Recherche et microdélétion22 en 2010

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UNIVERSITÉ DE GENÈVE

Différents domaines de recherche

- Génétique
- Développement cérébral
- Psychiatrie et développement intellectuel
- Models animaux

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J Genet Counsel
DOI 10.1007/s10897-010-9306-0

ORIGINAL RESEARCH

Patient and Family Experiences and Opinions on Adding 22q11 Deletion Syndrome to the Newborn Screen

Abigail M. Bales · Christina A. Zaleski · Elizabeth W. McPherson

Abstract 22q11 deletion syndrome (22qDS) has recently been proposed for addition to the newborn screening panel in Wisconsin and it seems likely that it may soon be considered in other states as well. Input from patients with 22qDS and their family was gathered from 21 phone interviews. Cardiac, palate, hypocalcemia, and multiple anomalies were common reasons for involved patients to be diagnosed, though age at diagnosis ranged from birth to adulthood. Many commented on their struggles with 22qDS, including worries about the future and the patient's independence. In general, respondents favored newborn screening for 22qDS because it would help prevent some medical problems, increase access to services, explain existing problems, and identify mild cases. However, a minority expressed reservations, including concerns that it would disrupt bonding, could be too costly, and would not be useful for mild cases.

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RESEARCH ARTICLE

AMERICAN JOURNAL OF medical genetics PART A

The Morphology of the Sella Turcica in Velocardiofacial Syndrome Suggests Involvement of a Neural Crest Developmental Field

Kirsten Mølsted,[1]* Maria Boers,[1] and Inger Kjär[2]

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[2]Department of Orthodontics, Faculty of Health Science, University of Copenhagen, Copenhagen, Denmark

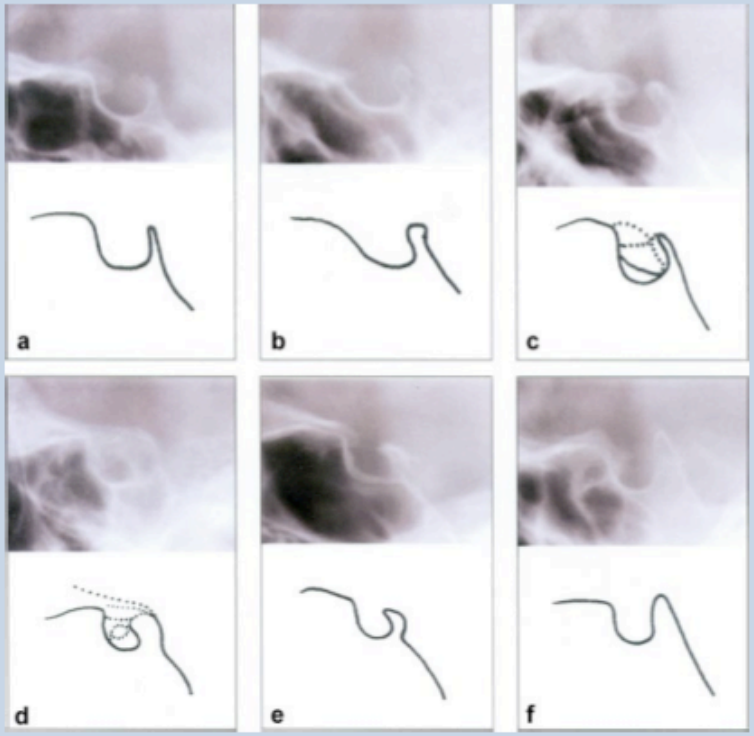

FIG. 1. Tracings and details from lateral cephalograms of the different morphological types of sella turcica: (a) normal sella turcica, (b) oblique anterior wall, (c) double contour of the floor, (d) sella turcica bridge, (e) irregularity (notching) in the posterior part of the sella turcica, (f) pyramidal shape of the dorsum sellae. The figure has previously been published in Axelsson et al. [2004b].

J Neurodevelop Disord (2010) 2:77–92
DOI 10.1007/s11689-010-9043-6

White matter microstructure in 22q11 deletion syndrome: a pilot diffusion tensor imaging and voxel-based morphometry study of children and adolescents

Frederick Sundram · Linda E. Campbell · Rayna Azuma · Eileen Daly · Oswald J. N. Bloemen · Gareth J. Barker · Xavier Chitnis · Derek K. Jones · Therese van Amelsvoort · Kieran C. Murphy · Declan G. M. Murphy

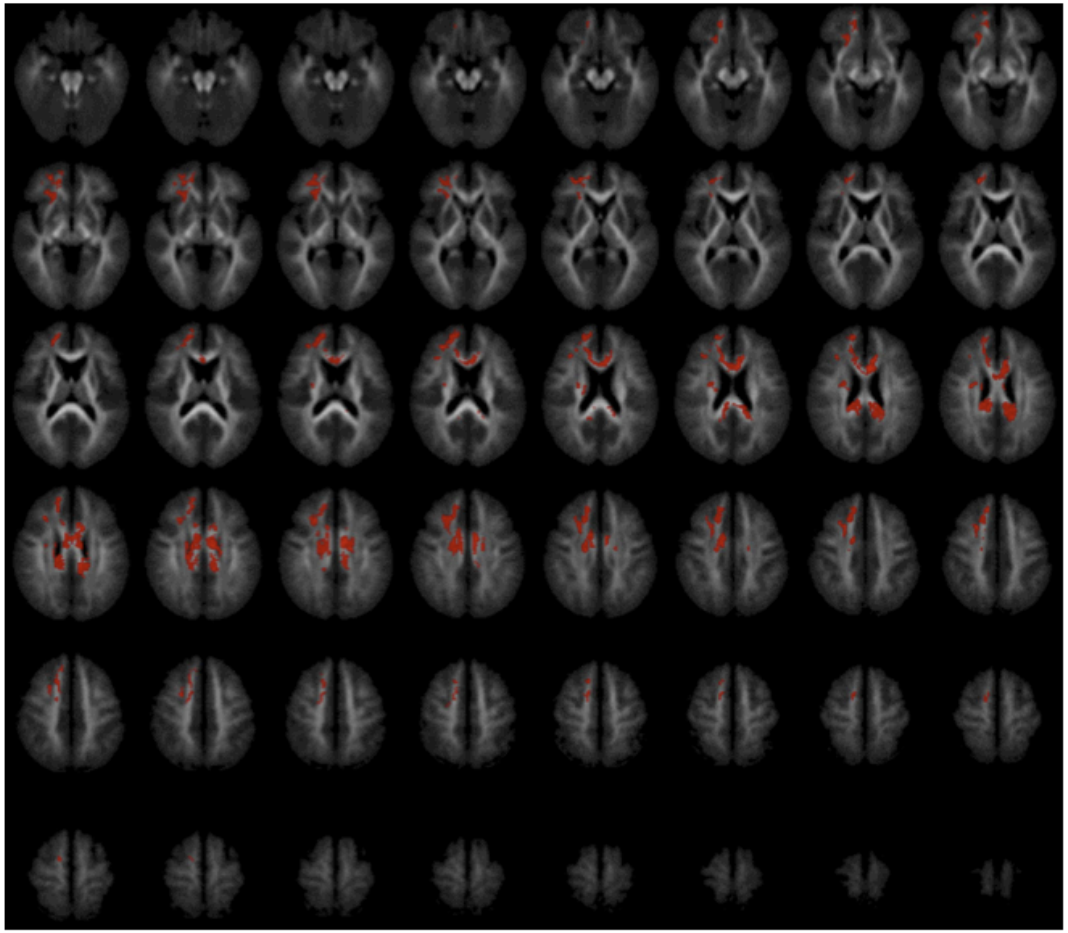

Fig. 3 Fractional anisotropy deficits within 22q11DS group in subjects with ^{V}COMT relative to ^{M}COMT. Ascending 2 mm transverse sections; (reversed where L = R, R = L)

Journal of Psychiatric Research xxx (2010) xxx–xxx

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Reduced NoGo-anteriorisation during continuous performance test in deletion syndrome 22q11.2

Marcel Romanos [a,*,1], Ann-Christine Ehlis [b,1], Christina G. Baehne [b], Christian Jacob [b], Tobias J. Renner [a], Astrid Storch [a,b], Wolfgang Briegel [c], Susanne Walitza [a,d], Klaus-Peter Lesch [b], Andreas J. Fallgatter [b,e]

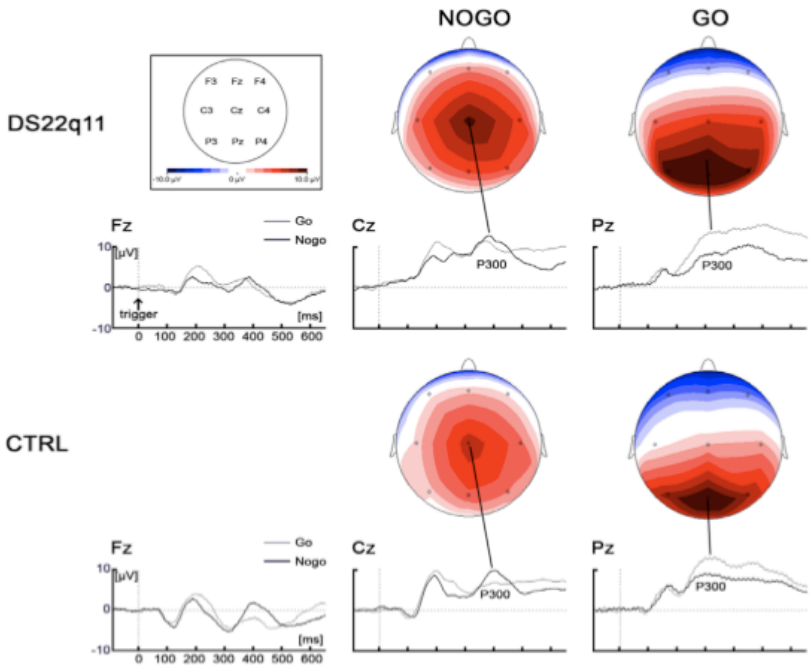

Fig. 1. Go- and NoGo-centroids, and P300 amplitudes at midline electrodes in patients with DS22q11.2 ('DS22q11') and healthy controls ('CTRL'). Go-centroid in 'DS22q11' is significantly more anterior compared to 'CTRL' ($p < .01$). No difference in localization of NoGo-centroid is found between groups. Amplitudes were higher in 'DS22q11' compared to 'CTRL' ($p < .05$) across task conditions.

Psychiatry Research: Neuroimaging 181 (2010) 1–8

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Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Evidence of gray matter reduction and dysfunction in chromosome 22q11.2 deletion syndrome

Vandana Shashi[a,b,*], Thomas R. Kwapil[c], Jessica Kaczorowski[c], Margaret N. Berry[b], Cesar S. Santos[b], Timothy D. Howard[b], Dhruman Goradia[d], Konasale Prasad[d], Diwadkar Vaibhav[e], Rajaprabhakaran Rajarethinam[e], Edward Spence[f], Matcheri S. Keshavan[e,g]

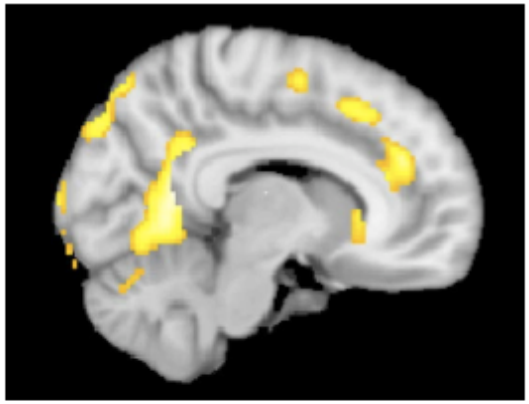

Fig. 1. Reduced gray matter in the cingulate gyrus in children with 22q11Ds compared to controls. Also evident is the decrease in gray matter in the occipital regions in the 22q11DS group.

