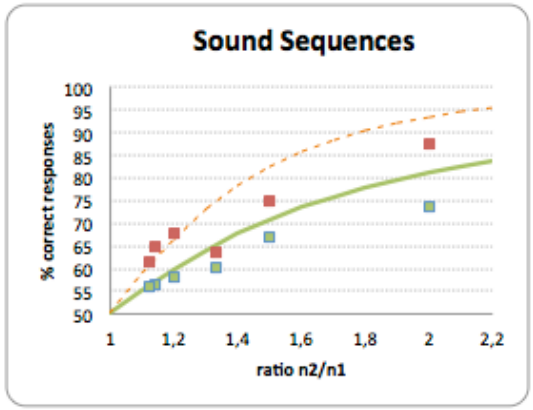
Turner


Lengths
Zone de graphique
% correct responses
ratio n2/n1
TS
TDv


Dot sequences
% correct responses
ratio n2/n1


Durations
% correct responses
ratio n2/n1


Collections
% correct responses
ratio n2/n1


Sound Sequences
% correct responses
ratio n2/n1

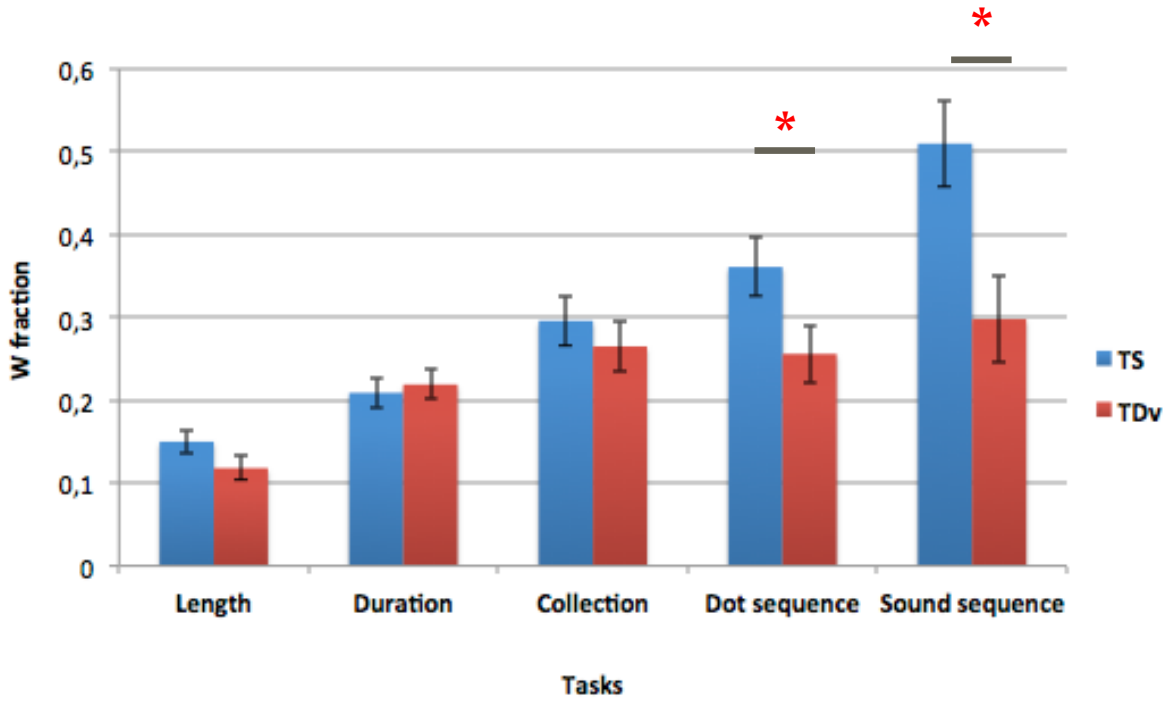
Turner

PLOS ONE

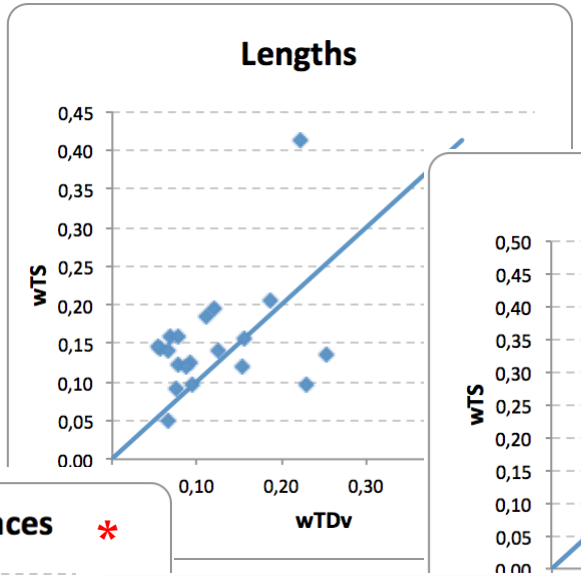
RESEARCH ARTICLE

The role of short-term memory and visuo-spatial skills in numerical magnitude processing: Evidence from Turner syndrome

Lucie Attout[1,2]*, Marie-Pascale Noël[1], Marie-Cécile Nassogne[3], Laurence Rousselle[2]



