Best clinical practice – when and how to diagnose ASD



Maria Luisa Scattoni

Coordinator of the Italian Network for early detection of Autism Spectrum Disorders (NIDA) Istituto Superiore di Sanità



EARLY DETECTION

In the absence of targeted pharmacological therapies, early surveillance and assessment leading to early intervention represents the only successful strategy to reduce the severity of symptoms and improve quality of life for children and their families.



Autism spectrum disorder (ASD) is often diagnosed after 3-4 years of age despite the presence of impairment in a range of skills from the earliest months of life

EARLY DETECTION: METHODS

- Parental reports
- Home-videos

Retrospective studies



PARENTAL REPORTS

First alarm signs retrospectively recognised between 14 and 19 months:

Medical consultation at 2 year of age requested for:

- ✓ Language delay
- ✓ Low reciprocity
- ✓ Regulation disorder
- ✓ Sterotipated behaviors

75% report them below 18 months of age

25% report them below 12 months of age

First reported alarm signs:

- ✓ No social smile
- No name response
 - Absence of initiative and responsivity
 - Motor development difficulties



From the study of the first symptoms to the study of the emergence of social skills and intersubjectivity, from the analysis of the developmental trajectories of vocalizations and movement to the analysis of the interactions between the child and his caregivers



Original article

An exploration of symmetry in early autism spectrum disorders: Analysis of lying

Gianluca Esposito^{a,*}, Paola Venuti^a, Sandra Maestro^b, Filippo Muratori^b

^a Department of Cognitive Science, University of Trento, Italy ^b Division of Child Neuropsychiatry, IRCCS Stella Maris and University of Pisa, Pisa, Italy Received 14 November 2007; received in revised form 9 April 2008; accepted 19 April 2008

Lying position at 5 months





Symmetry

No symmetry

Original article

Analysis of unsupported gait in toddlers with autism

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Received 14 April 2010; received in revised form 18 June 2010; accepted 21 July 2010

Unsupported gait at 12 months



Symmetry

No symmetry



JIDR

Journal of Intellectual Disability Research

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Research in Developmental Disabilities

Research

Differential brain responses to cries of infants with autistic disorder and typical development: An fMRI study

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disorder and typical development

Gianluca Esposito ^{a,b,*}, Jun Nakazawa ^{c,*}, Paola Venuti ^b, Marc H. Bornstein ^d

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RED FLAGS:



No big smiles or other warm, joyful expressions by six months or thereafter



No back-and-forth sharing of sounds, smiles or other facial expressions

by nine months

No babbling

by 12 months

No back-and-forth gestures such as pointing, showing, reaching or waving by 12 months

No words

by 16 months

No meaningful, two-word phrases (not including imitating or repeating) by 24 months





Disengagement/shifting attention



Contact searching



Visual attention to social stimoli



Reactivity for sensorial stimoli



Response to name



Any loss of speech, babbling or social skills at any age

Language trajectories



HIGH RISK INFANTS

PEDIATRACES

Recurrence Risk for Autism Spectrum Disorders: A Baby Siblings Research Consortium Study

Sally Ozonoff, Gregory S. Young, Alice Carter, Daniel Messinger, Nurit Yirmiya, Lonnie Zwaigenbaum, Susan Bryson, Leslie J. Carver, John N. Constantino, Karen Dobkins, Ted Hutman, Jana M. Iverson, Rebecca Landa, Sally J. Rogers, Marian Sigman and Wendy L. Stone *Pediatrics*; originally published online August 15, 2011; DOI: 10.1542/peds.2010-2825

Recurrence risk up to 18% (25.9% for boys 9.6% for girls)

Early detection: methods

- Parental reports
- Home-videos

Retrospective studies

Prospective studies

- Siblings
- At risk population



BRSC (USA) & BASIS (UK)

- 2003: Autism Speaks High Risk Baby Siblings Research Consortium (BSRC)
- 2011: British Autism Study of Infant Siblings (BASIS)



The Baby siblings network bring together research groups from around the world with the mission of discovering the earliest predictors of autism. Journal of Child Psychology and Psychiatry 54:7 (2013), pp 763-771