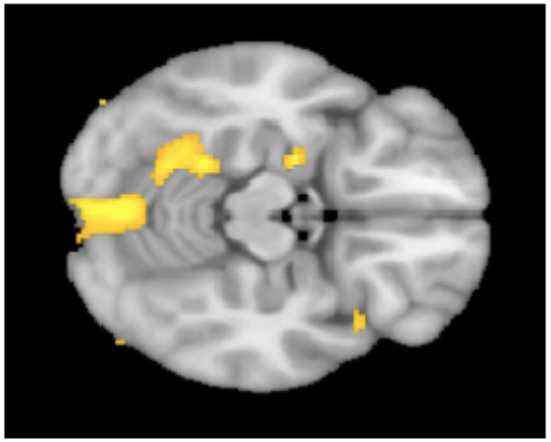

Fig. 2. Reduction in gray matter in the cerebellar regions in children with 22q11DS.

Schizophrenia Research 115 (2009) 182–190

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Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Deviant trajectories of cortical maturation in 22q11.2 deletion syndrome (22q11DS): A cross-sectional and longitudinal study

Marie Schaer [a,b,*], Martin Debbané [a], Meritxell Bach Cuadra [b], Marie-Christine Ottet [a], Bronwyn Glaser [a], Jean-Philippe Thiran [b], Stephan Eliez [a]

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[b] Signal Processing Laboratory, Swiss Federal Institute of Technology, CH-1015 Lausanne, Switzerland

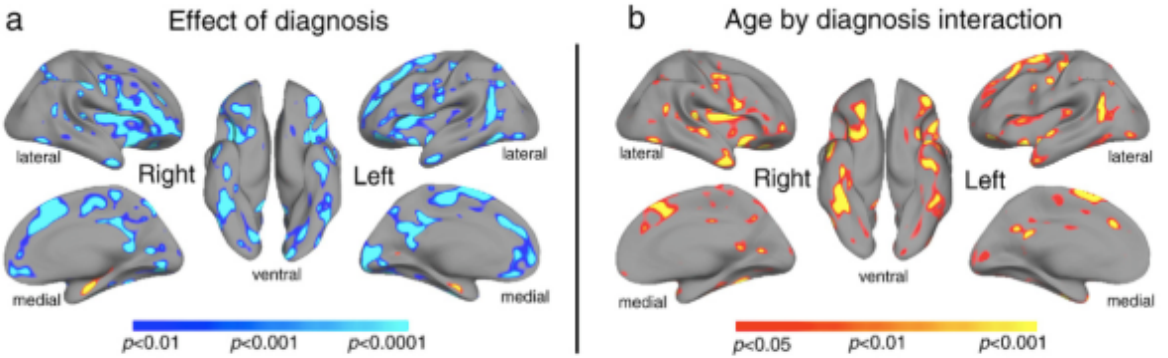

Fig. 1. Vertex-wise comparisons of cortical thickness between groups (cross-sectional). (a) When comparing the entire sample, we observe extensive areas of thicker cortex in patients with 22q11DS compared to controls (in blue). Small regions of thinner cortex in 22q11DS are shown around the bilateral entorhinal and parahippocampal regions. (b) Clusters in red/yellow show regions of significant age by diagnosis interaction, meaning that the regression line of cortical thickness changes with age shows a significantly steeper slope in patients with 22q11DS compared to controls.

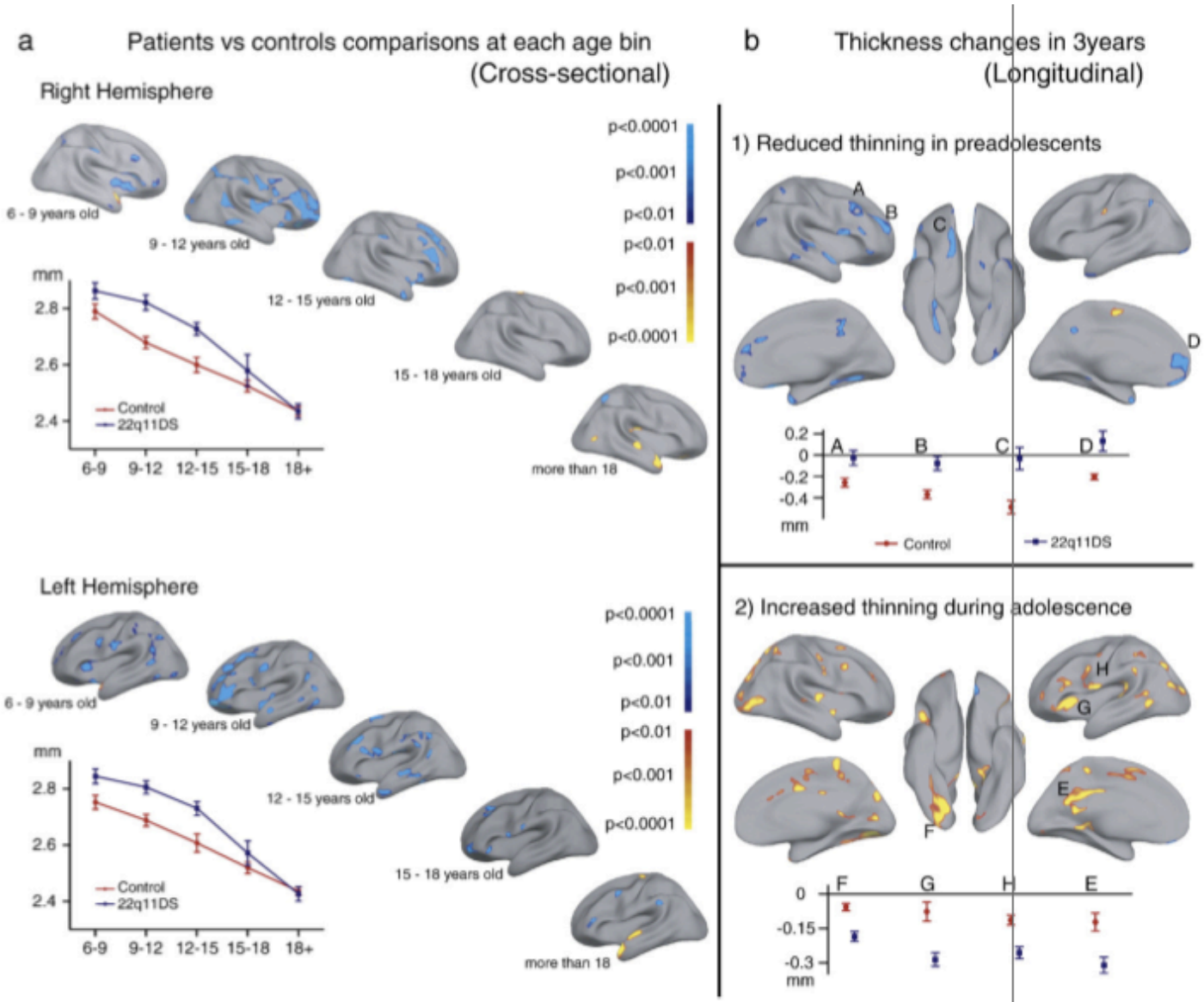

Fig. 2. Trajectories of cortical thickness change with age. a) Using a cross-sectional design to compute cortical thickness differences between patients and controls in each age bin, we observe that the larger clusters of thicker cortex (blue) are apparent between 9 and 12 years old in the prefrontal regions. Between 12 and 15 years old, clusters of thicker cortex are mostly located in the dorsal prefrontal region. In adults, prominent clusters of thinner clusters (yellow) are seen around the superior temporal gyrus, bilaterally. b) Using repeated-measures with the longitudinal subsample, we confirm the different trajectories of cortical thickness changes observed with cross-sectional design. In preadolescents (before 9 of age at Time 1), we observe numerous clusters where no thickness changes occur in patients, whereas thinning is observed in controls. In clusters A to D, this pattern of delayed thinning reach significance at threshold $p < 0.007$, with the following effect size (partial eta-squared): cluster A: 0.335, B: 0.467, C: 0.456, and D: 0.428. Contrarily, we observed greater thickness loss in affected adolescents compared to controls (older than 9 at Time 1). This larger thinning with age in patients compared to controls is significant at $p < 0.002$ and with the following partial eta-squared: cluster F: 0.342, G: 0.215, H: 0.285, and E: 0.239.

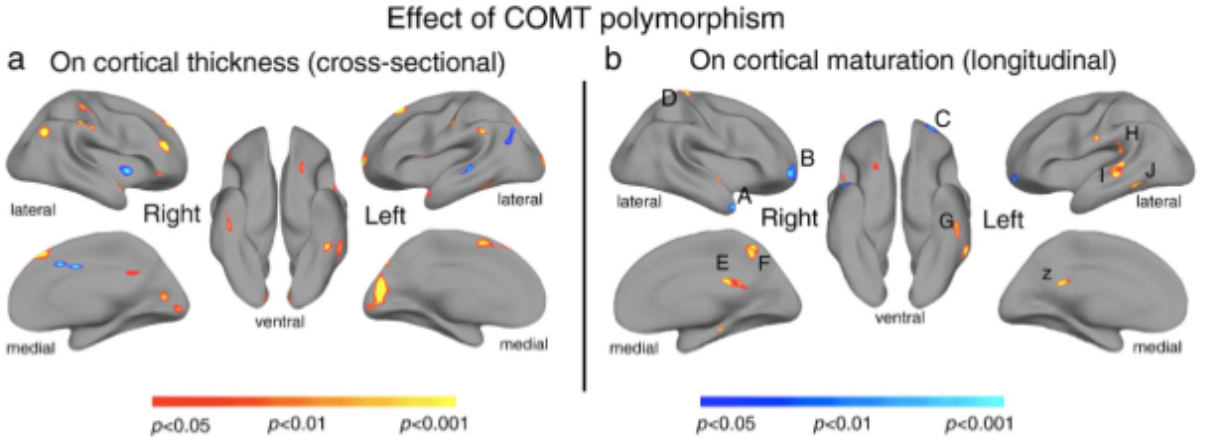

Fig. 3. Effect of COMT polymorphism on cortical thickness within 22q11DS. a) Apart from a cluster of thinner cortex at the left cuneus in patients with Met compared to Val allele (in yellow), only modest clusters of significant differences associated with COMT polymorphism are observed. b) Using repeated-measures in the longitudinal subsample, no compelling evidence for an unequivocal age by COMT polymorphism interaction is shown. Namely, clusters in blue illustrate larger thinning in Val compared to Met reaching the significance of $p < 0.023$ (partial eta-squared: A: 0.196, B: 0.225, C: 0.161). Clusters in yellow show greater cortical loss in Met compared to Val with significance of $p < 0.022$ (partial eta-squared: D: 0.205, E: 0.279, F: 0.256, G: 0.234, H: 0.164, I: 0.297, J: 0.244, K: 0.181).