Turner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0,35
0,30
0,25
0,20
0,15
0,10
0,05
0,00
wTS
0,10
0,20
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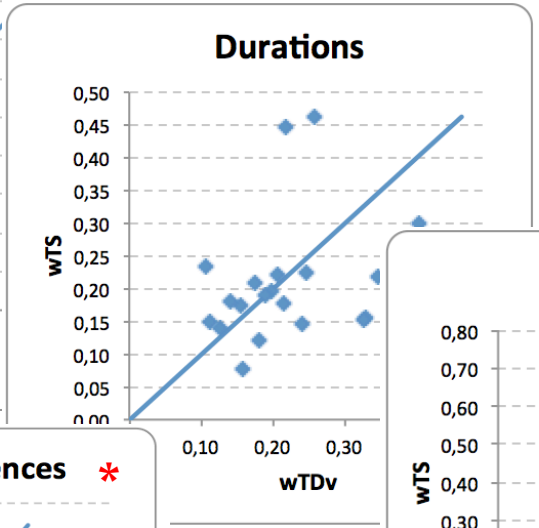
wTDv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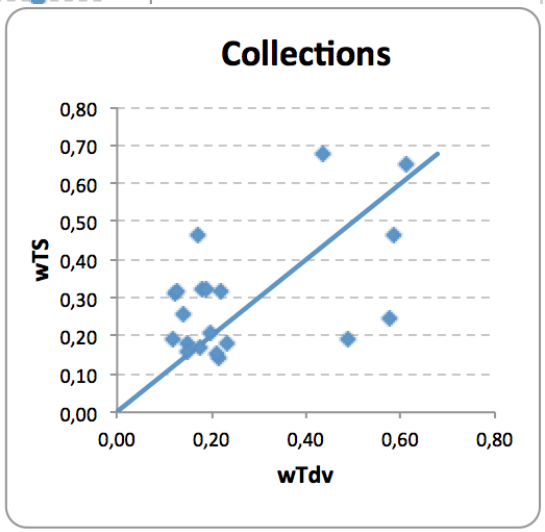
wTDv


Collections
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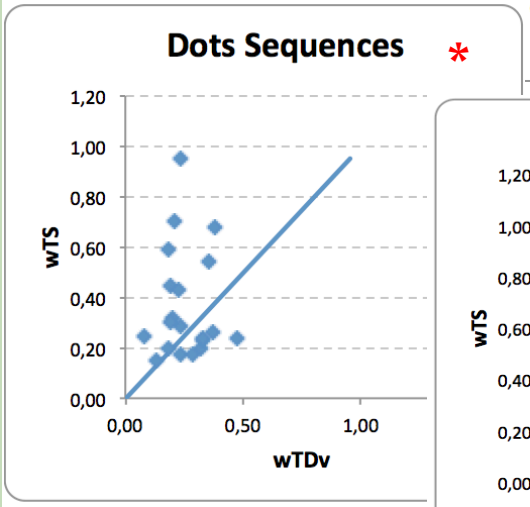
0,00
wTS
0,00
0,20
0,40
0,60
0,80
wTdv


Dots Sequences *
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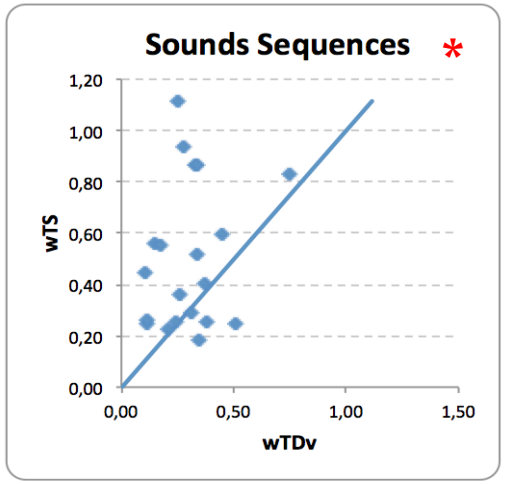
0,00
wTS
0,00
0,50
1,00
wTDv


Sounds Sequences *
1,20
1,00
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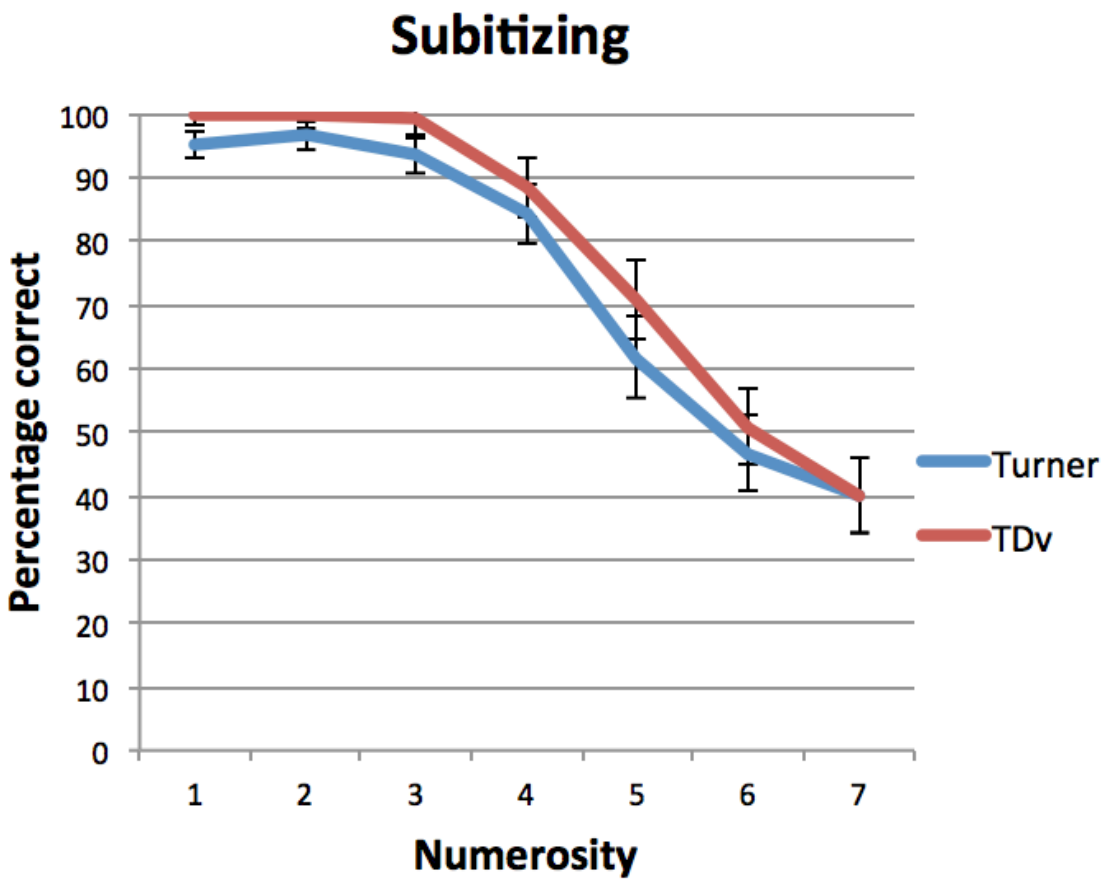
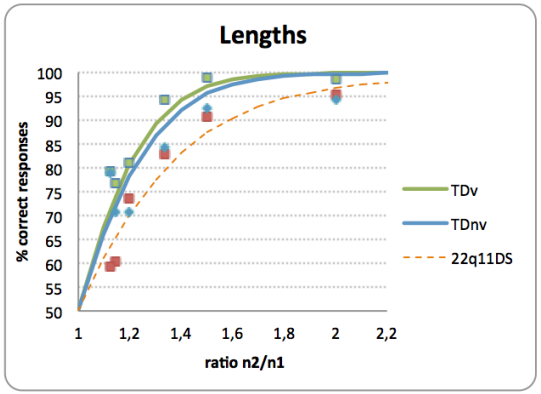
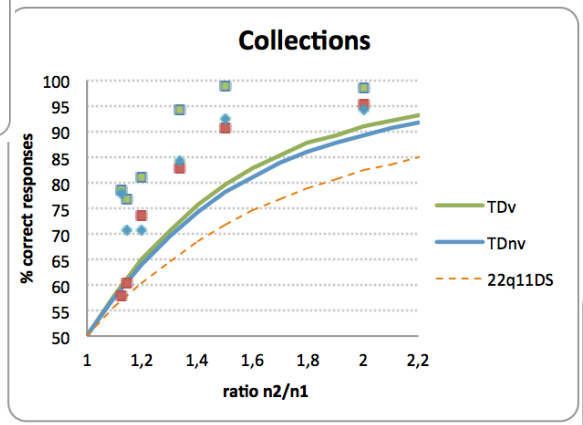
0,20
0,00
wTS
0,00
0,50
1,00
1,50
wTDv