PSYCHOLOGY AND PSYCHIATRY



Quality of interaction between at-risk infants and caregiver at 12–15 months is associated with 3-year autism outcome

Ming Wai Wan,¹ Jonathan Green,¹ Mayada Elsabbagh,² Mark Johnson,² Tony Charman,³ Faye Plummer,¹ and the BASIS Team*

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lings. **Results:** Parent nondirectiveness and sensitive responsiveness differed in relation to ASD/risk status (at-risk ASD, at-risk no-ASD and low-risk) at both 6 and 12 months. At 6 months, infant liveliness was lower in the at-risk groups; at 12 months, infant attentiveness to parent and positive affect were lower in the at-risk group later diagnosed with ASD. Dyadic mutuality and intensity of engagement showed a group effect at 12 months. Dyadic mutuality, infant positive affect and infant attentiveness to parent at 12 months (but not 6 months) predicted 3-year ASD outcome, whereas infant ASD-related behavioural atvoicality did not. **Conclusions:** This is the first prospective evidence that early dvadic

Mutual gaze (i.e. infant and parent making eye contact)

Infant affect





Joint attention



Infant/parent touching each other

THE JOURNAL OF CHILD PSYCHOLOGY AND PSYCHIATRY

Journal of Child Psychology and Psychiatry 52:5 (2011), pp 588-598

Out of the mouths of babes: vocal production in infant siblings of children with ASD

Rhea Paul,¹ Yael Fuerst,² Gordon Ramsay,^{1,3} Kasia Chawarska,¹ and Ami Klin¹

Background: Younger siblings of children with autism spectrum disorders (ASD) are at higher risk for acquiring these disorders than the general population. Language development is usually delayed in children with ASD. The present study examines the development of pre-speech vocal behavior in infants at risk for ASD due to the presence of an older sibling with the disorder. **Methods:** Infants at high risk (HR) for ASD and those at low risk, without a diagnosed sibling (LR), were seen at 6, 9, and 12 months as part of a larger prospective study of risk for ASD in infant siblings. Standard clinical assessments were administered, and vocalization samples were collected during play with mother and a standard set of toys. Infant vocal behavior was recorded and analyzed for consonant inventory, presence of canonical syllables, and of non-speech vocalizations, in a cross-sectional design. Children were seen again at 24 months for provisional diagnosis. **Results:** Differences were seen between risk groups for certain vocal behaviors. Differences in vocal production in the first year of life were associated with outcomes in terms of autistic symptomotology in the second year. **Conclusions:** Early vocal behavior is a sensitive indicator of heightened risk for autistic symptoms in infants with a family history of ASD. **Keywords:** Autism, speech, vocalization, infant siblings.

 Table 3 Mean (and s.d.) vocal productions in two risk groups

Age	Risk group	# Total vocalizations (speech + non-speech)	# Speech-like vocalizations	Total # consonants	# Early consonants	# Middle consonants	# Late consonants	% Canonical syllables	% Non-speech productions
6 mo.	HR	36.5 (27.4)	15.0 (16.0)	2.5 (2.9)	1.5 (1.7)	.5 (1.1)	.5 (.9)	4.5 (7.0)	60.2 (28.6)
	LR	39.2 (27.8)	18.3 (15.3)	37 (3.3)	2.1(2.2)	1.1 (1.4)	.5 (.9)	0.0 (11.5)	57.0 (25.2
9 mo.	HR	25.7 (19.6)	15.1 (16.2)	2.7 (3.0)	1.9 (1.7)	.5 (.9)	.4 (.8)	8.7 (11.5)	50 6 (21 7)
	LR	31.1 (18.6)	.2.6 (16.4	5.6 (3.9)	3.2 (2.1)	1.3 (1.4)	1.1 (1.1)	20.5 (17.6)	34.0 (24.2)
12 mo.	HR	35.2 (18.1)	12.6 (16.8)	0.26 (2.6)	3.8 (2.2)	1.6 (1.2)	.8 (.9)	27 1 (24.9)	36.5 (28.4)
	LR	39.1 (18.1)	31.9 (15.7)	7.3 (3.7)	4.5 (2.1)	1.8 (1.5)	1.0 (1.1)	28.8 (19.0)	19.3 (16.1)