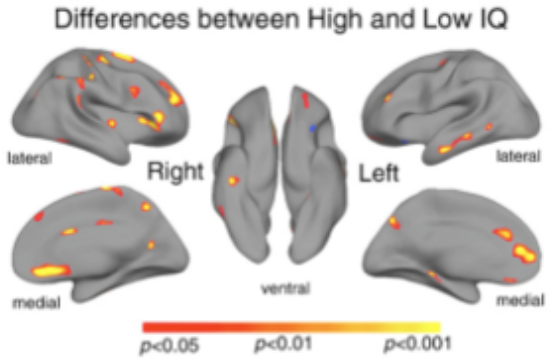

Fig. 4. Differences in cortical thickness related to cognitive abilities within 22q11DS. Clusters in red/yellow depict regions where children and adolescents with 22q11DS who score above 75 on the IQ tests show larger thickness values than those with IQ below 65. This association between thicker cortex and better performances seems to hold true at each age, as no significant clusters of group by age interaction were evidenced at $p < 0.05$ (statistical maps not shown).

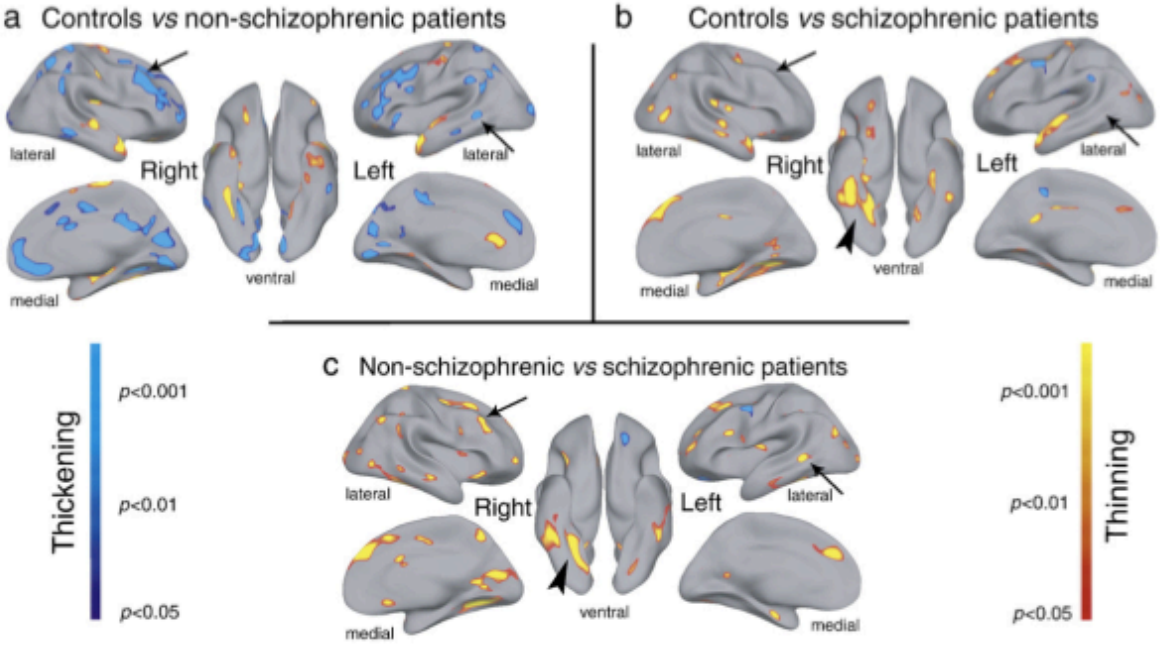

Fig. 5. Cortical thickness differences related to schizophrenia in adults. In the controls vs. non-schizophrenic patients, clusters in blue demonstrate thicker cortex in patients than controls, whereas red/yellow clusters show thinner cortex in patients compared to controls. When controls are compared to schizophrenic patients, only clusters of thinner cortex (red/yellow) are found in patients. Finally, the comparison within 22q11DS reveals mostly areas of cortical thinning (red/yellow) in schizophrenic compared to non-schizophrenic patients.

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- Psychiatrie et développement intellectuel
- Models animaux

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journal homepage: www.elsevier.com/locate/schres

Brief report

Attenuated positive symptoms of psychosis in adolescents with chromosome 22q11.2 deletion syndrome

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[b] Department of Psychiatry and Behavioral Sciences and the Imaging Research Center, UCDHS, United States

[c] Department of Psychiatry, University of California at San Francisco, United States

A B S T R A C T

Thirty percent of individuals with chromosome 22q11.2 deletion syndrome (22q11.2DS) develop a psychotic disorder, particularly schizophrenia. We assessed attenuated positive, negative and disorganized symptoms of psychosis and clinical-high-risk syndromes in 20 adolescents with 22q11.2DS (median age 15.1 years) using the Structured Interview for Prodromal Symptoms (SIPS). Two participants met criteria for the Attenuated Positive Symptom Syndrome, while nine participants (45%) experienced positive symptoms rated in the "moderate" to "severe and psychotic" range on the SIPS. Almost all presented with moderate to severe symptoms in the negative, disorganized, and general symptom domains.

Presentation of SIPS symptoms.

	22q11.2DS ($n = 20$)	
	n (%) having a score ≥ moderate [a]	Median (IQR) *range*
Positive symptoms [b]	9 (45)	4.0 (3.0) *0–14*
Unusual thought content	5 (25)	0.0 (2.5) *0–4*
Persecutory delusions/paranoia	2 (10)	0.0 (0.0) *0–3*
Grandiosity	2 (10)	0.0 (0.0) *0–6*
Perceptual abnormalities	5 (25)	1.0 (2.75) *0–4*
Disorganized communication	2 (10)	1.5 (2.0) *0–4*
Negative symptoms [b]	17 (85)	8.0 (11.5) *0–25*
Social anhedonia	7 (35)	1.5 (4.0) *0–6*
Avolition	10 (50)	2.0 (3.0) *0–5*
Expressions of emotion	7 (35)	0.5 (3.75) *0–5*
Experience of emotions and self	1 (5)	0.0 (0.75) *0–3*
Ideational richness	15 (75)	3.0 (1.75) *0–5*
Occupational functioning	4 (20)	1.0 (1.75) *0–4*
Disorganized symptoms [b]	11 (55)	3.0 (5.0) *0–15*
Odd behavior or appearance	3 (15)	0.0 (1.75) *0–3*
Bizarre thinking	1 (5)	0.0 (0.0) *0–4*
Problems with attention/focus	10 (50)	2.5 (1.75) *0–5*
Impairment in hygiene	5 (25)	0.0 (2.75) *0–4*
General symptoms [b]	12 (60)	6.0 (11.5) *0–18*
Sleep disturbance	5 (25)	0.0 (2.75) *0–4*
Dysphoric mood	9 (45)	2.0 (3.75) *0–5*
Motor disturbances	7 (35)	0.0 (3.0) *0–5*
Impaired tolerance to normal stress	8 (40)	2.0 (3.0) *0–6*

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Brief report

COMT and anxiety and cognition in children with chromosome 22q11.2 deletion syndrome

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ABSTRACT

The COMT gene is thought to contribute to the cognitive/psychiatric phenotypes in 22q11.2 deletion syndrome. We measured these manifestations against the Val/Met alleles of the COMT gene, in 40 nonpsychotic 22q11DS children. The Val allele was associated with poor IQ, processing speed, executive function and a higher frequency of anxiety disorders, underscoring the importance of the COMT gene in the childhood psychopathology in 22q11DS.

Table 1
Comparison of neuropsychological and behavioral manifestations in the Val and Met groups (independent samples *t*-test).

Test	Val/Met	*n*	Mean	SD	*t*-value	Cohen's *d*	*P* value
WISC full scale IQ	Met	21	76.24	9.55	2.39	0.76	<0.05
	Val	18	68.00	11.95			
WISC verbal comprehension factor	Met	21	79.52	11.91	1.55	0.51	0.13
	Val	17	73.71	10.99			
WISC working memory	Met	20	82.95	10.41	1.85	0.60	0.07
	Val	16	75.06	15.19			
WISC processing speed factor	Met	21	85.00	15.13	2.61	0.88	<0.05
	Val	16	72.88	12.02			
WISC perceptual organization factor	Met	22	78.73	10.72	1.77	0.55	0.08
	Val	17	71.24	15.59			
WCST conceptual level response	Met	22	84.36	7.73	117.5[a]		<0.05
	Val	17	80.41	14.31			
CBCL social *t*-score	Met	17	45.35	7.19	2.39	0.85	<0.05
	Val	14	38.14	8.82			
CBCL anxious/depressed (III) *t*-score	Met	18	56.17	6.24	−2.98	1.03	<0.01
	Val	14	64.35	9.33			
CBCL internalizing *t*-score	Met	18	53.61	15.54	−2.04	0.74	<0.05
	Val	14	64.07	12.74			
Parent SSRS total standard score	Met	18	102.11	13.50	2.60	0.88	0.01
	Val	16	82.5	28.62			
C-DISC any anxiety disorder	Met	5/22	Fisher's exact test $P = <0.01$				
	Val	13/18					

[a] Due to violation of the assumption of homogeneity of variance, Mann–Whitney *U* statistic computed. Please note that not all tests were performed on all the subjects.

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Visual scanning of faces in 22q11.2 deletion syndrome: Attention to the mouth or the eyes?

Linda Campbell [a,b,c,*], Kathryn McCabe [a,b], Kate Leadbeater [a], Ulrich Schall [a,b,c], Carmel Loughland [a,b,c], Dominique Rich [d]

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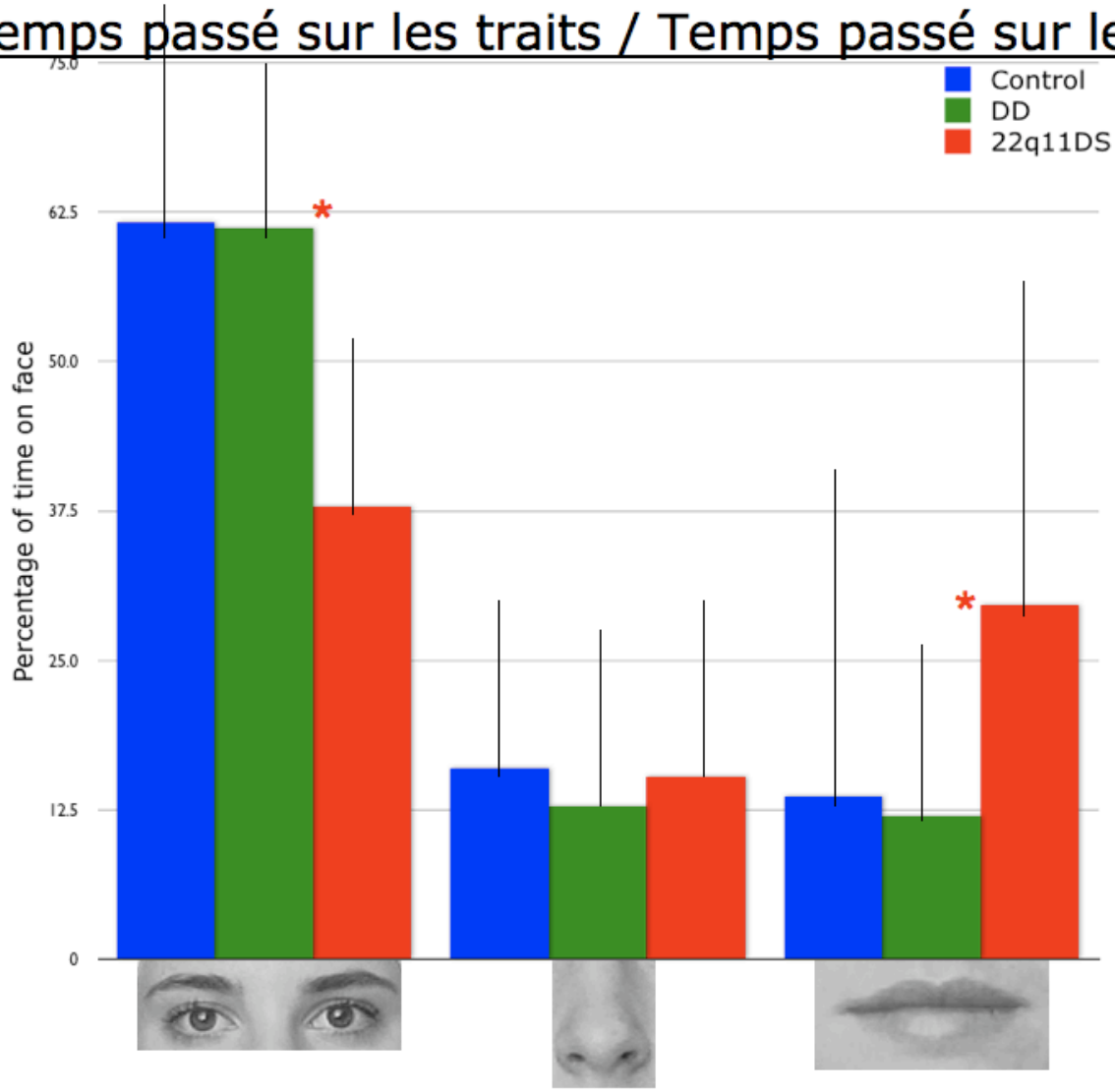
Table 2
Shows subjects mean accuracy as a function of emotion.