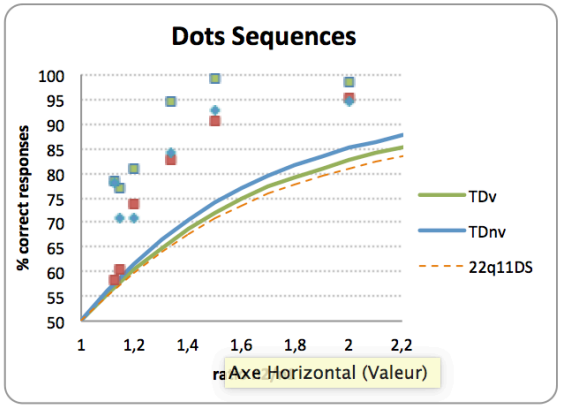
Turner

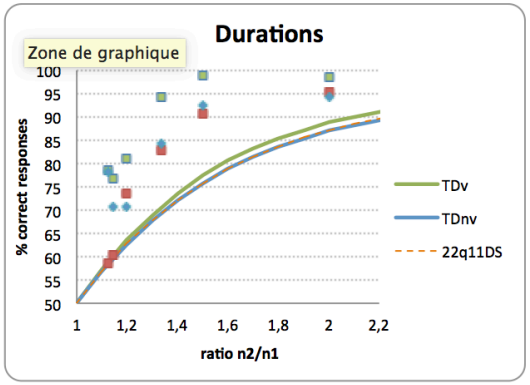

Subitizing
Percentage correct
100
90
80
70
60
50
40
30
20
10
0
1
2
3
4
5
6
7
Numerosity
Turner
TDv

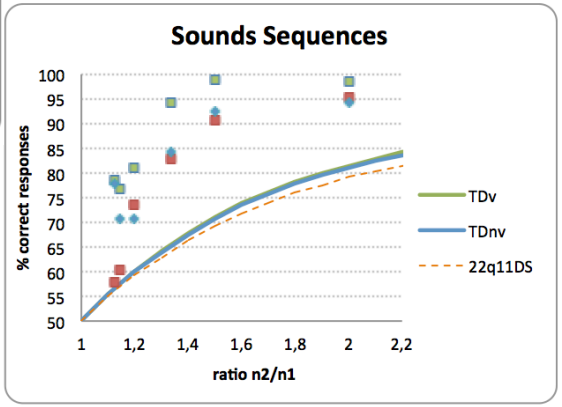
22q11DS


Lengths
% correct responses
ratio n2/n1
TDv
TDnv
22q11DS


Collections
% correct responses
ratio n2/n1
TDv
TDnv
22q11DS


Dots Sequences
% correct responses
TDv
TDnv
22q11DS
Axe Horizontal (Valeur)