HR = High Risk group; LR = Low R. L. g. and Significant difference between groups at p < .05.





doi:10.1111/j.1469-7610.2010.02332.x

Attention to eyes is present but in decline in 2–6–month–old infants later diagnosed with autism

Warren Jones^{1,2,3} & Ami Klin^{1,2,3}

Infants later diagnosed with autism spectrum disorders exhibit mean decline in eye fixation from 2 to 6 months of age, a pattern not observed in infants who do not develop ASD.



Infancy, 2013 Sep;18(5):639-661.



Posture Development in Infants at Heightened vs. Low Risk for Autism Spectrum Disorders.

Nickel LR¹, Thatcher AR, Keller F, Wozniak RH, Iverson JM.

Author information

Abstract

Evidence suggests that children and adults diagnosed with **autism** spectrum disorders (ASD) exhibit difficulties with postural control. Retrospective video studies of **infants** later diagnosed with ASD indicate that **infants** who eventually receive an ASD diagnosis exhibit delays in postural development. This study investigates early **posture** development prospectively and longitudinally in 22 **infants** at heightened biological risk for ASD (HR) and 18 **infants** with no such risk (Low Risk; LR). Four **HR infants** received an **autism** diagnosis (AD **infants**) at 36 months. **Infants** were videotaped at home at 6, 9, 12, and 14 months during everyday activities and play. All **infant** postures were coded and classified as to whether or not they were **infant**-initiated. Relative to LR **infants**, **HR infants** were slower to develop skill in sitting and standing postures. AD **infants** exhibited substantial delays in the emergence of more advanced postures and initiated fewer **posture** changes. Because **posture** advances create opportunities for **infants** to interact with objects and people in new and progressively more sophisticated ways postural delays may have cascading effects on opportunities for **infant** exploration and learnii These effects may be greater for **infants** with ASD, for whom **posture** delays are more significant.

HR infants were slower to develop skill in sitting and standing postures



Mean total duration of Lying, Sitting, and Standing postures for LR, HR, and AD infants at 6, 9, 12, and 14 months of age. Error bars indicate standard errors.





Ready, Set, Go! Low Anticipatory Response during a Dyadic Task in Infants at High Familial Risk for Autism



ORIGINAL RESEARCH published: 25 May 2016 doi: 10.3389/fpsyg.2016.00721

Rebecca J. Landa^{1,2*}, Joshua L. Haworth^{1,2} and Mary Beth Nebel^{3,4}

READY



SET (rolling)



GO (anticipation)



Visual- motor coupling, or action anticipation, during a dynamic, interactive ball-rolling activity.

LR and HR infants demonstrated context appropriate looking behavior, both before and during the ball's trajectory toward them.

HR infants were less likely to exhibit context appropriate anticipatory motor response to the approaching ball (moving their arm/hand to intercept the ball) than LR infants.

This finding did not appear to be driven by differences in motor skill between risk groups at 6 months of age and was extended to show an atypical predictive relationship between anticipatory behavior at 6 months and preference for looking at faces compared to objects at age 14 months in the HR group.

LETTER

Early brain development in infants at high risk for autism spectrum disorder

Heather Cody Hazlett^{1,2}, Hongbin Gu¹, Brent C. Munsell³, Sun Hyung Kim¹, Martin Styner¹, Jason J. Wolff⁴, Jed T. Elison⁵, Meghan R. Swanson², Hongtu Zhu⁶, Kelly N. Botteron⁷, D. Louis Collins¹¹, John N. Constantino⁷, Stephen R. Dager^{8,9}, Annette M. Estes^{9,10}, Alan C. Evans¹¹, Vladimir S. Fonov¹¹, Guido Gerig¹², Penelope Kostopoulos¹¹, Robert C. McKinstry¹³, Juhi Pandey¹⁴, Sarah Paterson¹⁵, John R. Pruett Jr⁷, Robert T. Schultz¹⁴, Dennis W. Shaw^{8,9}, Lonnie Zwaigenbaum¹⁶, Joseph Piven^{1,2} & the IBIS Network*





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High-Risk Infant with Increased Extra-Axial CSF; Diagnosed with ASD at 24



Example brain images indicating the presence of increased extra-axial CSF. (A) T1weighted coronal images of a low-risk infant with normal MRI at 6, 12, and 24 months. (B) T1-weighted coronal images of a high-risk infant with increased extra-axial CSF at 6, 12, and 24 months. This child was diagnosed with ASD at 24 months.