Emotion	Condition	Mean	(S.D.)	Emotion	Condition	Mean	(S.D.)	Emotion	Condition	Mean	(S.D.)
Anger**	*22q11DS*	2.59	(1.18)	Neutral*	*22q11DS*	3.65	(1.50)	Happy	*22q11DS*	4.88	(0.33)
	Control	4.06	(1.16)		*Control*	4.72	(0.46)		*Control*	5.00	(0.00)
Disgust*	*22q11DS*	1.65	(1.37)	Sad	*22q11DS*	3.65	(0.86)	Overall	*22q11DS*	22.12	(3.33)
	Control	2.94	(0.94)		*Control*	3.83	(0.99)		*Control*	27.61	(3.00)
Fear**	*22q11DS*	1.71	(1.26)	Surprise	*22q11DS*	4.00	(0.71)				
	Control	3.00	(0.84)		*Control*	4.06	(0.73)				

* Significant at $P<0.01$.
** Significant at $P<0.001$.

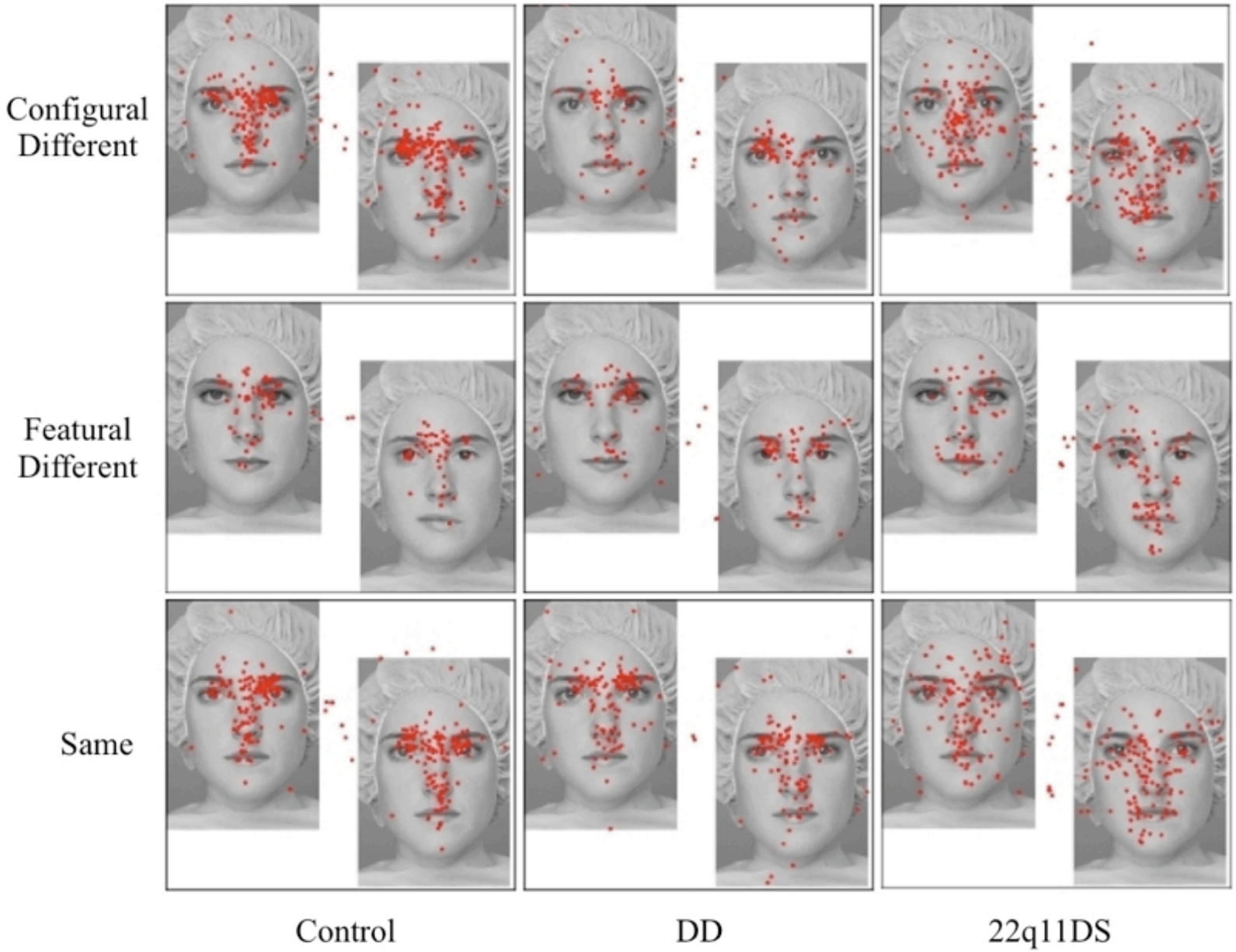
Temps passé sur les traits suivant les statuts

Temps passé sur les traits / Temps passé sur le visage



(Âge: 8-15)
22q11DS: N=26
DD: N=17
Contrôle: N=22

Zones fixées suivant le statut



(Âge: 8-15)
22q11DS: N=26
DD: N=17
Conttrôle: N=22

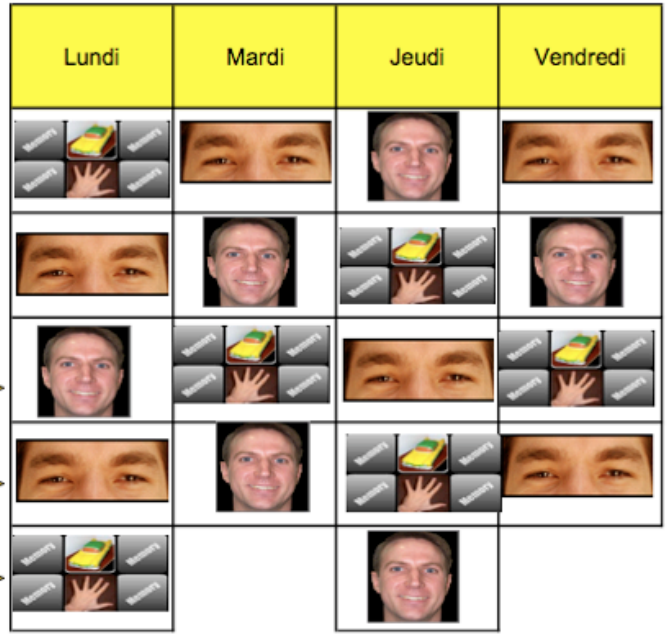
Vis-à-vis

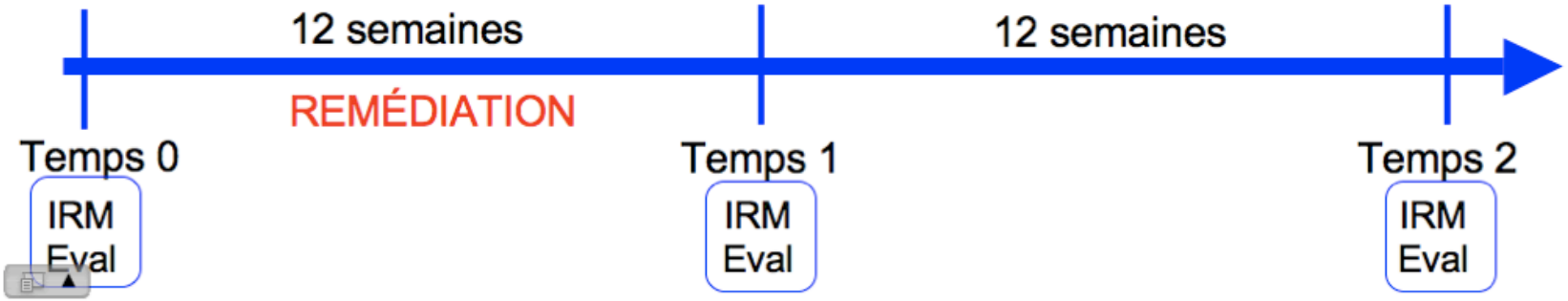
12 semaines
4 jours par semaine
15 minutes par jour
9 jeux
Niveau progressif