Durations
Zone de graphique
% correct responses
ratio n2/n1
TDv
TDnv
22q11DS


Sounds Sequences
% correct responses
ratio n2/n1
TDv
TDnv
22q11DS

22q11 DS

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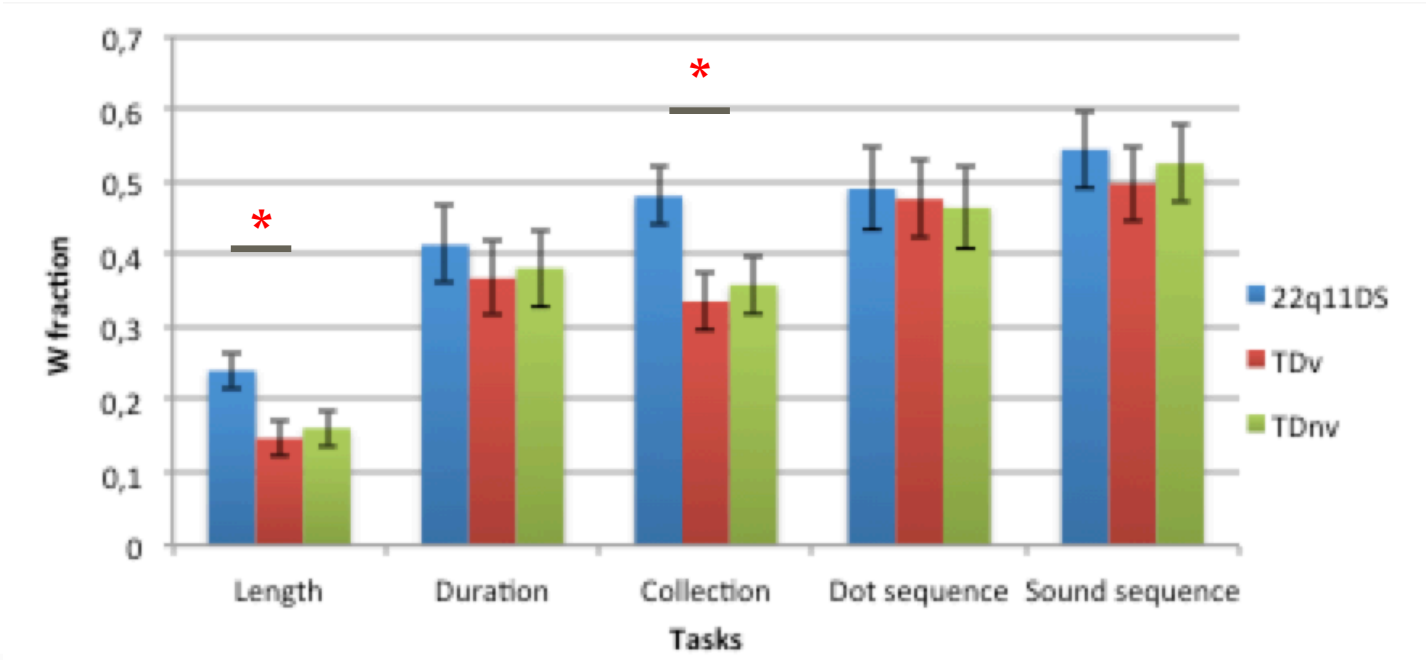
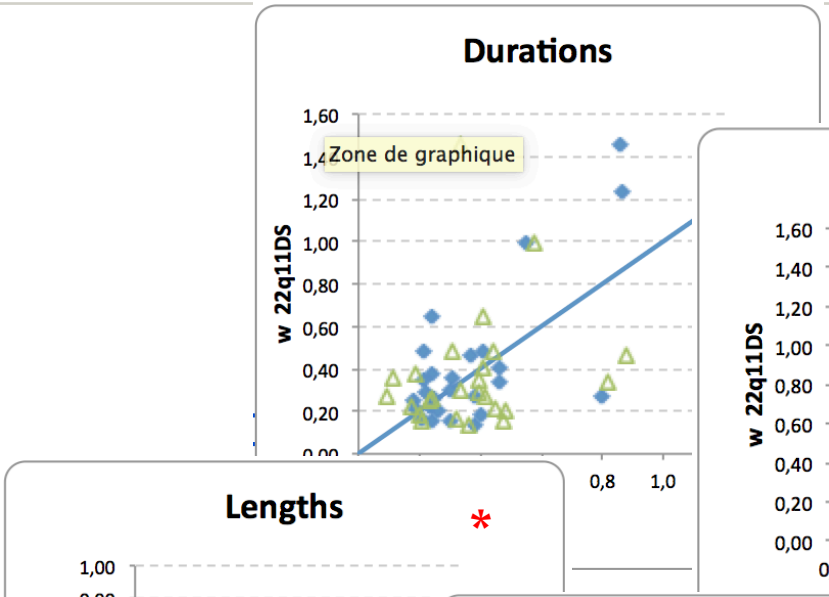
Evidence of the impact of visuo-spatial processing on magnitude representation in 22q11.2 microdeletion syndrome

Lucie Attout[a,b,*], Marie-Pascale Noël[b], Line Vossius[a], Laurence Rousselle[a]