Italian Network for early detection of Autism Spectrum Disorders (NIDA)

Project CCM 2012 Associazione Bambini delle Fate Italian Minister of Health Progetto BrainView (H2020) Fondazione Italiana Autismo Onlus



12 months: risk diagnosis

0-12 months: risk indexes





AIM of the NETWORK

Clinical and observational protocol for monitoring vocalsocial-motor-cognitive development (from birth to three years old) of low- and high risk infants/toddlers



A WORKING MODEL THAT MAY BE EXTENDED TO: 1. OTHER AT-RISK POPULATIONS, 2. OTHER CLINICAL CONTEXTS 3. THE ENTIRE ITALIAN TERRITORY





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- 11) Università di Trento (Paola Venuti e Gianluca Esposito)
- 12) Azienda Ospedaliera Universitaria Senese (Roberto Canitano-Valeria Scandurra)



RECRUITMENT

Inclusion criteria

- Low risk infants: born after 37 gestational weeks (GW) and with birth weight > 2400 gr
- Baby siblings (high risk): siblings of children diagnosed with ASD
- Small for Gestational Age (SGA) infants: birth weight below the 10th percentile
- **<u>Premature</u>**: born between 26 and 31 GW

Exclusion criteria

- Infant born before 37 GW and/or with birth weight < 2400 gr
- Presence of known genetic syndrome (in proband or infant) related to ASD (e.g. TSC, FXS, 22q11, 16p11.2, Rett'syndrome)
- Presence of severe cardiovascular, lung, kidney, endocrinological or hematological diseases

ACCOMPAGNA PER MANO LA RICERCA



Accompagnare per mano la ricerca vuol dire scegliere di avere un ruolo attivo nella costruzione di un futuro migliore per i nostri figli

Se siete interessati a partecipare ai nostri studi o a conoscere meglio le nostre attività, scrivete una mail a: marialuisa.scattoni@iss.it

Progetto di studio coordinato dall'Istituto Superiore di Sanità

Unità Operative

IRCCS Fondazione Stella Maris

Istituto di Scienze Applicate e Sistemi Intelligenti, Consiglio Nazionale delle Ricerche

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Dipartimento di Psicologia e Scienze Cognitive dell'Università di Trento

Azienda Ospedeliera Universitaria Integrata di Verona



Stai diventando mamma per la seconda volta?

Nessuno più di te sa quanto siano importanti i primi anni di vita di un bambino

Tu e il tuo bambino potete aiutarci a capire...

0



Spontaneous infant crying





<u>Crying can be viewed</u> <u>as both part of a first</u> <u>communicative system and</u> <u>an early social structure</u> <u>in human development</u>



A number of studies that examined cries of infants with specific medical conditions related to neurological damage have shown that fundamental frequency (f_0) is particularly influenced by neurological damage.

Higher level of f₀:

- Brain damage
- Meningitis
- Asphyxia

Lower levels of f₀:

- Hypothyroidism
- Children with Trisomy 13, 18, 21





F₀ developmental trajectory



Analysis of General Movements



DEVELOPMENTAL COURSE OF GENERAL MOVEMENTS



Postterm Age (weeks)

Prechtl's M GM Optimality L	t ements		
	(Ferrari et al 1990, modified)		
Name:			
Date of birth:	Gestational age at birth:	weeks	
Recording date:	3. Amplitude	variable, full range	2
		predominantly small range	1
1. Quality		predominantly large range	1
		mainly one range, not variable	1
	4. Speed	variable	2
		monotonously slow	1
2. Sequence		monotonously fast	1
		mainly one speed, not variable	1
	5. Space	from horizontal to vertical plane	2
		not the full space used	1
	6. Rotatory components	present, fluent and elegant	2
		no or just a few rotations	1
	7. Onset and offset	smooth	2
		minimal fluctuations or abrupt	1
	8. Tremulous movements	absent	2
		present	1
	GM Optimality Score :	Maximum 18	Minimum: 8.