Les émotions et leur contexte

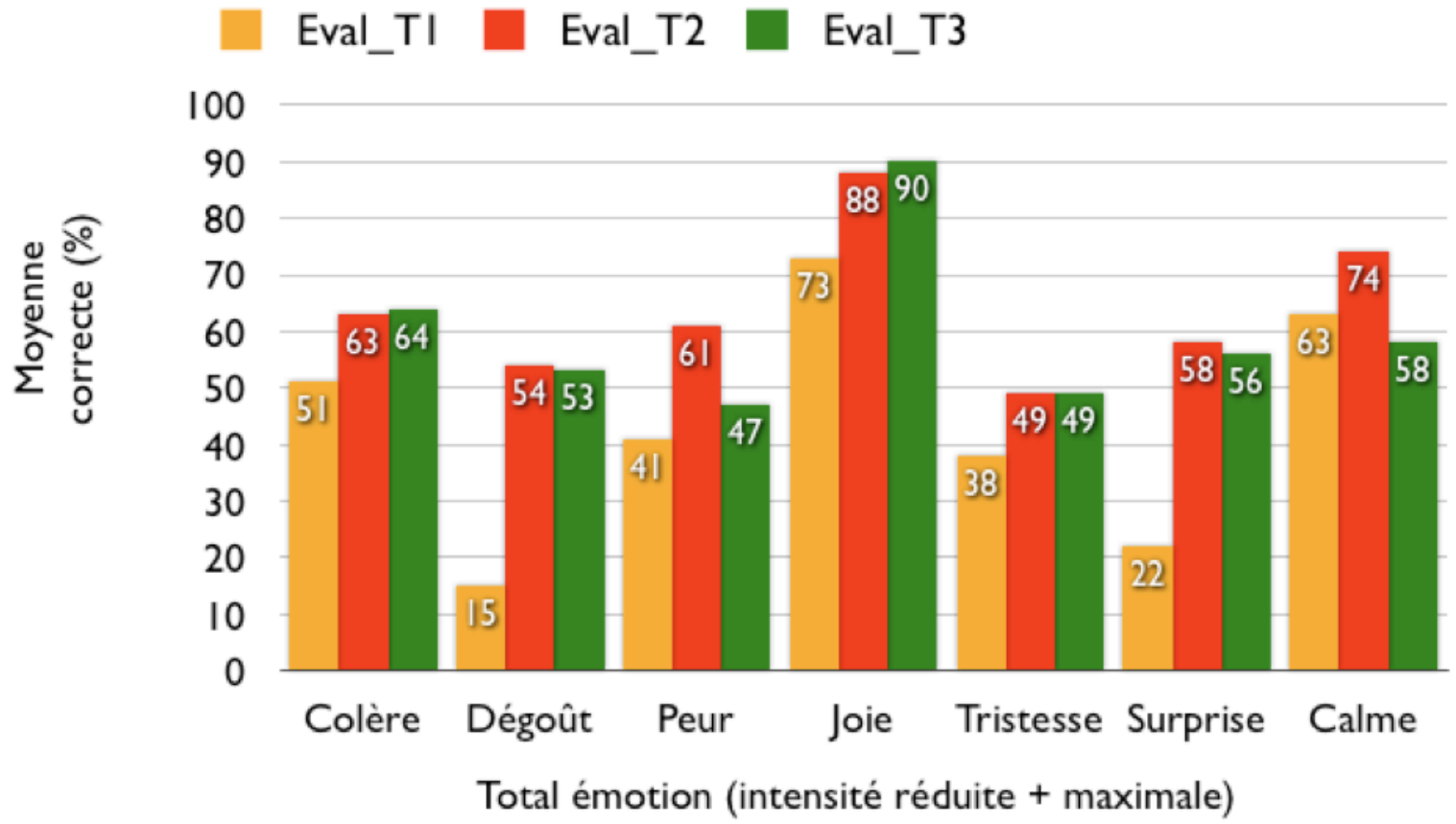
Fixation sur les yeux

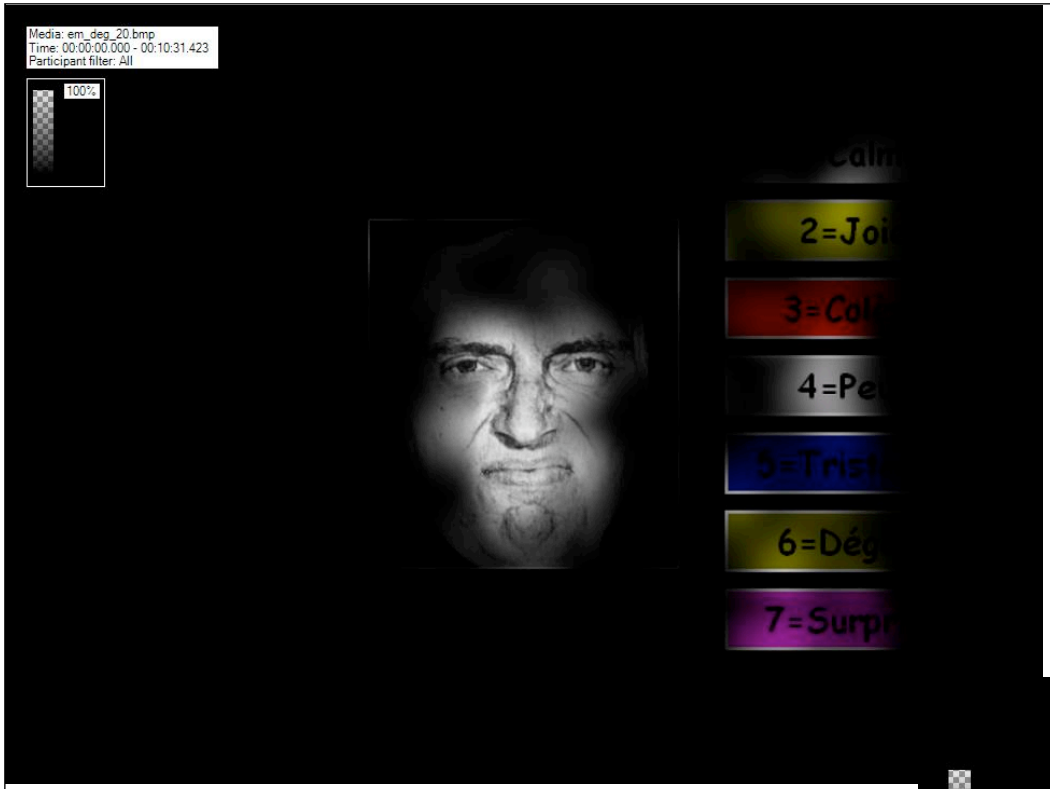
Mémoire de travail





Reconnaissance émotionnelle , groupe SVCF

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Participant filter: All
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2=Joi
3=Col
4=Pe
5=Tris
6=Dég
7=Surpr


2=J
3=Col
6=Dé

Executive functions and memory abilities in children with 22q11.2 deletion syndrome

Linda E. Campbell, Rayna Azuma, Fiona Ambery, Angela Stevens, Anna Smith, Robin G. Morris, Declan G.M. Murphy, Kieran C. Murphy

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Objective: Velo-cardio-facial syndrome or 22q11.2 deletion syndrome (22q11DS) is the most common known microdeletion syndrome. One of the genes in the deleted region is the *catechol-O-methyltransferase* (COMT) gene, which is thought to have significant effects on cognition through its influence on dopamine metabolism. The aim of the present study was to better characterize the cognitive phenotype in a large cohort children with 22q11DS compared with sibling controls and to investigate if the cognitive deficits in 22q11DS were modulated by COMT expression.

Method: The memory, executive function and attentional abilities of children with 22q11DS ($n = 50$) compared to sibling controls ($n = 31$), were measured. Also, within children with 22q11DS, a preliminary exploration was carried out of the relationship between cognitive ability and COMT genotype.

Results: Overall, the 22q11DS group had significantly reduced scores on tests of memory (especially in visual memory) and executive function (particularly in planning, working memory, and motor organization) compared with sibling controls. No association, however, was identified between COMT genotype and cognitive function.

Conclusions: Although 22q11DS children have specific cognitive deficits, differences in COMT do not account for these findings.

Key words: 22q11.2 deletion syndrome, *catechol-O-methyltransferase*, executive functions, memory, velo-cardio-facial syndrome

Table 3. Cognitive data

	22q11DS		Siblings				
	Mean	SD	Mean	SD	Statistic	p	η_p^2
Memory							
General memory	78.25	15.22	105.81	11.94	t = −8.52	0.0005***	
Visual Immediate	82.27	15.63	101.84	15.61	F = 29.90	0.0005***	0.28
Verbal Immediate	85.35	15.77	103.03	14.96	F = 23.72	0.0005***	0.24
Visual Delayed	84.73	13.69	103.32	10.26	F = 44.80	0.0005***	0.37
Verbal Delayed	85.48	15.29	105.03	13.49	F = 44.80	0.0005***	0.37
Learning	88.74	16.31	99.13	13.56	F = 8.63	0.004***	0.10
Delayed recognition	90.72	17.21	102.42	14.36	F = 9.81	0.002***	0.11
Executive functioning							
ID/ED task	(n = 45)		(n = 28)				
Stages passed	7.47	0.79	8.29	0.94	z = −3.6	0.0005***	
No. errors prior to the ED shift	10.02	7.40	7.59	3.68	z = −0.96	0.34	
No. errors in extradimensional shifting	22.13	9.01	14.21	11.09	z = −2.9	0.004**	
Switch	n = 37		n = 27				
Accuracy switch trials %	61.29	23.05	68.47	24.26	F = 1.20	0.28	
Accuracy report trials %	65.19	20.42	70.25	22.95			
Reaction time switch trials	824.12	194.85	831.19	194.26	F = 0.01	0.91	
Reaction time repeat trials	779.51	164.28	782.42	179.74			
Total omissions	36.00	34.32	44.43	39.76	t = −0.91	0.37	
Total premature responses	4.22	6.3	0.86	2.54	z = −3.8	0.0005***	
Stockings of Cambridge	(n = 44)		(n = 28)				
Moves above minimum	5.73	2.39	3.90	1.69	t = 3.05	0.004**	
Initial thinking time (ms) (3–5 moves)	12001.05	8275.40	14681.00	13377.08	F = 2.47	0.121	
Subsequent thinking time (ms) (3–5 moves)	4852.98	4307.88	2514.95	2283.24	F = 14.90	0.0005***	0.19
Spatial Working Memory	(n = 44)		(n = 28)				
Between search errors	60.30	15.93	40.72	20.75	F = 21.8	0.0005***	0.24
Within-search errors(4–8 boxes)	3.64	3.16	2.32	2.91	z = −2.09	0.04*	
Strategy score	39.25	3.16	36.04	4.48	z = −3.3	0.001***	
Digit span (WISC–III)	(n = 50)		(n = 31)				
	6.32	2.15	9.71	2.82	t = −6.1	0.005***	
Attention/inhibition							
Attention/concentration (CMS)	80.51	11.62	104.29	12.59	F = 73.19	0.005***	0.49
Go–NoGo	(n = 40)			(n = 27)			
Reaction time to go signals	394.50	60.93	402.74	74.63	t = −0.50	0.62	
Probability of inhibition % (left)	79.48	22.99	80.74	22.08	z = −1.2	0.2	
Probability of inhibition % (right)	69.76	24.39	80.37	16.82	z = −2.0	0.05*	
Probability of inhibition % (summed)	74.62	15.82	80.55	15.60	z = −1.9	0.05*	
Premature responses to all go's	6.62	7.02	2.33	4.52	z = −3.6	0.005***	
Omission to all go's	18.71	18.9	19.3	22.85	t = 0.07	0.948	
Stroop	(n = 39)		(n = 25)				
Reaction time Stroop trials	612.66	156.76	594.28	136.00	F = 0.37	0.59	
Reaction time to non-Stroop signals	502.52	93.53	506.54	97.66			
Stroop omissions %	10.81	12.73	8.42	10.02	z = −0.69	0.49	
Non-Stroop omissions %	10.44	11.61	7.69	8.64			
Stroop errors %	31.87	11.75	26.65	15.36	F = 4.86	0.03*	0.07
Non-Stroop errors %	9.03	7.29	5.14	6.07			
Stroop effect	110.15	107.39	87.74	71.75	t = 0.95	0.35	

22q11DS, 22q11 deletion syndrome; CMS, Children's Memory Scale; ED, extradimensional; ID, intradimensional; WISC, Wechsler Intelligence scales for Children. *p<0.05, **p<0.01, ***p<0.001.

Table 4. COMT genotype and cognitive data

	COMT	n	Mean	SD	Statistic	p
Intellectual functioning						
FSIQ	val	11	64.91	8.215	0.23	0.82
	met	23	64.17	9.099		
Performance IQ	val	11	65.45	8.371	0.28	0.79
	met	23	64.48	10.215		
Verbal IQ	val	11	69.36	12.90	t = 0.03	0.98
	met	23	69.26	10.09		
Memory						
Immediate Faces	val	11	6.91	2.587	t = 1.40	0.17
	met	22	5.32	3.301		
Executive functioning						
ID/ED						
EDS errors	val	10	21.30	11.27	U = 94.50	0.81
	met	20	21.25	9.50		
Stages completed	val	10	7.40	.70	U = 98.50	0.95
	met	20	7.45	.83		
Switch						
Premature switch errors	val	9	1.80	1.91	U = 64.50	0.40
Stockings of Cambridge						
Moves above minimum	val	9	3.19	1.26	*t* = 1.25	0.22
	met	19	2.50	1.43		
Subsequent thinking time, seconds	val	9	19.97	2.65	U = 84.00	0.96
	met	19	19.48	3.21		
Spatial Working Memory						
Between-search errors	val	10	12.50	1.21	U = 88.00	0.62
	met	20	11.59	2.71		
Strategy	val	10	40.60	2.76	t = 1.30	0.21
	met	20	39.20	2.80		
Digit span	val	11	6.36	2.063	t = 0.074	0.94
	met	23	6.30	2.245		
Attention/inhibition						
Go–NoGo						
Premature responses to go's	val	11	8.36	9.32	U = 65.00	0.13
	met	18	3.39	3.15		
	met	18	7.66	11.13		

COMT, *catechol-O-methyltransferase*; ED, extradimensional; EDS: extradimensional set-shift, FSIQ, full-scale IQ; ID, intradimensional.