22q11DS


Durations
Zone de graphique
w 22q11DS
1,60
1,40
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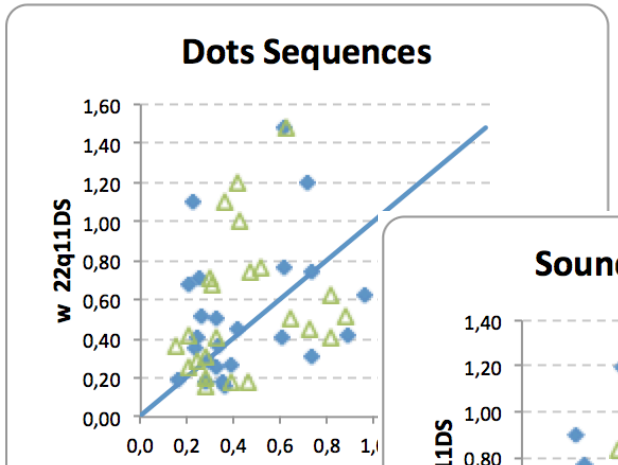
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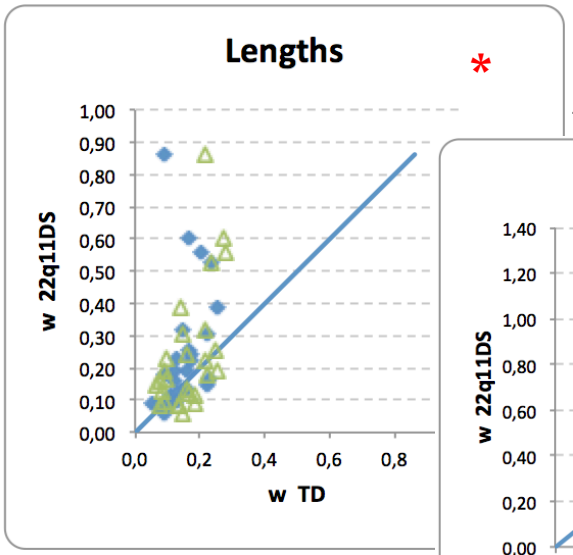
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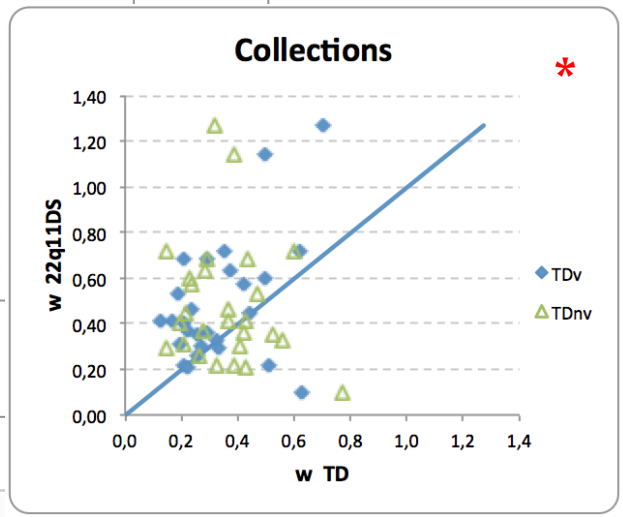
w TD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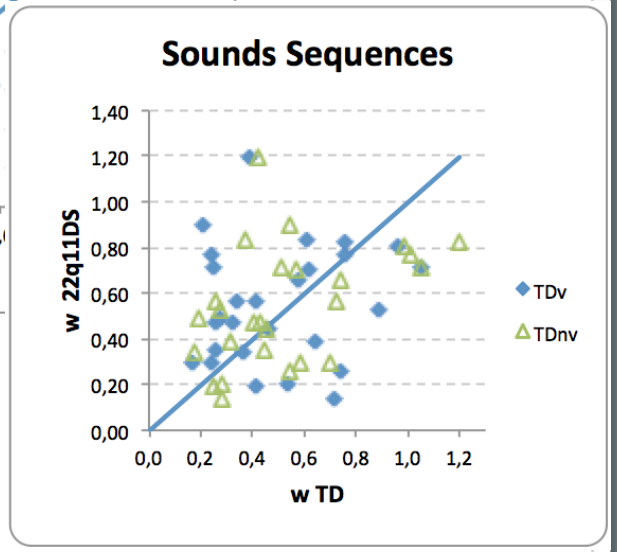
w TD
TDv
TDnv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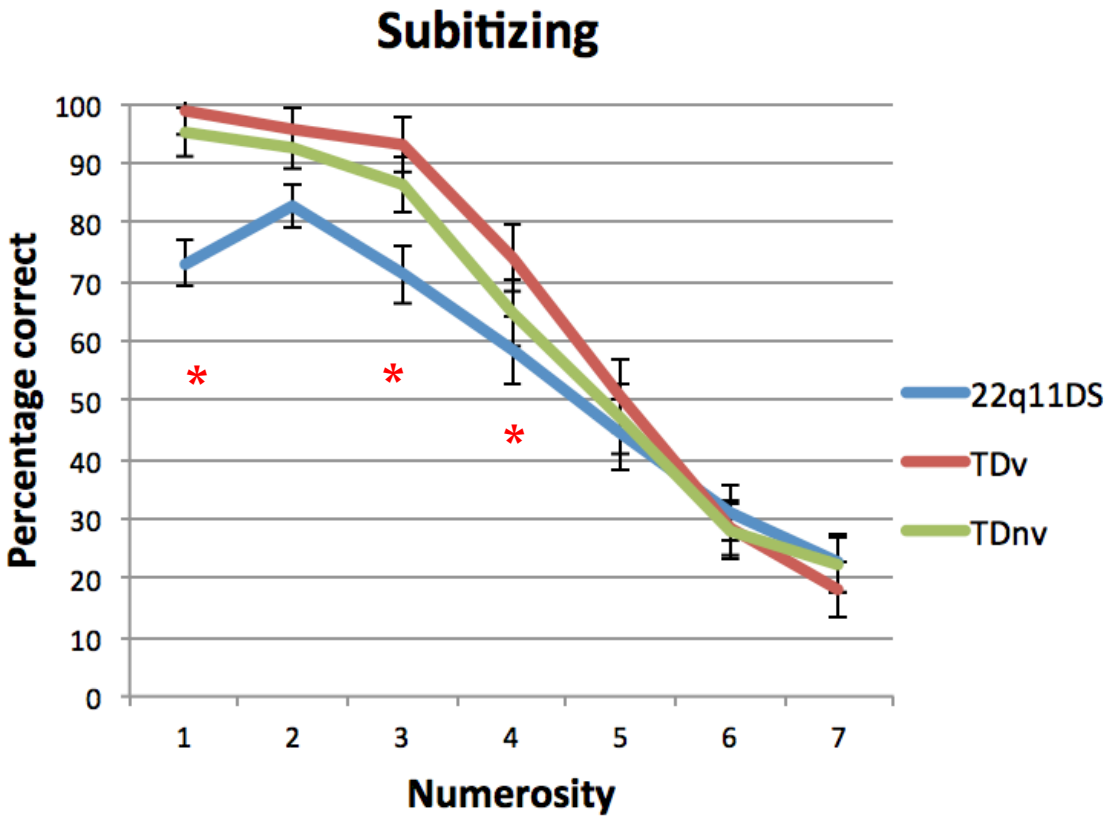
1,2
w TD
TDv
TDnv

22q11DS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10
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3
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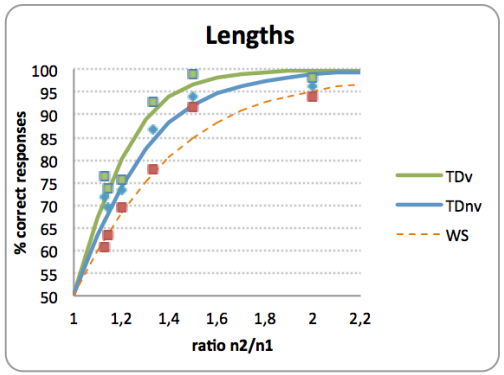
6
7
Numerosity
*
*
*
22q11DS
TDv
TDnv