TRAJECTORY OF GENERAL MOVEMENTS

GM optimality score: Maximum 18; Minimum 8







Attention to social stimuli SCIENTIFIC REPORTS

OPEN Difference in Visual Social Predispositions Between Newborns at Low- and High-risk for Autism

Received: 03 August 2015 Accepted: 29 April 2016 Published: 20 May 2016

Elisa Di Giorgio¹, Elisa Frasnelli^{1,2}, Orsola Rosa Salva¹, Scattoni Maria Luisa³, Maria Puopolo³, Daniela Tosoni¹, NIDA-Network[§], Francesca Simion^{4,5} & Giorgio Vallortigara¹



AREA OF INTEREST: FACE AND EYE GAZE

Di Giorgio e al., Sci Rep 2016



HR

12

LR

14



LR

14

DIRECT *vs.* AVERTED EYE-GAZE HR 12

NIDA Network Protocol Summary

Assessment/Diagnostic tools	6m	12m	18m	24m	36m
VinelandAdaptive Behavior Questionnaire (VABS PL) II		x	X	Х	Х
MacArthur Communicative Development Inventory		x	X	Х	X
Questionario Temperamento (QUIT)	Х	X	х	Х	Х
M-CHAT			Х		
Child Behavior Checklist (CBCL)			Х	Х	Х
Griffiths (GMDS)	Х	X	X	Х	Х
Autism Observation Scale for Infants (AOSI)	Х	X			
ADOS-2 (modulo Toddler)		X	X	Х	
ADOS-2 (modulo 1 o 2)					Х
Autism Diagnostic Interview –Revised (ADI-R)					X
Parenting Stress Index (PSI)	Х	Х	Х	Х	Х





OMICS panel:

1) High risk infants

At 6 and 12 months





At the twelve-month-visit of the high risk infants:

Urines

(10 ml)

EDTA

tubes

(10 ml)

2) Unaffected and ASD siblings

3) Parents

Tempus for

RNA tube

At 18 and 24 months





CONCLUSIONS

Establishment of normative values for the vocal, motor and social maturation profile in infants can be used not only for early diagnosis of ASDs, but also to identify other neurodevelopmental disabilities (i.e. intellectual disability, language or motor delay).

A WORKING MODEL THAT MAY BE EXTENDED TO OTHER AT-RISK POPULATIONS

Early detection: methods

- Parental reports
- Homevideos

Retrospective studies

Prospective studies

- Siblings
- High-risk populations

• Large scale screening (paediatricians/parents)

- Well-child surveillance protocol by paediatricians
- Kindergarten teachers training

Screening



Eur Child Adolesc Psychiatry (2014) 23:1005-1021

101

Map of the ASD European screening studies



Over 70,000 children have been screened in Europe using 18 different screening procedures