Cognitive and Psychiatric Predictors to Psychosis in Velocardiofacial Syndrome: A 3-Year Follow-Up Study

Kevin M. Antshel, Ph.D., Robert Shprintzen, Ph.D., Wanda Fremont, M.D., Anne Marie Higgins, N.P., Stephen V. Faraone, Ph.D., Wendy R. Kates, Ph.D.

Objective: To predict prodromal psychosis in adolescents with velocardiofacial syndrome (VCFS). **Method:** A total of 70 youth with VCFS, 27 siblings of youth with VCFS, and 25 community controls were followed from childhood (mean age = 11.8 years) into mid-adolescence (mean age = 15.0 years). Psychological tests measuring intelligence, academic achievement, learning/memory, attention, and executive functioning as well as measures of parent and clinician ratings of child psychiatric functioning were completed at both time points. **Results:** Major depressive disorder, oppositional defiant disorder, and generalized anxiety disorder diagnoses increased in the VCFS sample. With very low false positive rates, the best predictor of adolescent prodromal psychotic symptoms was parent ratings of childhood odd/eccentric symptoms and child performance on a measure of executive functioning, the Wisconsin Card Sorting Test. **Conclusions:** Similar to the non-VCFS prodromal psychosis literature, a combination of cognitive and psychiatric variables appears to predict psychosis in adolescence. A child with VCFS who screens positive is noteworthy and demands clinical attention. J. Am. Acad. Child Adolesc. Psychiatry, 2010;xx(x):xxx. **Key Words:** velocardiofacial syndrome (VCFS), 22q11 deletion syndrome, cognition, psychosis, longitudinal

TABLE 1 Number of Participants (Percentage of Sample) with Schedule for Affective Disorders and Schizophrenia for School-Aged Children–Present and Lifetime Version (K-SADS-PL) Diagnoses

	VCFS		Siblings		Control	
Diagnosis	Time 1	Time 2	Time 1	Time 2	Time 1	Time 2
Schizophrenia	0	0	0	0	0	0
Major depressive disorder	14 (18%)	45 (64%)***	1 (3%)	8 (30%)*	2 (5%)	2 (8%)
Bipolar disorder	3 (4%)	0	0	0	0	0
Any mood disorder	17 (21%)	45 (64%)	1 (3%)	8 (30%)*	2 (5%)	2 (8%)
Panic disorder	2 (3%)	0	0	0	0	0
Separation anxiety disorder	4 (5%)	4 (6%)	0	0	0	0
Simple phobia	19 (24%)	12 (17%)*	4 (12%)	2 (7%)	2 (5%)	2 (8%)
Social phobia	2 (3%)	5 (7%)	0	0	0	0
Generalized anxiety disorder	14 (18%)	19 (27%)*	3 (9%)	2 (7%)	6 (15%)	4 (16%)
Obsessive compulsive disorder	3 (4%)	2 (3%)	0	0	0	0
Posttraumatic stress disorder	1 (2%)	0	0	0	0	0
Any anxiety disorder	35 (44%)	37 (53%)	6 (18%)	4 (15%)	7 (17%)	4 (16%)
Enuresis	12 (15%)	6 (9%)*	0	0	0	0
Encopresis	3 (4%)	0	0	0	0	0
Anorexia	0	0	0	0	0	0
Bulimia	0	0	0	0	0	0
ADHD	36 (45%)	29 (41%)	4 (12%)	2 (7%)	15 (38%)	8 (32%)
Oppositional defiant disorder	7 (9%)	14 (20%)**	0	2 (7%)	3 (8%)	4 (16%)
Conduct disorder	0	0	0	0	0	0
Tic disorder	0	0	0	0	0	0
Tourette's disorder	0	0	0	0	0	0
Substance abuse	0	0	0	0	0	0
Substance dependence	0	0	0	0	0	0

Note: McNemar χ^2 tests comparing Time 1 and Time 2 between groups. ADHD = attention-deficit/hyperactivity disorder; VCFS = velocardiofacial syndrome.

*$p < .05$; **$p < .01$; ***$p < .001$.

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ORIGINAL PAPER

Age-dependent clinical problems in a Norwegian national survey of patients with the 22q11.2 deletion syndrome

Kari Lima · Ivar Følling · Kristin L. Eiklid · Solveig Natvig · Tore G. Abrahamsen

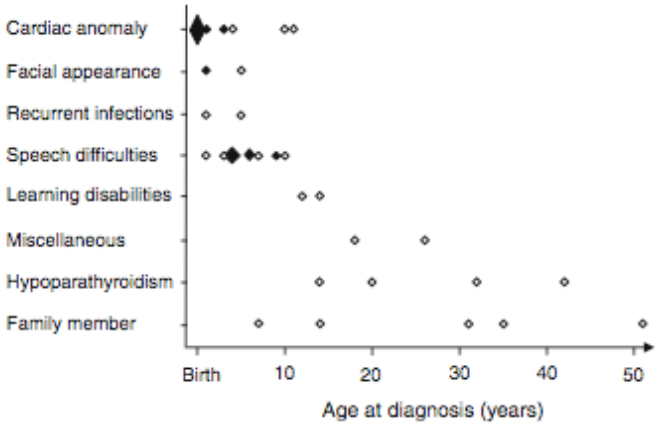

Fig. 1 The main phenotypic feature leading to the positive FISH-test versus age at diagnosis. The *symbols* represent: one patient (◇), two (◆), four (◆), five (◆), and 20 patients (◆). Median age at diagnose 4 years, range 0–51 years. Miscellaneous features: one patient with a muscular VSD, overt cleft palate, hernias, and recurrent infections and one patient with developmental delay, mental retardation, scoliosis, and transient neonatal hypocalcemia

Table 3 Age-related main problems defined by the patients/parents

Age (years)	Number of cases	Main problems
1–2	7	Speech problems
		Recurrent infections
		Feeding difficulties
3–5	11	Speech problems
		Social behavior
		Concentration deficit
		Feeding difficulties
		Cardiac problems
6–10	18	Social behavior
		Concentration deficit and learning disabilities
		Speech problems
11–15	12	Concentration deficit and schoolwork
		Social relations
		Depressive mood
		Hypotonia
16–25	6	Learning disabilities
		Psychiatric problems
		Social relations
26–54	6	Psychiatric diseases
		Social relations
		Money matters

Research in Developmental Disabilities 31 (2010) 864–868

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Research in Developmental Disabilities

Memory in intellectually matched groups of young participants with 22q11.2 deletion syndrome and those with schizophrenia

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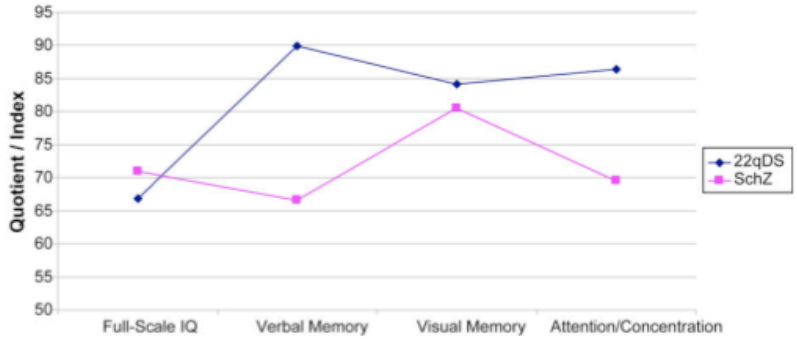
Table 1
Demographic and clinical characteristics of young participants with 22qDS and of those with schizophrenia.

	22qDS ($n = 29$)	Schizophrenia ($n = 15$)	t/χ^2, d.f., P
Males, females: n	15, 14	9, 6	0.27, 1, 0.60
Age			
Range	7.1–14.7	14.2–21.4	
Mean (SD)	11.7 (1.9)	16.8 (1.8)	8.37, 42, <0.001
White, African/Caribbean, Other: n	25, 1, 3	7, 6, 2	Fisher's exact, <0.01
Familial, de novo: n	2, 27	N/A	N/A
On typical, atypical, no medication: n	N/A	4, 9, 2	N/A
Chlorpromazine equivalents: mean (SD)	N/A	286.5 (247.5)	N/A
PANSS positive symptoms: mean (SD)	N/A	15.8 (5.5)	N/A
PANSS negative symptoms: mean (SD)	N/A	18.6 (6.5)	N/A

Table 2
IQ, memory and attention/concentration in young participants with 22qDS and in those with schizophrenia.

	22qDS ($n = 29$)	Schizophrenia ($n = 15$)	t, d.f., P
Full-Scale IQ	66.9 (8.1)	71.0 (10.3)	1.46, 42, 0.15
Verbal memory	89.9 (14.2)	69.2 (15.3)	4.47, 42, <0.001
Visual memory	84.1 (16.3)	80.5 (22.1)	0.62, 42, 0.54
Attention/concentration	86.4 (17.3)	71.3 (13.8)	2.95, 42, <0.01



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journal homepage: www.elsevier.com/locate/jad

Brief report

Affective disorders and other psychiatric diagnoses in children and adolescents with 22q11.2 Deletion Syndrome

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A B S T R A C T

Background: 22q11.2 Deletion Syndrome (22qDS) is a common chromosome deletion syndrome that has been associated with severe psychopathology, including bipolar disorder and schizophrenia, in adults. Assessment of psychiatric diagnoses in children and adolescents with 22qDS is in the early stages of investigation.

Methods: 24 children and adolescents with 22qDS established by chromosomal analysis were randomly selected from a 22qDS clinic. Children and their parents were interviewed by trained psychometricians with a standardized structured diagnostic interview. A diagnosis was considered present if DSM-IV diagnostic criteria were met on either the parent or the child interview.

Results: 24 22qDS subjects (mean age 9.7 ± 3.3 years) had a mean of two DSM-IV psychiatric disorders. 79% met criteria for at least one DSM-IV psychiatric disorder and over one third had three or more diagnoses. 12.5% met criteria for major depression but none had bipolar disorder. Anxiety disorders (54%), attention-deficit/hyperactivity disorder (38%), and oppositional defiant disorder (38%) were common. Although 29% reported at least one psychotic-like symptom, none met criteria for a psychotic disorder.

Limitations: Small sample size may have obscured significant associations. Other limitations included non-blinded interviewers and lack of a simultaneously studied control group.

Conclusion: Affective, anxiety, attentional, and behavioral disorders were relatively common in this randomly selected group of children and adolescents with 22qDS. No child met criteria for bipolar disorder or schizophrenia. Prospective, longitudinal study is needed to determine whether early psychiatric symptomatology in children with 22qDS predicts continuing or more severe psychopathology later in life. Early psychiatric screening and monitoring appears warranted in 22qDS patients.

