






Identifying signs of risk in the early development of autism: Current challenges and new research proposals in Europe

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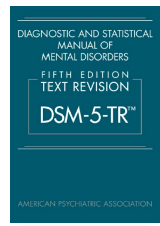
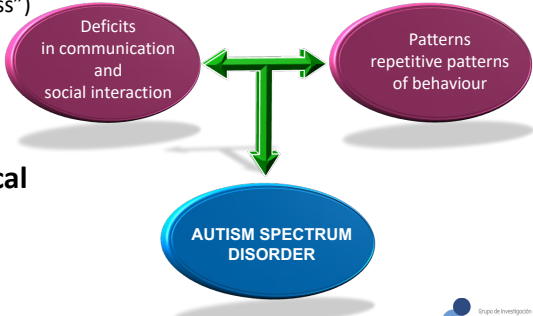


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Autism Spectrum Disorder (ASD)

- Diagnostic category encompassing all those patients who share two essential characteristics :
 - Deficits in social interaction and communication
 - Behavioral abnormalities, in the form of either
 - Rrepetitive behaviors (“stereotypies”),
 - Difficulties in adapting to change (“insistence on sameness”)
 - Restricted interests.

High degree of inter-individual variability in clinical symptomatology (severity levels & specifiers)



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Increased interest in the early detection of autism spectrum disorder (ASD)

- Can improve the quality of life of people with autism.
- May provide an important opportunity for timely intervention
 - Has been considered “essential to achieving the best outcomes”
- It may be the best opportunity to influence neural connectivity at a time of optimal brain plasticity.
- Early detection for families:
 - More positive experience than dealing with a generally slow and unexpected diagnostic process
 - Higher levels of acceptance of the diagnosis
 - Lower levels of stress
 - More effective coping strategies

(French & Ellis, 2018; Pierce, Courchesne, & Bacon, 2016)

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Early detection is the gateway to early intervention

- Early intervention is a beneficial strategy
 - Leads to better outcomes for the child (brain plasticity)
 - Provides better understanding of the child
 - Provides support for parents
 - Allows for adaptation of the environment
 - Strengthens resource networks
 - Prevents or reduces concurrent or secondary problems
 - Improves quality of life for the child and family
 - Family planning
 - ...

Dawson, Rieder & Johnson, 2023; French & Kennedy, 2018; Sandbank et al., 2020

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ASD as a neurodevelopmental disorder and early detection & intervention

Early Detection and Early Intervention

- The longer the child maintains an atypical developmental pattern, the more difficult it is to recover a typical developmental trajectory.
- The earlier the risk of ASD is detected, the more likely it is that intervention will succeed in changing the atypical trajectory.

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Early detection research started 30 years ago ...

- First studies of early detection of ASD in the 1990s. :
 - Johnson, Siddons, Frith y Morton (1992)
 - Visual/auditory tests - Autism at 18m
 - Baron-Cohen, S., Allen, J., y Gillberg, C. (1992; 1996, 2000)
 - CHAT

CAN AUTISM BE PREDICTED ON THE BASIS OF INFANT SCREENING TESTS?

Mark H. France, Uta Frith, John M. ...

Brief Reports

British Journal of Psychiatry (1996), 168, 158-163

Can Autism be Detected by The Needle, the Hay?

SIMON BARON-COHEN, JANE ALLAN ...

Autism is currently detected only at about three years of age. This study aimed to establish if detection of autism was possible at 18 months of age. We screened 41 18-month-old toddlers who were at high genetic risk for developing autism, and 50 randomly selected ...

A Screening Instrument for Autism at 18 Months of Age: A 6-Year Follow-up Study

GILLIAN BAIRD, F.R.C.PAED., TONY CHARMAN, PH.D., SIMON BARON-COHEN, PH.D., ANTONY COX, F.R.C.PSYCH., JOHN SWETTENHAM, PH.D., SALLY WHEELWRIGHT, B.A., AND AURIOL DREW, M.A.

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But making an early diagnosis of autism is easier said than done

- Access to diagnosis:
 - 42 months for children under 7 years old
 - 36 months for children under 9 years of age
 - Most cases detected between 32 and 46 months
 - Being female and having better language are associated with later diagnosis (Salomone et al., 2015)
 - Children diagnosed very early may represent only a sub-set of the autism constellation
- Age of entry into intervention: 42.2 months

Child: care, health and development
Original Article doi:10.1111/ich.12261

Child's verbal ability and gender are associated with age at diagnosis in a sample of young children with ASD in Europe

E. Salomone,^{*} T. Charman,^{*} H. McConachie[†] and P. Warreyn[‡]

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<https://doi.org/10.1007/s10803-019-04253-0>

ORIGINAL PAPER

Early Detection, Diagnosis and Intervention Services for Young Children with Autism Spectrum Disorder in the European Union (ASDEU): Family and Professional Perspectives

Alvaro Bejarano-Martin¹ · Ricardo Canal-Bedia¹ · María Magán-Maganto¹ · Clara Fernández-Alvarez¹

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In Spain 20 years ago...

Study on diagnostic delay in ASD; N= 646 families. (Ministry of Health, 2003)

22 months 26 months 54 months

← Diagnostic delay →

← Gap between concern and diagnosis →

Birth 1 2 3 4 5 6

Age in years →

First concerns (32 months) Diagnosis

First query to the paediatrician

EARLY INTERVENTION

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Why is autism detected and diagnosed so late?

Variety of Symptoms and Clinical Presentations

Development of Symptoms

Lack of Public Knowledge and Awareness

Limited Access to Specialised Health Care

Denial or Normalisation of Symptoms

What underlies this reality?

There is no single biological or behavioural marker with a robust positive predictive value for autism

We do not know which early signs are unequivocal.

We need to identify signs with predictive value at different ages



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Looking for early signs

- Retrospective studies
 - Based on the use of home video footage and questionnaires about the first months/years of life of children with autism.
 - Helped to better understand the development of autism in the first years of life.
- Longitudinal (prospective) studies
 - This type of research follows groups of high-risk babies over time to observe how autism develops.
 - E.g., babies who already have an older sibling with ASD; preterm babies, etc.
 - Allow early signs of autism to be identified before the disorder develops.
 - Provide precise information about the sequence and course of autism development.
 - Help to determine risk factors for autism.