Williams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80
75
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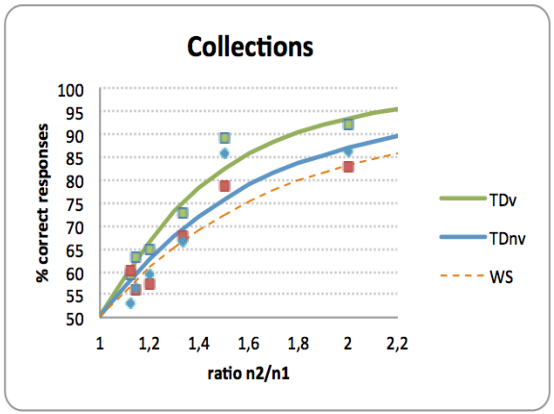
2
2,2
ratio n2/n1
TDv
TDnv
WS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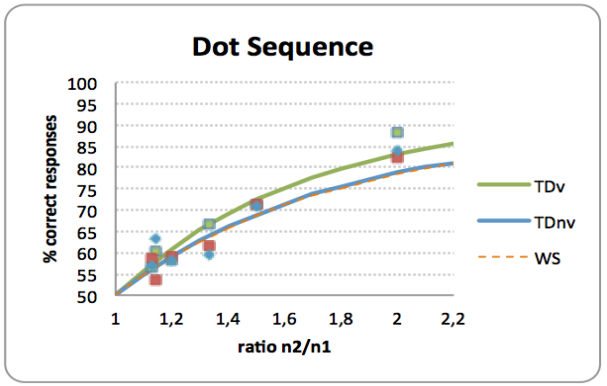
2
2,2
ratio n2/n1
TDv
TDnv
WS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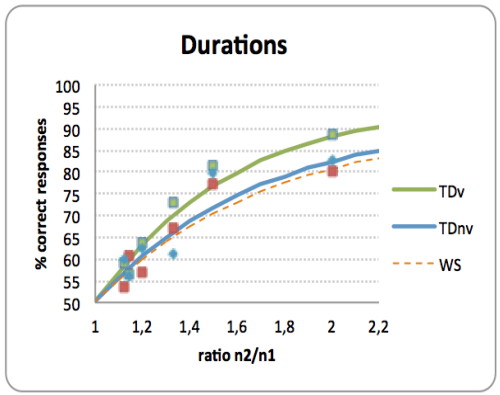
2
2,2
ratio n2/n1
TDv
TDnv
WS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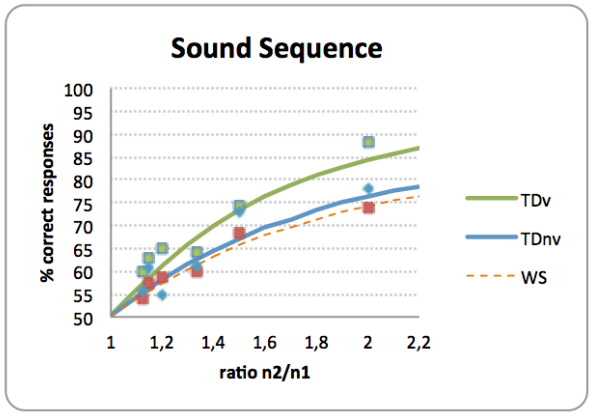
2,2
ratio n2/n1
TDv
TDnv
WS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50
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1,4
1,6
1,8
2
2,2
ratio n2/n1
TDv
TDnv
WS

Williams

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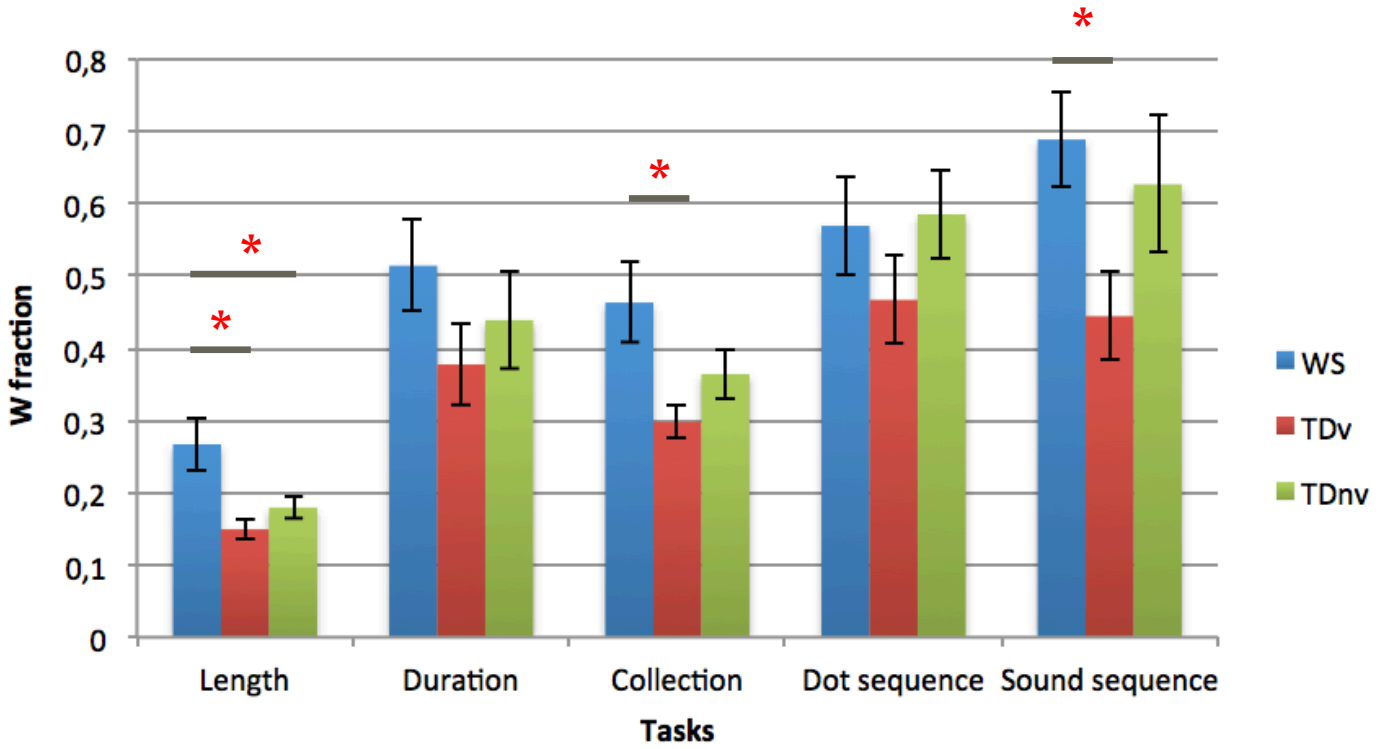
PLOS ONE