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Research in Developmental Disabilities

The neuropsychology of 22q11 deletion syndrome. A neuropsychiatric study of 100 individuals

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ABSTRACT

The primary objective of this study was to study the impact of ASD/ADHD on general intellectual ability and profile, executive functions and visuo-motor skills in children and adults with 22q11 deletion syndrome (22q11DS). A secondary aim was to study if gender, age, heart disease, ASD, ADHD or ASD in combination with ADHD had an impact on general intellectual ability and profile. One hundred consecutively referred individuals aged 1–35 years with 22q11DS were given in-depth neuropsychological assessments. Mean full scale IQ was 71 with a normal distribution around this mean. Higher IQ for females than males, and a negative trend for IQ with higher age were found. Intellectual impairment, as well as visuo-motor dysfunction, was found to be related to 22q11DS per se and not to ASD/ADHD. In the area of executive function, the presence of ASD/ADHD predicted poor planning ability in the children in the study.

Psychiatric Disorders and Intellectual Functioning Throughout Development in Velocardiofacial (22q11.2 Deletion) Syndrome

TAMAR GREEN, M.D., DORON GOTHELF, M.D., BRONWYN GLASER, PH.D., MARTIN DEBBANE, PH.D., AMOS FRISCH, PH.D., MOSHE KOTLER, M.D., ABRAHAM WEIZMAN, M.D., AND STEPHAN ELIEZ, M.D.

ABSTRACT

Objective: Velocardiofacial syndrome (VCFS) is associated with cognitive deficits and high rates of schizophrenia and other neuropsychiatric disorders. We report the data from two large cohorts of individuals with VCFS from Israel and Western Europe to characterize the neuropsychiatric phenotype from childhood to adulthood in a large sample. **Method:** Individuals with VCFS (n = 172) aged 5 to 54 years were evaluated with structured clinical interviews for psychiatric disorders and age-appropriate versions of the Wechsler intelligence tests. **Results:** The frequency of psychiatric disorders was high and remarkably similar between samples. Psychotic disorders and depression were uncommon during childhood but increased in rates during adulthood (depressive disorders: 40.7% in young adults [aged 18–24 years]; psychotic disorders: 32.1% in adults [age >24 years]). Cognitive scores were inversely associated with age in subjects with VCFS, including patients without psychosis. Specifically, Verbal IQ (VIQ) scores negatively correlated with age, and the subjects with VCFS and psychotic disorders had significantly lower VIQ scores than nonpsychotic VCFS subjects. **Conclusions:** Neuropsychiatric deficits in individuals with VCFS seem to follow a developmental pattern. The VIQ scores are negatively associated with age and rates of mood, and psychotic disorders increase dramatically during young adulthood. The data presented here support careful monitoring of psychiatric symptoms during adolescence and young adulthood in VCFS. Prospective longitudinal studies are needed to examine the nature of age-related cognitive changes and their association with psychiatric morbidity in VCFS. *J. Am. Acad. Child Adolesc. Psychiatry,* 2009;48(11):1060–1068. **Key Words:** 22q11.2 deletion syndrome, schizophrenia, Verbal IQ, depression mood disorders, neurodevelopmental disorder.

TABLE 1

Prevalence of Current *DSM-IV-TR* Psychiatric Disorders (%) in Individuals With Velocardiofacial Syndrome

Diagnosis	All (n = 172)	Tel Aviv (n = 86)	Geneva (n = 86)	p
Age, y	15.9 ± 9.1	15.7 ± 9.7	16.0 ± 8.5	NS
Male/female, %	90/82 (52.3/47.7)	53/33 (61.6/38.4)	37/49 (43.0/57.0)	.011
Any *DSM-IV* disorder	126 (73.3)	70 (81.4)	56 (65.1)	.012
Any psychotic disorder	17 (9.9)	8 (9.3)	9 (10.5)	NS
Schizophrenia	10 (5.8)	5 (5.8)	5 (5.8)	NS
Schizoaffective disorder	4 (2.3)	2 (2.3)	2 (2.3)	NS
Schizophreniform disorder	1 (0.6)	0	1 (1.2)	NS
Psychotic disorder NOS	1 (0.6)	0	1 (1.2)	NS
Any anxiety disorder	90 (52.3)	48 (48.8)	42 (48.8)	NS
SA[a]	9 (7.7)	5 (8.6)	4 (6.8)	NS
GAD	19 (11.0)	10 (11.6)	9 (10.5)	NS
OCD	27 (15.7)	21 (24.4)	6 (7.0)	.001
PTSD	4 (2.3)	4 (4.7)	0	NS
Panic disorder	1 (0.6)	1 (1.2)	0	NS
Specific phobia	62 (36.0)	30 (34.9)	32 (37.2)	NS
Social phobia	16 (9.3)	9 (10.5)	7 (8.1)	NS
Any mood disorder	26 (15.1)	17 (19.8)	11 (12.8)	NS
Major depressive disorder	10 (5.8)	6 (7.0)	4 (4.7)	NS
Dysthymic disorder	20 (11.6)	14 (16.3)	6 (7.0)	.047
Bipolar affective disorder	1 (0.6)	0	1 (1.2)	NS
Suicide ideation	11 (6.4)	7 (8.1)	4 (4.7)	NS
Suicide attempt	2 (1.2)	2 (2.3)	0	NS
Any disruptive disorder[b]	60 (41.2)	41 (47.7)	19 (32.2)	NS
ADHD[b]	52 (35.9)	37 (43.0)	15 (25.4)	.022
ODD[a]	23 (19.0)	14 (23.3)	9 (15.3)	NS
Conduct disorder	0	0	0	NS
Eating disorder	2 (1.2)	1 (1.2)	1 (1.2)	NS

Note: ADHD = attention-deficit/hyperactivity disorder; GAD = generalized anxiety disorder; NOS = not otherwise specified; NS = not significant; OCD = obsessive-compulsive disorder; ODD = oppositional defiant disorder. PTSD = posttraumatic stress disorder; SA = separation anxiety.

[a]The disorder was evaluated for in individuals younger than 18 years only.

[b]The disorder was evaluated for in individuals younger than 18 years only in the Geneva sample.

Différents domaines de recherche

- Génétique
- Développement cérébral
- Psychiatrie et développement intellectuel
- Models animaux

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LETTERS

Impaired hippocampal–prefrontal synchrony in a genetic mouse model of schizophrenia

Torfi Sigurdsson[1], Kimberly L. Stark[1,2], Maria Karayiorgou[1,4], Joseph A. Gogos[2,3] & Joshua A. Gordon[1,4]

Abnormalities in functional connectivity between brain areas have been postulated as an important pathophysiological mechanism underlying schizophrenia[1,2]. In particular, macroscopic measurements of brain activity in patients suggest that functional connectivity between the frontal and temporal lobes may be altered[3,4]. However, it remains unclear whether such dysconnectivity relates to the aetiology of the illness, and how it is manifested in the activity of neural circuits. Because schizophrenia has a strong genetic component[5], animal models of genetic risk factors are likely to aid our understanding of the pathogenesis and pathophysiology of the disease. Here we study *Df(16)A*$^{+/-}$ mice, which model a microdeletion on human chromosome 22 (22q11.2) that constitutes one of the largest known genetic risk factors for schizophrenia[6]. To examine functional connectivity in these mice, we measured the synchronization of neural activity between the hippocampus and the prefrontal cortex during the performance of a task requiring working memory, which is one of the cognitive functions disrupted in the disease. In wild-type mice, hippocampal–prefrontal synchrony increased during working memory performance, consistent with previous reports in rats[7]. *Df(16)A*$^{+/-}$ mice, which are impaired in the acquisition of the task, showed drastically reduced synchrony, measured both by phase-locking of prefrontal cells to hippocampal theta oscillations and by coherence of prefrontal and hippocampal local field potentials. Furthermore, the magnitude of hippocampal–prefrontal coherence at the onset of training could be used to predict the time it took the *Df(16)A*$^{+/-}$ mice to learn the task and increased more slowly during task acquisition. These data suggest how the deficits in functional connectivity observed in patients with schizophrenia may be realized at the single-neuron level. Our findings further suggest that impaired long-range synchrony of neural activity is one consequence of the 22q11.2 deletion and may be a fundamental component of the pathophysiology underlying schizophrenia.

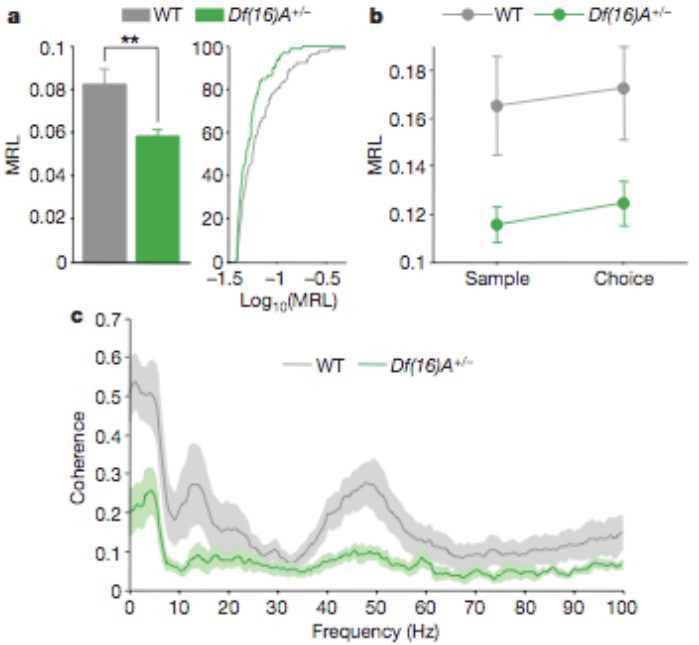

Figure 2 | Reduced hippocampal–prefrontal synchrony in *Df(16)A*$^{+/-}$ mice. **a**, Phase-locking of prefrontal neurons to hippocampal theta (left) and cumulative distribution of phase-locking values (right) in the two genotypes. Phase-locking is stronger in wild-type mice. $^{**}P < 0.01$; WT, wild type. **b**, Phase-locking strength in the centre arm during sample and choice phases. **c**, Coherence between hippocampal and prefrontal field potentials during the choice phase as in **b**. Coherence is lower in *Df(16)A*$^{+/-}$ mice. Data shown, mean ± s.e.m.

Diminished dosage of 22q11 genes disrupts neurogenesis and cortical development in a mouse model of 22q11 deletion/DiGeorge syndrome

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The 22q11 deletion (or DiGeorge) syndrome (22q11DS), the result of a 1.5- to 3-megabase hemizygous deletion on human chromosome 22, results in dramatically increased susceptibility for "diseases of cortical connectivity" thought to arise during development, including schizophrenia and autism. We show that diminished dosage of the genes deleted in the 1.5-megabase 22q11 minimal critical deleted region in a mouse model of 22q11DS specifically compromises neurogenesis and subsequent differentiation in the cerebral cortex. Proliferation of basal, but not apical, progenitors is disrupted, and subsequently, the frequency of layer 2/3, but not layer 5/6, projection neurons is altered. This change is paralleled by aberrant distribution of parvalbumin-labeled interneurons in upper and lower cortical layers. Deletion of *Tbx1* or *Prodh* (22q11 genes independently associated with 22q11DS phenotypes) does not similarly disrupt basal progenitors. However, expression analysis implicates additional 22q11 genes that are selectively expressed in cortical precursors. Thus, diminished 22q11 gene dosage disrupts cortical neurogenesis and interneuron migration. Such developmental disruption may alter cortical circuitry and establish vulnerability for developmental disorders, including schizophrenia and autism.

flect changes in cortical neurogenesis. We focused on two distinct classes of cortical progenitors: basal progenitors–transit amplifying progenitors in the cortical subventricular zone (SVZ)–and apical progenitors–self-renewing radial glial stem cells present in the cortical VZ. Each class can be recognized with combinations of proliferative and molecular markers (Fig. 1). We found reduced frequency of mitotic basal progenitors, identified by phosphohistone 3 labeling (PH3; a G_2/M-phase cell-cycle marker) as well as SVZ location, throughout the embryonic day (E)13.5 LgDel cortex (79% of WT, $P = 0.05$, $n = 5$ per genotype) (Fig. 1 *A–C*; Fig. S1). Analysis of dual BrdU (90-min exposure; S-phase marker) and Tbr2 labeling (basal progenitors) confirms this deficit (76% of WT, t test, $P = 0.049$, $n = 5$) (Fig. 1 *D–F*). When systematically sampled at dorsal, medial, and lateral cortical locations, LgDel S-phase basal progenitor frequency was diminished by 32% in medial cortex ($n = 5$; t test, $P = 0.045$) (Fig. 1*F Middle*), 20% laterally (nonsignificant), and similar to normal dorsally.