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Longitudinal (prospective) studies

- There are two major international consortia
 - Bring together several research groups that are focused on this methodology
 - Autism Baby Siblings Research Consortium
 - Several groups mainly from North America, Canada and Europe and
 - The Studying Autism and ADHD in the eaRly yearS (STAARS) project
 - Several groups from Europe
- These studies have identified four core domains
 - Attentional flexibility,
 - Social attention and engagement
 - Prelinguistic development,
 - Sensory and motor differences
- Many group differences have been found
 - But the field requires more repetitions before any test can begin to achieve candidate marker status (Jones et al., 2014).

Dawson, Rieder & Johnson, 2023; Fletcher-Watson & Happé, 2019; French & Kennedy, 2018)

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Looking for early signs (Studies on new screening tools)

- Are parent-reported early detection tools or direct observation protocols.
 - These are tools that assess a range of behaviours (social communication, repetitive behaviours, sensory sensitivity).
 - E.g. in Europe:
 - Checklist for Autism in Toddlers (Baron-Cohen, et al., 1992)
 - Checklist for Early Signs of Developmental Disorders (Dereu et al., 2010)
 - Spanish version of the Modified Checklist for Autism in Toddlers (M-CHAT & M-CHAT-R/F) (Canal-Bedia et al., 2018)
 - Joint Attention- Observation Schedule - JA-OBS preschool (Linnsand et al., 2022)
- Screening tools can give false positives or miss subtle signs of autism.

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Why are no clear risk indicators with predictive validity found?

- There are different reasons:
 - 1. Complexity of the Autism Spectrum:**
 - Autism is a complex and heterogeneous disorder
 - 2. Subtlety of Early Signs:**
 - Are often subtle.
 - 3. Variability in Symptom Presentation:**
 - Symptoms can vary widely between individuals and may change over time.
 - 4. Confounding Factors and Comorbidities:**
 - The symptoms may overlap with those of other neurodevelopmental disorders.
 - 5. Need for Further Research:**
 - is still needed to validate their usefulness as reliable predictors in the clinical context.

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ASD screening in Spain Castilla y León ASD Screening Programme

*Dirección General de Asistencia Sanitaria. Dirección Técnica de Atención Primaria
Instituto Universitario de Integración en la Comunidad - INICO*

*Servicio de Asistencia Psiquiátrica y Coordinación Sociosanitaria
INFOAUTISMO*

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ASD screening in Spain (Castilla y León)

- At 18 and 24 months of age
 - Children with risk factors
 - Children with signs and symptoms of suspicion by parents or professionals
- Risk indicators for selection
 - Existence of a **direct relative diagnosed with ASD** (especially siblings).
 - **Genetic syndrome related to autism**: Fragile X syndrome, tuberous sclerosis, neurofibromatosis, phenylketonuria.
 - **Pre- and perinatal pathology**:
 - High blood pressure, gestational diabetes, exposure to drugs and medications (valproate, teratogens), viral infection in the 1st trimester, foetal distress, dystocic delivery, prematurity, low birth weight, metabolic diseases.
 - **Adopted children** with unknown obstetric and family history.
 - **Advanced age** of the father or mother at birth.
 - **Either parent with severe mental disorder** (schizophrenia, bipolar disorder, depression).



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The M-CHAT-R/F tool (Spanish version)

	Sólo para uso oficial (no relevar)
1. Si usted señala algo al otro lado de la habitación, ¿su hijo le mira? (POR EJEMPLO ¿Si usted señala a un juguete, un peluche o un animal, ¿su hijo lo mira?)	SI NO
2. ¿Alguna vez se ha preguntado si su hijo es sordo?	SI NO
3. ¿Su hijo juega o juega de fantasía o imaginación? (POR EJEMPLO ¿hace como que bebe de una taza vacía, habla por teléfono o da de comer a una muñeca o peluche...?)	SI NO
4. ¿A su hijo le gusta subirse a cosas? (POR EJEMPLO ¿a una silla, escaleras, o tobogán...?)	SI NO
5. ¿Hace su hijo movimientos inusuales con sus dedos cerca de sus ojos? (POR EJEMPLO mueve sus dedos cerca de sus ojos de manera inusual)	SI NO
6. ¿Su hijo señala con un dedo cuando quiere pedir algo o pedir ayuda? (POR EJEMPLO señala un juguete o algo de comer que está fuera de su alcance?)	SI NO
7. Su hijo señala con un dedo cuando quiere mostrarle algo que le llama la atención? (POR EJEMPLO ¿señala un avión en el cielo o un camión muy grande en la calle)	SI NO
8. ¿Su hijo se interesa en otros niños? (POR EJEMPLO ¿mira con atención a otros niños, les sonríe o se les acerca?)	SI NO
9. ¿Su hijo le muestra cosas escondidas o levantándolas para que usted las vea - no para pedir ayuda sino solamente para compartirlas con usted? (POR EJEMPLO ¿le muestra una flor o un peluche o un coche de juguete)	SI NO
10. ¿Su hijo responde cuando usted le llama por su nombre? (POR EJEMPLO ¿se vuelve, habla o balbucea, o deja de hacer lo que estaba haciendo para mirarle?)	SI NO
11. ¿Cuándo usted sonríe a su hijo, él o ella también le sonríe?	SI NO
12. ¿La madre o el hijo ríen espontáneamente? (POR EJEMPLO ¿la aspiradora o la música, incluso cuando está no está excesivamente alta?)	SI NO
13. ¿Su hijo camina solo?	SI NO
14. ¿Su hijo le mira a los ojos cuando usted le habla, juega con él o ella, o lo viste?	SI NO
15. ¿Su hijo imita sus movimientos? (POR EJEMPLO ¿dece ados con la mano, aplaudir o algún ruido, gracioso que usted haga?)	SI NO
16. Si usted se gira a ver algo, ¿su hijo trata de mirar hacia lo que usted está mirando?	SI NO
17. ¿Su hijo intenta que usted le mire/levele atención? (POR EJEMPLO ¿busca que usted le haga un cumplido, o le dice "mira" o "mirame")	SI NO
18. ¿Su hijo le entiende cuando usted le dice que haga algo? (POR EJEMPLO ¿si usted no hace caso, su hijo entiende "no el biberón de la silla" o "tráeme la manita")	SI NO
19. Si algo nuevo pasa, ¿su hijo le mira para ver como usted reacciona al respecto? (POR EJEMPLO ¿si ore un ruido extraño o ve un juguete nuevo, se gira a ver su cara?)	SI NO
20. La gustan a su hijo los juegos de movimiento? (POR EJEMPLO le gusta que le balances, o que le haga "el caballo" señalándole en sus rodillas)	SI NO