		Tuble T Tibb Screening (0015							
		Screening tool (long name)	Short name	Admin. time (min)	Admin. age (months)	Admin. method ^b	Items	Sensitivity	Specificity
	<	Level 1 ^a Checklist for Autism in Toddlers [16, 17]	CHAT	5-10	18	Parent + clinician	9 + 5	0.18-0.38	0.98-1.0
Population-based		Social Communication Ouestionnaire [18]	SCO	15-20	36-82	Parent rated	40	0.74	0.54
screening		Modified-Checklist for Autism in Toddlers [19]	M-CHAT	5-10	18-30	Parent rated	23	0.87	0.99
		Quantitative Checklist for Autism in Toddlers [20]	Q-CHAT	5	16-30	Parent rated	25	-	-
		Communication and Social Behaviour Scale- Infant and Toddlers Checklist [21]	CSBS-DP	5-10	16-30	Parent rated	24	-	-
	$\boldsymbol{\mathcal{C}}$	Level 2 ^a							
ASD specific		Developmental Behaviour Checklist-primary care version [28]	DBC-ES	5-10	18-48	Parent rated	96	0.83	0.48
screening tool		Screening tool for autism in 2 years old [29]	STAT	20	24-35	Child care worker rated	12	0.83	0.86
performed on		Screening for infants with developmental deficits and/or autism [30]	SEEK	30-40	8	Parent + clinician rated	9 + 28	-	-
development delay		Pervasive Developmental Disorders Rating Scale [31]	PDDRS	60	>12	Parent rated	51	-	-
		Autistic behavioural indicators instrument [32]	ABII	30	24-72	Clinician rated	18	-	-
		Autism Behaviour Checklist [33]	ABC	15	>36	Parent rated	57	0.58	0.76
		Childhood Rating Scale [34]	CARS	15 - 20	>24	Clinician rated	15	0.92-0.98	0.85
		Autism detection in early childhood [35]	ADEC	12	12	Parent or nurse rated	16	0.79–0.94ª	0.88-1.00ª
		Baby and Infant Screen for Children with Autism Traits [36–39]	BISCUIT	15	17-37	Parent rated	42	0.84	0.86
		Three-item direct observation screen test [40]	TIDOS	5	18-60	Clinician rated	3	0.95	0.85

Table 1 ASD screening tools

^a Level 1 = population-based screening; level 2 = ASD specific screening tool after developmental delay risk confirmation at a routine developmental surveillance

^b Clinician = usually paediatrician or primary care physician

Web-based platform



Diagnostic Assessment

ADOS

3

1

- Griffiths' Mental Development
 Scale
- Vineland Adaptive Behavior
 Scale

CHAT-MCHAT-QCHAT



2

7. Per quanto tempo il vostro bombino può mantenene il suo interesse su un oggetto che giro (es. lovatrice, ventilotore, ruate della naccchinice)?
O dienzi ora deci muni or pool di muniti meno du vi minto
8. Quarte parele à ventre banches à la grado di dire? Researe: ente la tomore latate e parlex Presed 20 parle 15-60 parle 9: di Doparle più di Doparle
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Intellify 2000 Constant of general gen
12. Il voitro banbino 'usa' la vostra mana per compiene urizzione che non se fane? (es. mette la vostra mana sulla moniglia della parta ganda vole che la apriote o su un giocattele quando voale che la attiviste).
Refer unite al giarne gastiche wirts al giarne gastiche wirts a sertimono nesi dura witho a settimono nesi



Well-child surveillance protocol



Neurodevelopment assessment (with a special focus on socio-comunicative skills) by paediatricians



Kindergarten teachers training



Early signs identification



Paediatrician assessment



Unusual visual fixations Unusually strong Abnormal and persistent examrepetitive ination of objects behaviors Spending unusually long periods of time repeating (()an action, such as looking at their hands

Delayed

Neutral facial tones and

intentional

decreased efforts to gesture

and gain parent attention

communication

Lack of ageappropriate sound development

Delayed development of vowel sounds, such as "ma ma, da da, ta ta"

or rolling an object

AUTISM EARLY SIGNS IN INFANTS





Greater interest in objects than people and difficult to sustain face-to-face interactions

UCDAVIS MIND INSTITUTE

BEST CLINICAL PRACTICES: suggestions

- Screening procedures ASD-specific questionnaires (M-CHAT, Q-CHAT etc.)
- Protocol for assessing and promoting neurodevelopment (well-child surveillance protocol – paediatricians)
- Web-based platform to connect paediatricians/ neonatologists with the child psychiatric/neurologic units
- Monitoring of at-risk populations: siblings of children with ASD, prematures and SGA etc.



Thank you for your attention



Italian Network for early detection of Autism Spectrum DIsorders (NIDA) BRAINVIEW Marie Skłodowska-Curie Actions (MSCA) Innovative Training Networks (ITN) H2020-MSCA-ITN-2014







EUROSIBS The European Babysibs Autism Research Network