Magnitude Representations in Williams Syndrome: Differential Acuity in Time, Space and Number Processing

Laurence Rousselle[1]*, Guy Dembour[2], Marie-Pascale Noël[1]



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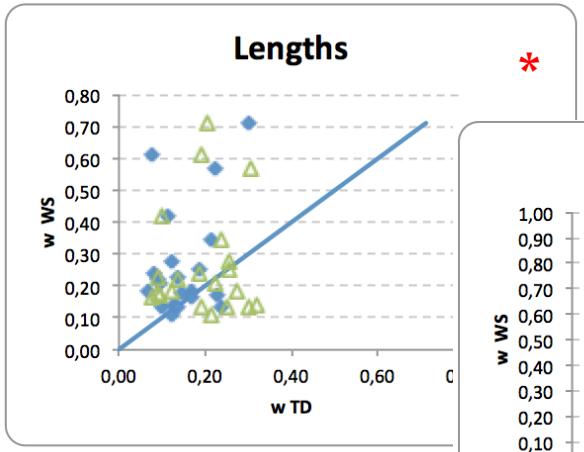
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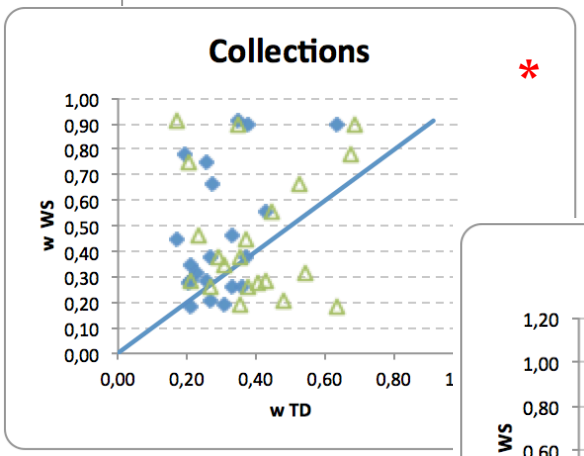
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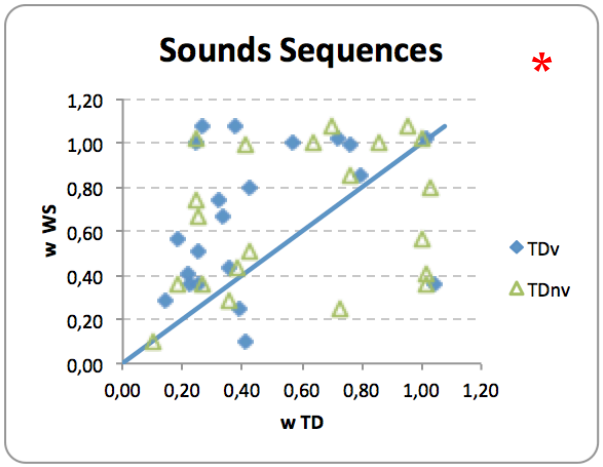
Sounds Sequences
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TDv
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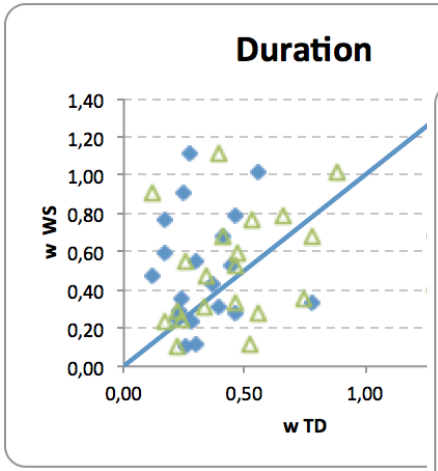
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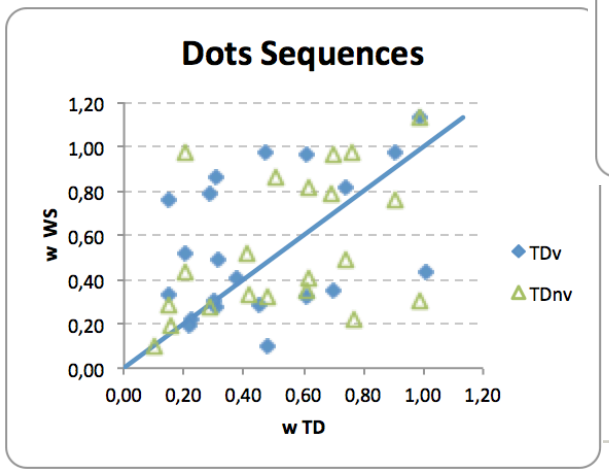
Dots Sequences
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TDv
TDnv
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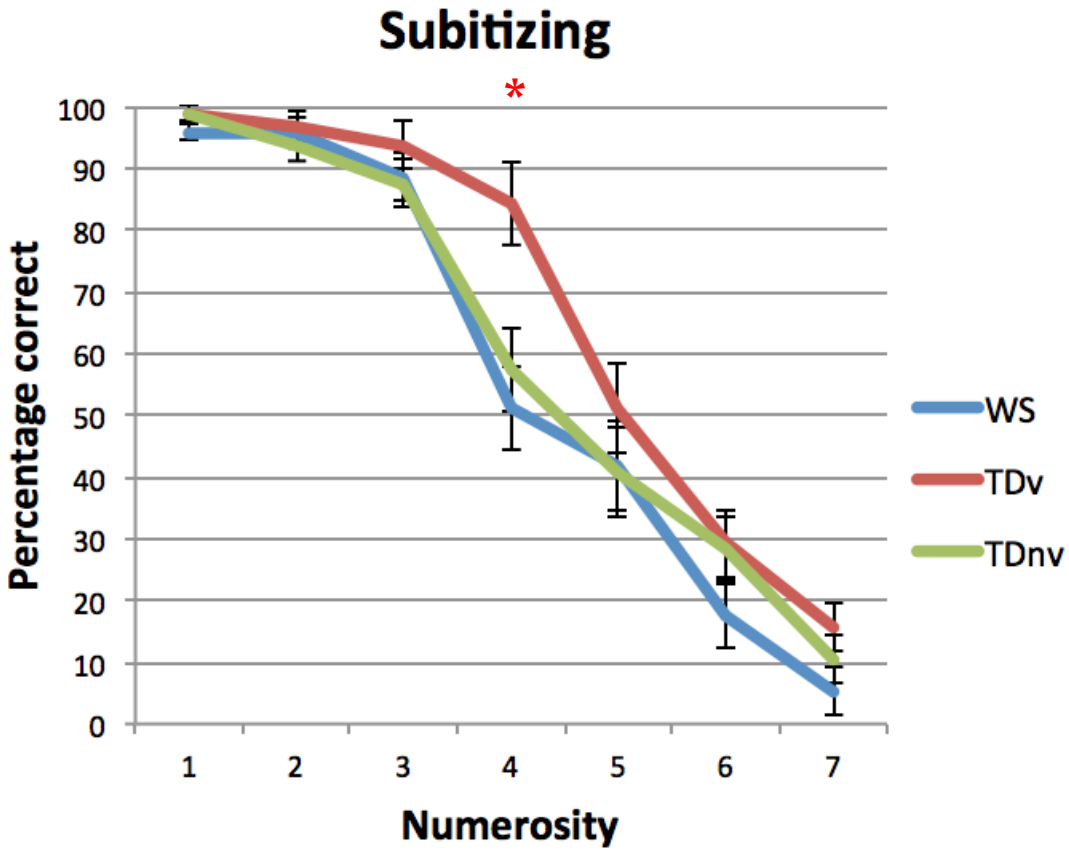
Williams