Fecha de hoy: _____ SELLO CIAS

DATOS CONFIDENCIALES DEL NIÑO o la NIÑA

NOMBRE Y APELLIDOS: _____
 FECHA DE NACIMIENTO: _____
 SEXO: Varón Mujer TELEFONO de CONTACTO: _____
 DIRECCIÓN: _____ CP: _____ LOCALIDAD: _____

Nombre de la persona que rellena el cuestionario: _____
 Parentesco con el niño/la: Madre Padre Otro (especificar): _____

Recommended age

• 16-30 months

Screening (Well-child visits)

• A los 18 meses
• A los 24 meses

J Autism Dev Disord (2011) 41:1342-1351
DOI 10.1007/s10803-010-1163-z

ORIGINAL PAPER

Modified Checklist for Autism in Toddlers: Cross-Cultural Adaptation and Validation in Spain

Ricardo Canal-Bedia · Patricia Garcia
José Santos-Borbujo · Zoila Guisura


Journal of Autism and Developmental Disorders
<https://doi.org/10.1007/s10803-018-3777-5>

ORIGINAL PAPER

Spanish Cultural Validation of the Modified Checklist for Autism in Toddlers, Revised

María Magán-Maganto¹ · Ricardo Canal-Bedia² · Aránzazu Hernández-Fabian² · Álvaro Bejarano-Martin¹ · Clara J. Fernández-Álvarez¹ · María Martínez-Velarte³ · María V. Martín-Cilleros¹ · Noelia Flores-Robaina⁴

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M-CHAT-R/F (Spanish version)

QUESTIONARIO DEL DESARROLLO COMUNICATIVO Y SOCIAL EN LA INFANCIA (M-CHAT-R/F)

La información que contiene este cuestionario es totalmente confidencial. Los datos personales que aparezcan al final serán separados del resto del cuestionario para proteger la confidencialidad de sus respuestas. Le garantizamos que no se realizará ninguna difusión de los datos aquí contenidos.

Por favor responda a estas preguntas sobre su hijo/a. Tome en cuenta cómo se comporta generalmente su hijo/a. Si usted ha visto a su hijo/a comportarse de una de estas maneras algunas veces, pero no es un comportamiento usual, por favor responda "NO". Seleccione: SI NO SI/NO. Muchas gracias.

	Solo para uso clínico (no revelar)	
	SI	NO
1. Si usted señala algo al otro lado de la habitación, ¿su hijo/a lo mira? (POR EJEMPLO, ¿Si usted señala a un juguete, un peluche o un animal, ¿su hijo/a lo mira?)	SI	NO
2. ¿Alguna vez se ha preguntado si su hijo/a es sordoblo?	SI	NO
3. ¿Su hijo/a juega a juegos de fantasía o imaginación? (POR EJEMPLO, ¿hace como que bebe de una taza vacía, habla por teléfono o se come a una muñeca de peluche...?)	SI	NO
4. ¿A su hijo le gusta subirse a cosas? (POR EJEMPLO, a una silla, escaleras, o tobogán...?)	SI	NO
5. ¿Hace su hijo/a movimientos inusuales con sus dedos cerca de sus ojos? (POR EJEMPLO, mueve sus dedos cerca de sus ojos de manera habitual)	SI	NO
6. ¿Su hijo/a señala con un dedo cuando quiere pedir algo o pedir ayuda? (POR EJEMPLO, señala un juguete o algo de comer que está fuera de su alcance?)	SI	NO
7. Su hijo/a señala con un dedo cuando quiere mostrarle algo que le llama la atención? (POR EJEMPLO, señala un avión en el cielo con gesto muy grande en la cabeza)	SI	NO
8. ¿Su hijo/a se interesa en otros niños? (POR EJEMPLO, juega con atención a otros niños, les señala o se les acerca?)	SI	NO
9. ¿Su hijo/a le muestra cosas acercándose o levantándose para que usted las vea - no para pedir ayuda sino solamente para compartirlas con usted? (POR EJEMPLO, le muestra una flor o un peluche a un niño de su juego?)	SI	NO
10. ¿Su hijo/a responde cuando usted le llama por su nombre? (POR EJEMPLO, ¿se vuelve, habla o babbea, o diga de hacer lo que estaba haciendo para mirarlo?)	SI	NO
11. ¿Cuánto usted sonríe a su hijo/a, él o ella también le sonríe?	SI	NO
12. ¿Le molestara a su hijo/a ruidos solidarios? (POR EJEMPLO, ¿le aspiradora o la música, incluso cuando está no está excesivamente alta?)	SI	NO
13. ¿Su hijo/a camina solo?	SI	NO
14. ¿Su hijo/a le mira a los ojos cuando usted le habla, juega con él o ella, o lo viste?	SI	NO
15. ¿Su hijo/a imita sus movimientos? (POR EJEMPLO, decir adios con la mano, aplaudir o algún tipo de gesto que usted haga?)	SI	NO
16. Si usted se gira a ver algo, ¿su hijo/a trata de mirar hacia lo que usted está mirando?	SI	NO
17. ¿Su hijo/a intenta que usted le muestre atención? (POR EJEMPLO, busca que usted le haga un comentario, o le dice "mira" o "mirame")	SI	NO
18. ¿Su hijo/a le entiende cuando usted le dice que haga algo? (POR EJEMPLO, ¿si usted no hace gestos, su hijo/a entiende "pon el libro encima de la silla" o "támete la manita")	SI	NO
19. Si algo nuevo pasa, ¿su hijo/a le mira, para ver como usted reacciona al respecto? (POR EJEMPLO, si oye un ruido extraño o se ve un juguete nuevo, se gira a ver su caso?)	SI	NO
20. Le gustan a su hijo/a los juegos de movimiento? (POR EJEMPLO, le gusta que le balancee, o que le haga "el caballo" señalándole en sus rodillas)	SI	NO

Fecha de hoy: SELLO CIAS

DATOS CONFIDENCIALES DEL NIÑO o LA NIÑA

NOMBRE Y APELLIDOS:

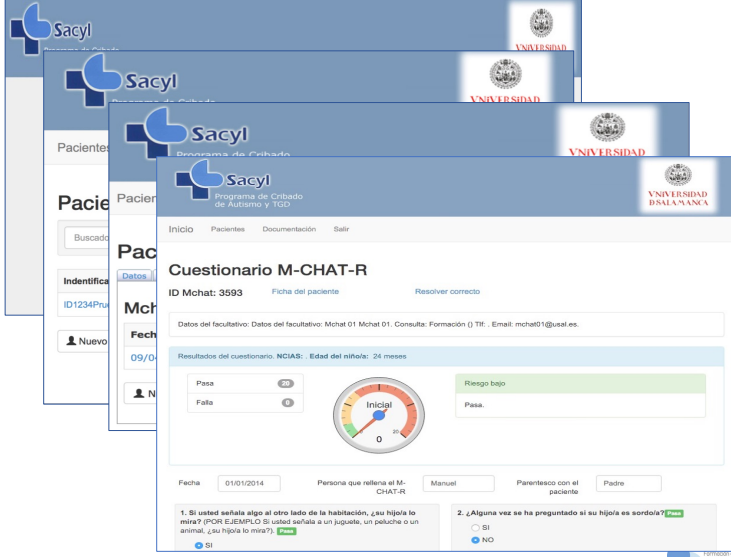
FECHA DE NACIMIENTO:

SEXO: Varón Mujer


DIRECCIÓN: TELÉFONO DE CONTACTO: CP: LOCALIDAD:

Nombre de la persona que rellena el cuestionario:


Parentesco con el niño/a: Madre Padre Otro respectivamente



The screenshot shows the web interface for the M-CHAT-R/F questionnaire. It includes a header with the Sacyl logo and the text 'Programa de cribado de Autismo y TCC'. The main content area displays the questionnaire ID (ID Mchat: 3593) and the patient's name. Below this, there are fields for 'Fecha' (Date) and 'Personas que rellena el M-CHAT-R' (Person filling out the M-CHAT-R), with options for 'Manual', 'Parentesco con el paciente', and 'Padre'. A central gauge shows the 'Riesgo bajo' (Low risk) result. At the bottom, there are two sample questions with radio button options for 'SI' (Yes) and 'NO' (No).




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Psychometric properties of the M-CHAT-R/F (Sp. version) by age range

	14-22 months	23-36 months
Sensitivity	0.818	0.75
Specificity	0.997	0.995
PPV	0.474	0.33
NPV	0.999	0.999
LR+*	285.136	165.054
LR-*	0.182	0.251

*Calculated at 95% Confidence Interval
 *Conventional
 PPV Predictive Positive Value, NPV Negative Predictive Value, LR+ Positive Likelihood Ratio, LR- Negative Likelihood Ratio



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High number of false positives

Low sensitivity

The positive predictive value for ASD only

Tool	PPV	Reference
M-CHAT	0,6	Chlebowski, et al. (2013)
M-CHAT-R / F	0, 54	Chlebowski, et al. (2013)

Positive predictive value for any developmental delay

Herramienta	PPV	Referencia
M-CHAT	98%	Chlebowski, et al. (2013)
M-CHAT-R / F	94%	Robins et al. (2013)
M-CHAT con JA-OBS	90%	Nygren et al. (2012)
CESDD	83%	Dereu et al. (2010)
ESAT	99%	Dietz et al. (2006)
Infant Toddler Checklist (ITC)	93%	Wetherby et al. (2008)

High number of False Negatives

Low specificity

May be a consequence of variability in the presentation of ASD symptoms.

- Different patterns of symptom presentation
- Variability depending on the type and predictive power of symptoms for a diagnosis of autism (how and when these symptoms are expressed).

Unequal parental involvement Circumstantial involvement of professionals

- Parental collaboration
 - **Greater** collaboration if children have more evident atypical behaviour.
 - **Less** collaboration if children are younger
- Better several informants
 - Parents as informants
 - Paediatricians + nurses + carers
- Need for good training programmes and an appropriate toolkit
 - E.g. DIANE project
 - Training reduces fear of misidentification

(Branson, 2008; Glascoe, 1997; Dereu et al., 2012; Oosterling et al., 2010; Nice, 2017)

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Early diagnosis of ASD today Lights and Shadows

- **Reliable diagnosis possible at 24 months**
 - Today in Spain paediatricians detect suspected cases between 18 and 24 months.
 - Access to early intervention leads to better outcomes
 - More children now have access to EI
- **But most cases go unnoticed**
 - Sibling follow-up programmes
 - They leave more than 50% of cases undiagnosed (see Ozonoff et al., 2015; Zwaigenbaum et al., 2016).
 - Population-based programmes have a large number of false-positive ASD (e.g. in preterm infants - Hernandez et al., 2018) and false-negative ASD (Siu, et al., 2016).
- **There is a diagnostic delay affecting 2 out of 3 diagnosed cases.**
- **The delay is not because autism is not expressed at 24 months or earlier**
 - It is because the instruments are not precise and sensitive enough.
 - Difficulty in identifying signs of risk that appear in subtle ways (Bacon et al., 2018)

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Symptoms of ASD may emerge or attenuate over time (Landa et al. 2022).

- The sensitivity and stability of the diagnosis of ASD is significantly increased.
 - From time 1 (sensitivity: 52%; stability: 63%)
 - Till time 2 (sensitivity: 86%; stability: 68%)
- Predictors of belonging to different diagnostic groups:
 - Presence of restricted and repetitive behaviours
 - Limitations in the initiation of joint attention
 - Expressive language skills

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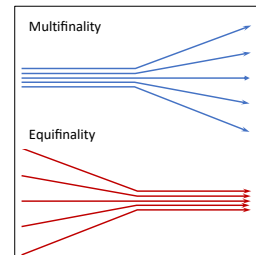
What have we learned?

- We wanted to identify specific markers in infants with ASD.
 - Defined categorically.
- The usefulness of markers in screening tools has been evaluated in terms of sensitivity and specificity.
 - But these markers have not been useful for prediction at the individual level.
- The sensitivity and specificity of early markers increases during the second year of life.
 - It is higher for markers closer to ASD symptoms.
 - It is lower than expected
 - Because some are predictive only at specific ages.
 - E.g., speed of identifying a visual target among distractors at 9 and 15 months predicts later autism; but at 2 years it does not (Cheung et al., 2018).
 - Inaccuracy of measurement in infants also plays a role.
 - There is evidence that there may be protective factors
 - Or other modifying factors in developmental trajectories.

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Towards a prospective approach

- Research indicates that ASD is not a consequence of simple mechanistic causal pathways.
 - ASD phenotypes show convergence ("equifinality") and divergence of pathways ("multifinality").
 - Different genetic, environmental and brain factors can lead to a diagnosis of ASD.
 - Nearly identical causal factors may increase the likelihood of different atypical phenotypes.
 - This discourages simple reductionist approaches.
 - We need to understand the emergent properties of the system as it develops.
 - Systems neuroscience approach
 - Because they are phenomena in which events appear over multiple time scales.