Aberrant apical progenitor proliferation or radial migration is not the basis for the basal progenitor proliferation defect. There

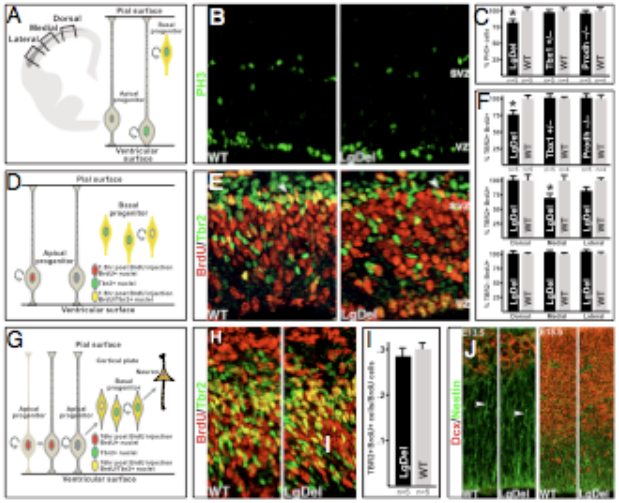

Fig. 1. Diminished 22q11 gene dosage disrupts cortical basal progenitor proliferation. (*A*) Schematic representation of a coronal section through the mouse E13.5 forebrain with the cortical SVZ indicated in gray. Proliferating cells were counted at probe locations shown by boxes, or throughout the entire cortex (*Left*). Schematic representation showing that basal and apical progenitors, both labeled by PH3, are discerned by their positions in the SVZ versus VZ (*Right*). (*B*) PH3 immunolabeling in the E13.5 cortex of WT and Large Deletion mice (LgDel) (10). (*C*) PH3 labeled cell frequency in the SVZ throughout its entire lateral to dorsal extent is significantly reduced in the LgDel cortex (•, $P \leq 0.05$). However, in Prodh$^{-/-}$ deficient or Tbx1$^{+/-}$ mutants, frequency is unchanged. (*D*) Schematic representation of short-pulse BrdU paradigm used to label the S-phase SVZ progenitors. Dual BrdU/Tbr2 immunolabeling allows assessment of S-phase basal (Tbr2+/BrdU+) as well as apical (Tbr2-/BrdU+) progenitor frequency. (*E*) BrdU (90-min exposure) and Tbr2 immunolabeling in the WT and LgDel E13.5 cortex (arrowheads: double-labeled cells). (*F*) Tbr2+/BrdU+ SVZ cells, throughout the entire cortex, are more frequent in WT versus LgDel (•, $P \leq 0.05$). However, their frequency is not changed in *Prodh*$^{-/-}$ or *Tbx1*$^{+/-}$ (*Top*). There is a significant decrease of Tbr2+/BrdU+ cells in the medial and a trend in the lateral E13.5 LgDel cortex (*Middle*). Tbr2-/BrdU+ cell frequency is unchanged at all WT and LgDel E13.5 cortical probe locations (*Lower*). (*G*) BrdU paradigm used to assess apical progenitor production of basal progenitors. The 16-h BrdU exposure provides enough time for a fraction of labeled apical progenitor progeny to migrate toward the SVZ, and express Tbr2. Concurrently, BrdU-labeled basal progenitors down-regulate Tbr2 and migrate toward the cortical plate. The fraction of BrdU+ cells that are also Tbr2+ reflect basal progenitor generation by apical progenitors (54). (*H*) Tbr2+/16 h BrdU+ cells (yellow) in WT and LgDel E13.5 cortex. (*I*) Apical progenitor genesis of basal progenitors (Tbr2+BrdU/BrdU cells) is not significantly different between E13.5 WT and LgDel cortex (medial probe). (*J*) Immunofluorescent labeling in E13.5 and E15.5 WT and LgDel cortex show no disruption of migrating neuroblasts (Dcx, doublecortin) or radial glial processes (nestin) (arrowheads).

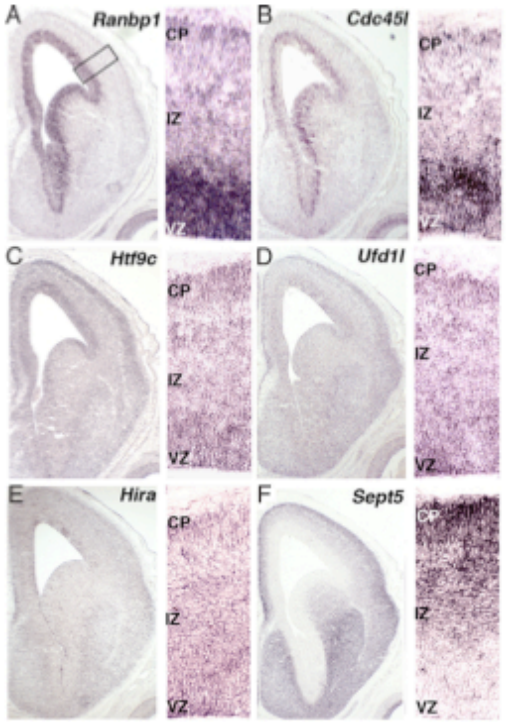

Fig. 2. Expression localization of 22q11 cell-cycle genes during cortical neurogenesis. In all images, the entire cortical hemisphere from an E14.5 WT embryo is shown (*Left*), whereas higher magnification of VZ, intermediate zone (IZ), and cortical plate (CP) is shown (*Right*). ISH shows that 22q11 cell-cycle genes are enhanced in the VZ [*Ranbp1* (*A*); *Cdc45l* (*B*)] enhanced in both the VZ and CP [*Htf9c* (*C*); *Ufd1l* (*D*)] lightly, but broadly expressed [*Hira* (*E*)] or enhanced in the CP [*Sept5* (*F*)].

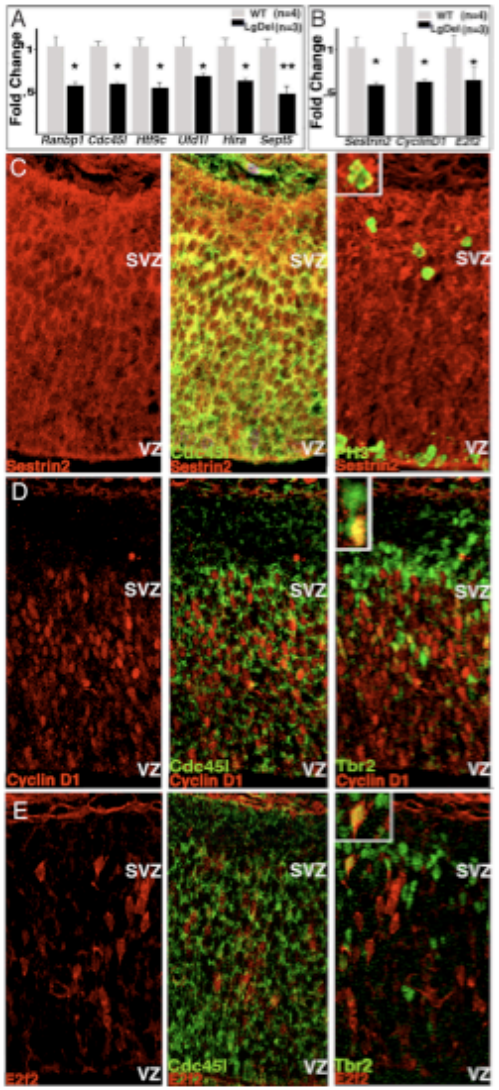

Fig. 3. Changes in cell-cycle gene expression in embryonic LgDel cortex. (*A*) Six 22q11 putative cell-cycle genes show diminished expression by ~50% (•, $P \leq 0.05$; ••, $P \leq 0.001$) relative to WT E13.5 cortex. (*B*) Quantitative PCR verifies that three cell-cycle gene transcripts are diminished by ~50% (•, $P \leq 0.05$) in E13.5 LgDel cortex relative to WT as suggested by cell-cycle array. (*C–E*) Protein products of these three genes are detected in cells that also express Cdc45l, PH3, or Tbr2. (*C*) Sestrin2 (*Left*), colabeled with Cd45l (*Center*), or PH3 (*Right*). (*D*) CyclinD1 in E13.5 cortex (*Left*), colabeled with Cdc45l (*Center*), or Tbr2 (*Right*). (*E*) E2f2 in E13.5 cortex (*Left*), colabeled with Cdc45l (*Center*), or Tbr2 (*Right*).

laminar specificity of this change using markers for molecularly distinct cortical neurons. There was a 20% decrease in the frequency of neurons labeled for Cux1, a layer 2–4 selective marker (23), in the medial LgDel cortex ($n = 5$ per genotype; t test, $P = 0.02$) (Fig. 4*D*). In contrast, the frequency of neurons labeled for Tbr1, a layer 5/6 selective marker (24), is unchanged (Fig. 4*D*). Also, Cux1 neuron frequency is unchanged at all cortical sites in $Tbx1^{+/-}$ mice and $Prodh^{-/-}$ deficient mice (data not shown).

To determine whether this specific change in layer 2–4 neuron frequencies reflects altered basal progenitor proliferation at E13.5 (Fig. 1), we analyzed the frequency of E13.5 birth-dated Cux1 or Tbr1 neurons in the P5 cortex. The frequency of E13.5 BrdU birth-dated/Cux1 double-labeled neurons was diminished by 50% only at the medial location ($n = 4$ LgDel, $n = 5$ WT; $P = 0.01$) (Fig. 4*E*). However, there was no significant difference in E13.5 BrdU injected/Tbr1 labeled layer 5/6 cells (Fig. S4). There was no evidence of compensation by accelerated neurogenesis later in development. We found no significant difference in E18.5 BrdU/Cux1 cell frequency between genotypes (Fig. 4*E*). Last, we did not see prolonged neurogenesis. E19.5 birth-dated neurons were not present in LgDel or WT P5 cortex (data not shown). Apparently, proliferative changes in E13.5 basal progenitors prefigure a corresponding change in the frequency of supragranular projection neurons in the medial cortex of LgDel mice.

Conclusions

- Un domaine de recherche très actif
- Impact majeur des neurosciences sur la compréhensions des troubles associés au 22q11

Perspectives futures

- Recherches sur des molécules modifiant ou modulants les cascades métaboliques en rapport avec le 22q11
- Essais médicamenteux et validation des traitements par des approches de neuroimagerie
- Synapsy: un acteur majeur dans la recherche européenne sur le 22q11

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