Subitizing
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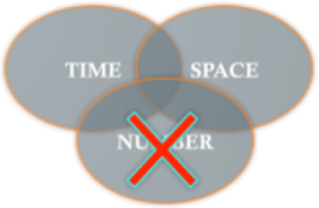
Numerosity
WS
TDv
TDnv

Conclusion

None the genetic condition is associated with a global magnitude deficit



None of them presented a specific deficit non symbolic number magnitude

Their deficit in basic numerical processing tasks results from other non-numerical impairment :

- Working memory impairement in Turner syndrome
- Visuo-spatial deficit in 22q11DS syndrome
- A mix of both for Williams syndrome

Thanks

Prof. M-P Noël

Lucie Attout

Line Vossius

Prof. M-C Nassogne

Dr G Dembour

Table 2. Data and paired t-tests for general measures in TS and C groups.

	TS group		C group			
	Mean	**SD**	**Mean**	**SD**	**t**	**p**
Age (months)	219.20	87.09	219.75	91.75	-.21	.83
IQ measures						
Vocabulary (max. 68)	32.85	11.08	33.90	10.21	-1.57	.13
Similarities (max. 44)	20.15	6.12	20.35	6.11	-.45	.66
Block design (max. 68)	35.40	11.50	42.45	10.07	-3.45	**.003**
Picture concepts (max. 28)	17.45	4.32	18.70	2.92	-1.70	.11
Working memory						
Visuo-spatial sketchpad (max. 42)	35.15	7.00	38.75	5.54	-2.52	**.02**
Phonological loop (max. 16)	7.70	1.63	9.00	2.29	-2.80	**.01**
Central executive (max. 16)	6.75	1.86	7.25	2.20	-.85	.41
Mathematical fluency						
Addition (Accuracy) (max. 81)	42.55	23.51	49.95	23.53	-1.90	.07
Subtraction (Accuracy) (max. 81)	33.75	20.19	40.00	18.32	-2.01	.06
Multiplication (Accuracy) (max. 81)	25.05	17.18	34.50	16.21	-2.74	**.01**
Complex arithmetic (Accuracy) (max. 36)	10.71	5.02	13.65	5.29	-2.53	**.02**
Counting speed (ms/item)	437.83	151.26	433.20	113.70	.14	.89
Speed processing (ms)	567.62	98.11	565.40	95.28	.08	.94

doi:10.1371/journal.pone.0171454.t002

Table 3
Data and paired *t*-tests for general measures in 22q11DS, verbal and visuo-spatial control groups.

	22q11DS		TD_{VERBAL}		TD_{VSSP}	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age	127.52	49.69	94.59***	28.38	86.74***	30.44
IQ measures (raw score)						
Vocabulary	22.44	7.78	23.63	8.25	23.00	10.52
Similarities	18	5.88	17.04	5.32	15.63	8.65
Block design	25.19	10.64	29.19	9.64	25.37	10.54
Concept identification	14.48	3.83	15.93	3.32	13.15	4.64
Working memory						
Visuo-spatial sketchpad	4.48	1.67	5.11	1.63	4.19	1.44
Phonological loop	6.04	2.01	6.04	1.43	5.67	1.57
Central executive	5.00	2.22	5.26	1.70	4.96	1.74
Mathematical fluency						
Pictorial additive fluency	8.00	6.13	11.27[a]	5.71	10.82[a]	6.29
Pictorial additive fluency (errors)	4.45	3.33	1.00[a*]	1.55	2.00[a*]	1.90
Addition fluency	24.93	13.19	19.07[b]	10.96	20.60[c]	7.37
Subtraction fluency	19.40	11.35	16.27[b]	9.96	19.60[c]	6.33
Multiplication fluency	18.80	12.62	12.60[b]	9.65	16.90[c]	11.29

Table 2. Mean Chronological Age and Mean Performance in Working Memory, Processing Speed and Counting Speed by Group.

			WS		TDv		TDnv	
		N	Mean	SD	Mean	SD	Mean	SD
Age (months)		20	265.4	139.4	90.4**	22.2	72.8**	21.5
Working Memory	Visuo-spatial span	20	8.1	3.3	11.6**	2.9	9.4	3.3
	Letter span	20	5.2	1.8	5.9	1.0	5.2	1.4