(Ahn, Tewari, Poon, & Phillips, 2006 ; Cicchetti and Rogosch, 1996; Davies, 2017; Lord et al., 2020)

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Towards a prospective approach

- ASD are best understood **not only as simple point categories** (categorical diagnosis)
 - **But also, as graded areas** of a multidimensional space (dimensional traits).
 - Individual variation can arise
 - Directly from genetic variation
 - Indirectly from the non-linear developmental process
 - Prospective studies have the potential to help integrate the categorical and the dimensional approach
 - Because the population of interest is defined independently of, and prior to, clinical diagnosis.

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What to do?

- To identify early processing atypicalities
 - These would be deviations from the norm
 - Associated at the group level with an atypical outcome.
- To identify neurocognitive moderators
 - Associated with typical outcomes in infants with identified early atypicality.
 - These moderators would act as transdiagnostic factors of resilience.

Johnson et al., 2021

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AUTISM RESEARCH FOR EUROPE

COMPLEJO ASISTENCIAL UNIVERSITARIO DE SALAMANCA

THE MR-BRAIN PROJECT

Integrated body tracking technologies for the follow-up of preterm infants at risk of neurodevelopmental disorders


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InFoAutismo
Universidad de Salamanca

INSTITUTO UNIVERSITARIO DE INTEGRACIÓN A LA COMUNIDAD
UNIVERSIDAD DE SALAMANCA

Grupo de Investigación y Formación en Autismo


Este proyecto cuenta con el apoyo del programa de investigación e innovación Horizonte 2020 de la Unión Europea y de FPPIA a través de Innovative Medicines Initiative 2 Ref. nº 777394; del Ministerio de Ciencia e Innovación mediante las ayudas ref.: PID2019-107177RB-I00 y TED2021-129301B-I00; de la Consejería de Educación de Castilla y León mediante subvención Ref.: SA0119P20; y la Fundación Mutua Madrileña

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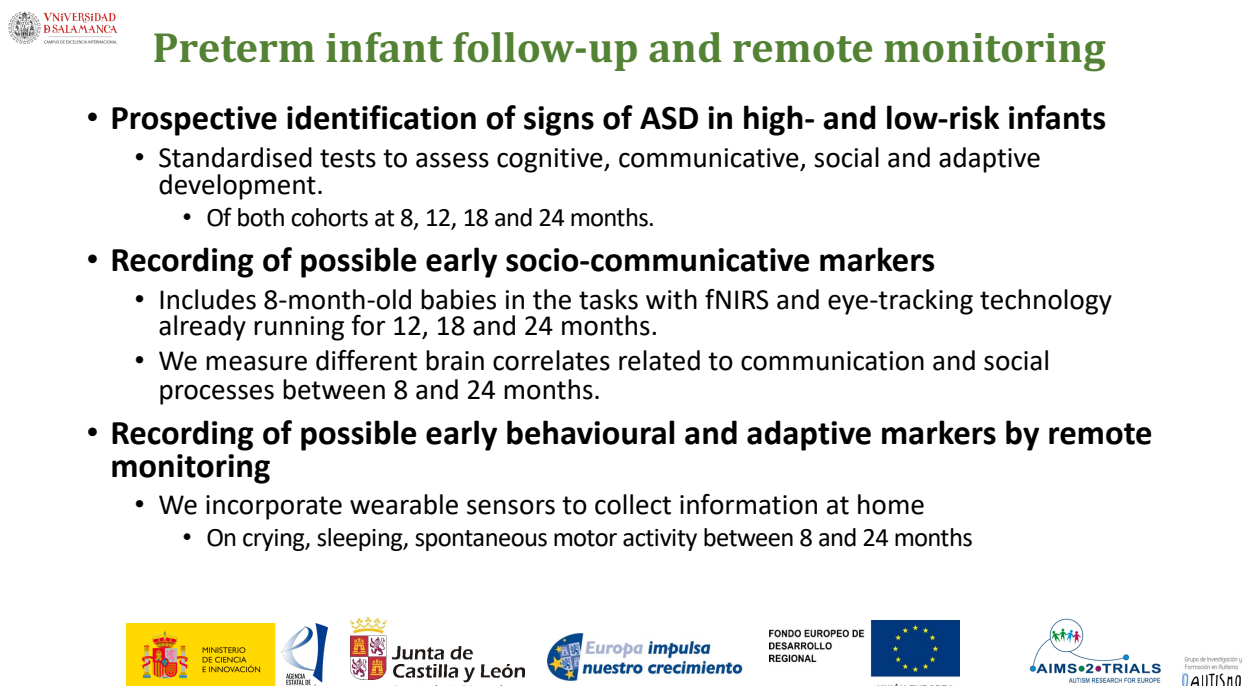


Aims

1. To enhance the identification of markers related to social communication and adaptive functioning associated with ASD risk signs.
2. To build a platform for remote monitoring of PTNBW infants or infants with BPEG.




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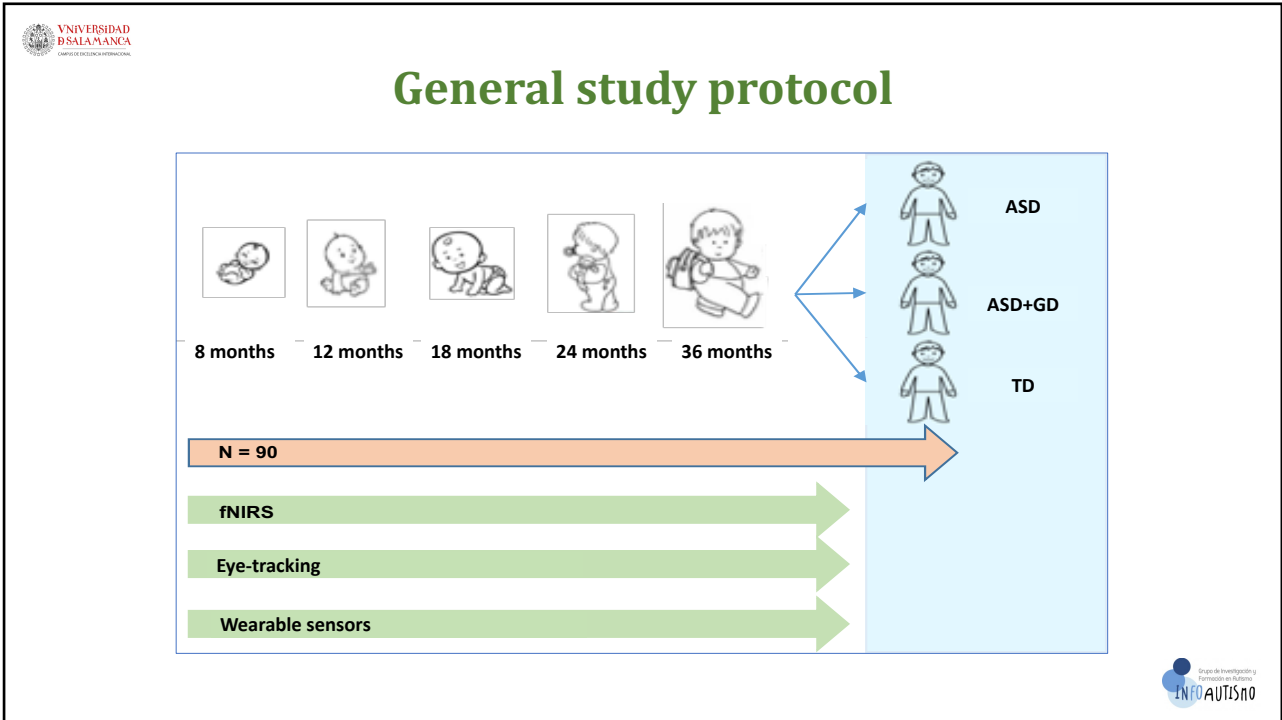


Preterm infant follow-up and remote monitoring

- **Prospective identification of signs of ASD in high- and low-risk infants**
 - Standardised tests to assess cognitive, communicative, social and adaptive development.
 - Of both cohorts at 8, 12, 18 and 24 months.
- **Recording of possible early socio-communicative markers**
 - Includes 8-month-old babies in the tasks with fNIRS and eye-tracking technology already running for 12, 18 and 24 months.
 - We measure different brain correlates related to communication and social processes between 8 and 24 months.
- **Recording of possible early behavioural and adaptive markers by remote monitoring**
 - We incorporate wearable sensors to collect information at home
 - On crying, sleeping, spontaneous motor activity between 8 and 24 months



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Appointments schedule

	Age	0-6 months	8 months	12 months	18 months	24 months	30 months	36 months
Invitation & Consent		X						
Clinical information		X	X	X	X	X	X	X
Parental temperament				X				
AQ parents				X				
SACS				X	X	X		X
M-CHAT-R					X	X		
Bayley III			X	X	X	X		X
Vineland			X	X	X	X		X
MacArthur Inventory					X	X		
ADOS-2					X	X		X
fNIRS				X	X	X		
Eyetracking				X	X	X		
Wearable sensors			X	X	X	X	X	X

Legend: Hospital (Green), Research Unit / Home (Yellow)

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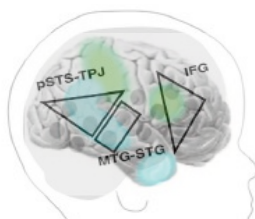
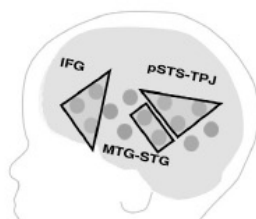
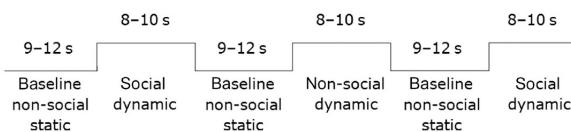
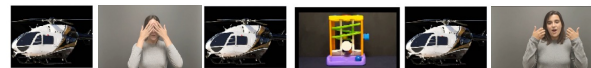
Specific protocols

- **fNIRS protocol:** Dynamic social and non-social stimuli without sound, compared to a static non-social base line.
- **Eye-Tracking Protocol :** Pupillary response (dilation), gaze fixations, and eye movements in response to dynamic social and non-social stimuli.
- **Wearable sensors:** Recording of crying episodes, sleep quality and spontaneous motor activity of the baby at home from 18:00h to 9:00h.

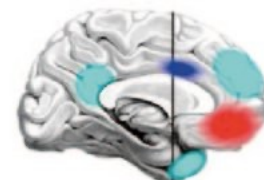
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Experimental setting (fNIRS & Eye-Tracking)

Similar to Braukman et al. (2017)



- Amygdala Network
- Mentalizing Network
- Empathy Network
- Mirror/Simulation/Action-Perception Network



- **fNIRS: 3 regions of interest :**
 - Inferior frontal gyrus (IFG)
 - Anterior middle temporal gyrus/superior temporal gyrus (aMTG-STG)
 - Posterior superior temporal sulcus/temporoparietal junction (pSTS-TPJ).

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Eye-Tracking

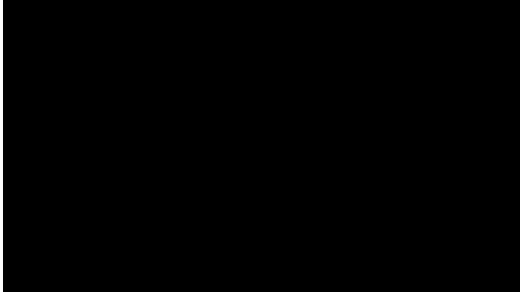

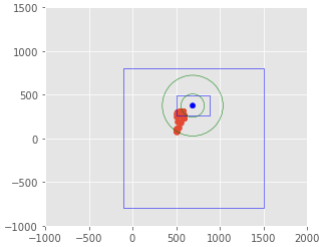


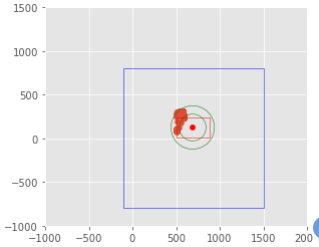
Image of the experiment



Centre of eyes



Centre of the mouth




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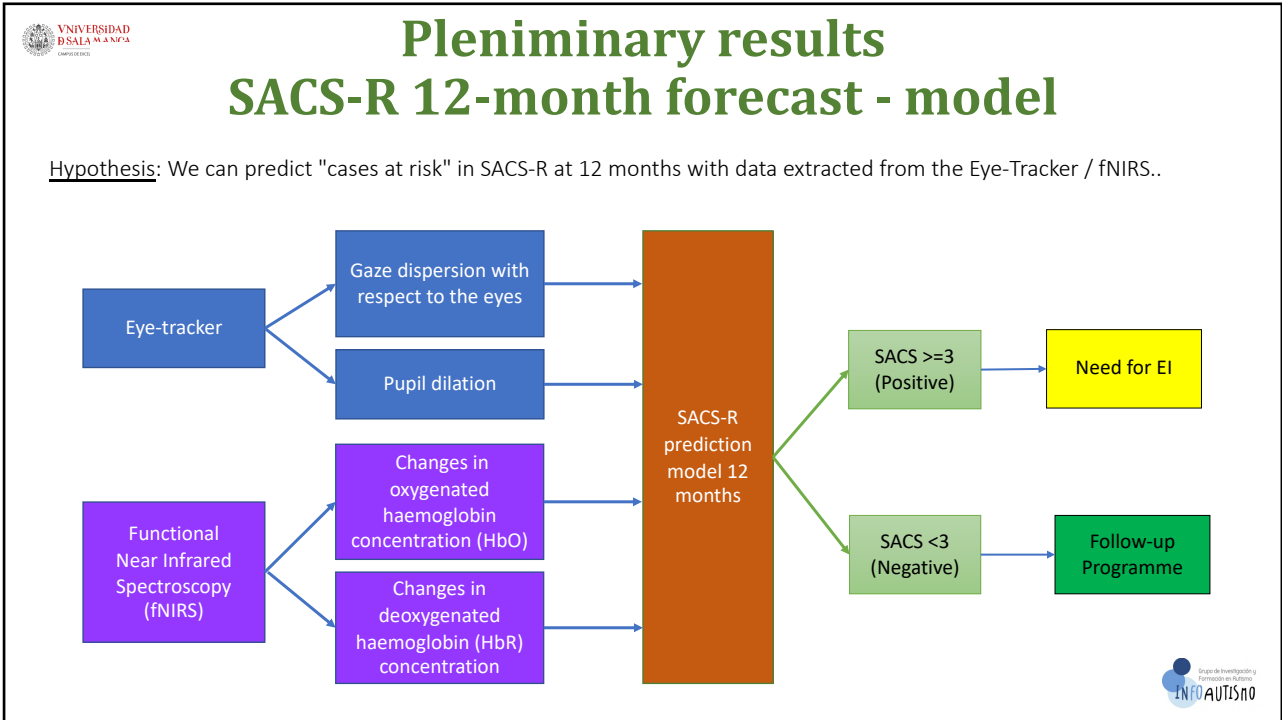
Wearable sensors

- Nappy with two integrated ECG textile electrodes designed for infant sleep monitoring (Ilen et al., 2019).

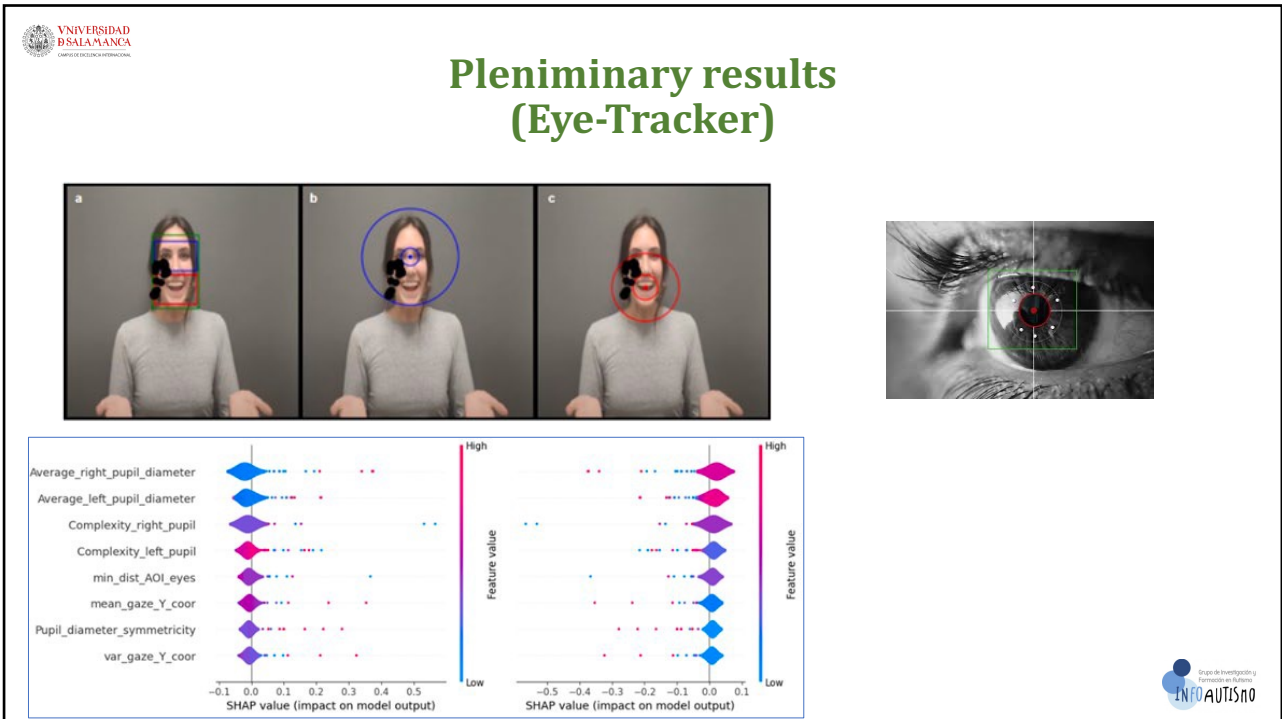


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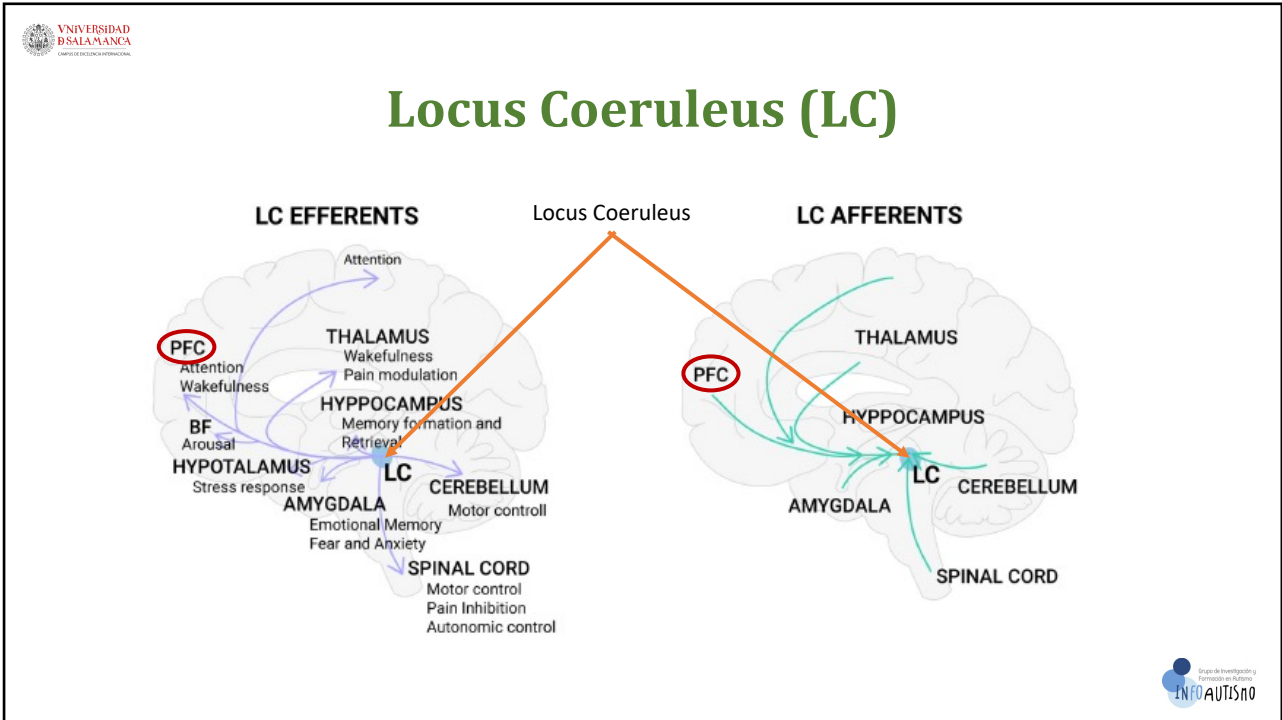
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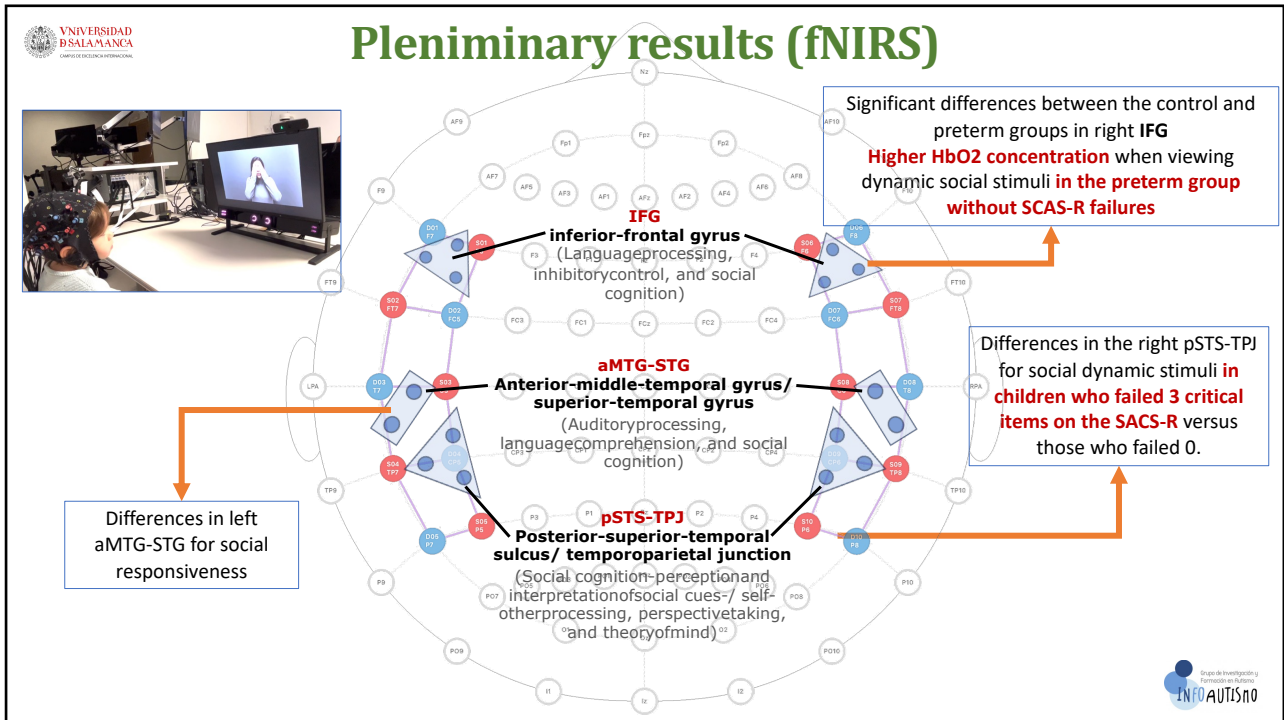
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Psychometric values of the Eye-Tracker algorithm

Algorithm	Accuracy	PPV	NPV	Recall /Sensitivity	Specificity	F1 Score	MCC	AUC score
Random Forest	0.94	0.6	0.98	0.75	0.96	0.67	0.67	0.94

- 5 preterm babies identified as being at risk of ASD
- Potential biomarker of risk for social communication impairment

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Wearable sensors
Neurodevelopment Portal - MR-BRAIN
<https://neurodesarrollo.usal.es/>

- **Development of a Remote Monitoring Platform for Infants at Increased Risk of Neurodevelopmental Incidence**
 - Will allow
 - Data aggregation and integration
 - Visualisation, analysis and representation
 - Tailored to pre-defined profiles, for the participation of families, health professionals and researchers.
 - Taking special care of privacy, security, legal liability and ethics of data collection and storage
 - Participation of Primary Care Paediatrics teams
 - Participate in early intervention follow-up for infants in need of it

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Conclusions

- Early detection is technically difficult, but essential
 - Benefits children with ASD or at risk and their families and promotes a preventive approach to services.
- In interpreting results of screening studies, several factors inherent to ASD need to be taken into account.
- Despite the number of existing tools, there is no "best" detection tool.
- We should move towards monitoring protocols based on dimensional measurements.
- The challenge is to identify indicators of atypical processing and neurocognitive modifiers.

In the near future...

- For supporting children with or at risk of ASD
 - Increased capacity for detecting ASD earlier.
 - Identify early signs that anticipate trajectories on which to intervene.
 - Provide support services at earlier ages.
 - Achieving a brighter future for children at risk
 - Promote an active attitude towards the prevention of ASD in the framework of childcare.
- To improve knowledge of ASD
 - Improved knowledge of the early development of at-risk newborns.
 - Identify mediating and moderating factors for the development of ASD.

