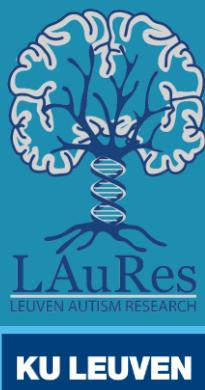


# HOW CAN WE OBJECTIVELY QUANTIFY SOCIO-COMMUNICATIVE SENSITIVITY? INNOVATIVE NEUROIMAGING APPROACHES IN AUTISM AND BEYOND

BART BOETS

[bart.boets@kuleuven.be](mailto:bart.boets@kuleuven.be)

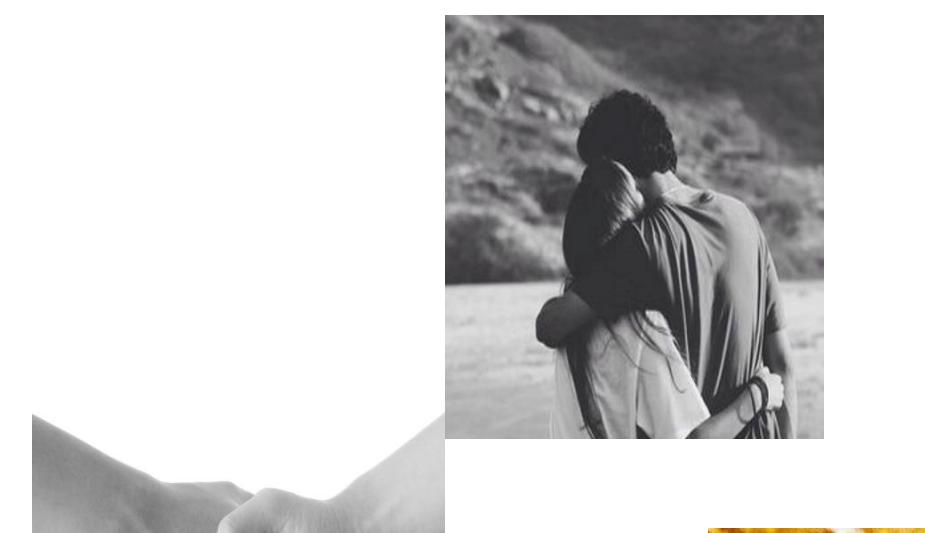
CENTER FOR  
DEVELOPMENTAL  
PSYCHIATRY



KU LEUVEN

# Humans are social beings

Psychopathology ~ social impairments

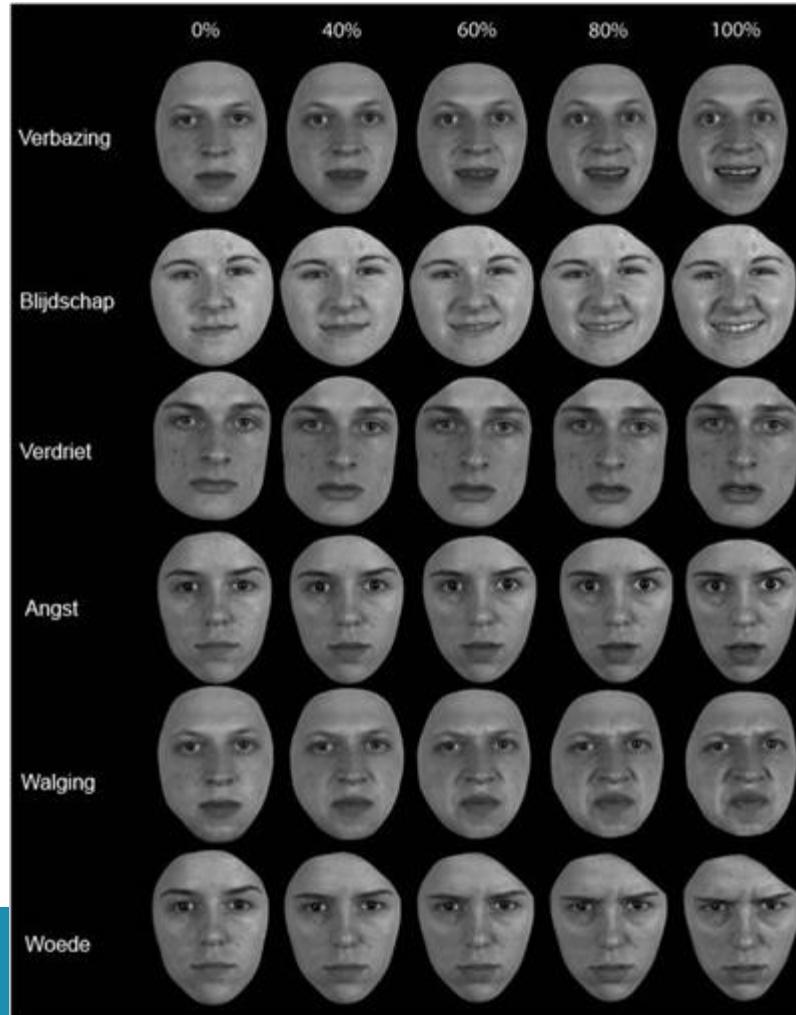
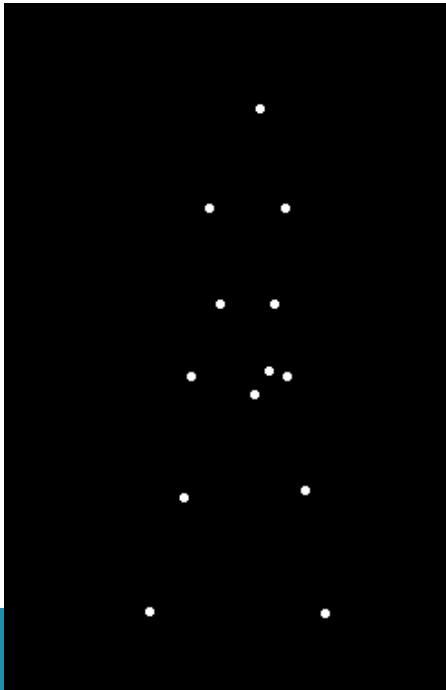
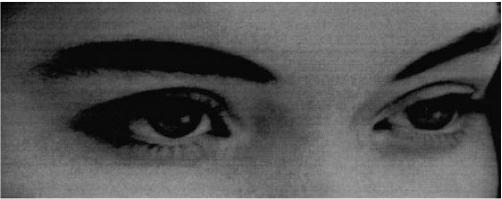
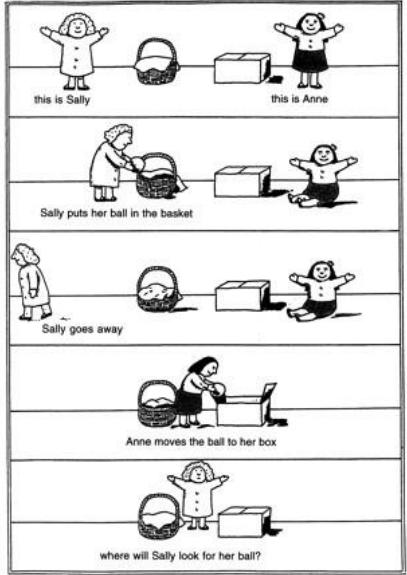


# How to measure socio-communicative impairments?

- Need for diagnostic tools to quantify this
  - Clinical expertise

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- Need for diagnostic tools to quantify this
  - Clinical expertise
  - Behavioural social cognition tests
    - But lab performance does not reflect daily life functioning
    - Explicit compensatory strategies versus automatic, implicit processing



# How to measure socio-communicative impairments?

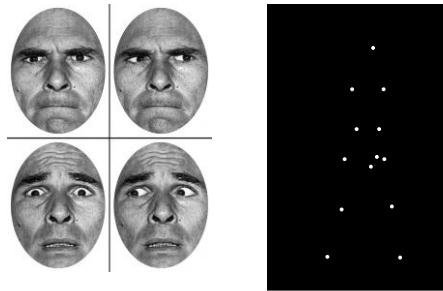
- Need for diagnostic tools to quantify this
  - Clinical expertise
  - Behavioural social cognition tests
    - But lab performance does not reflect daily life functioning
    - Explicit compensatory strategies versus automatic, implicit processing
- Need for more sensitive objective tools
  - Automatic, implicit, momentary processing → fMRI
  - Fast, straightforward, user friendly, cheap → EEG, eye-tracking, stress physiology
  - Ecologically valid
  - Within the context of real-life interactions → two-person neuropsychiatry approach

# Autism Spectrum Disorders (ASD)

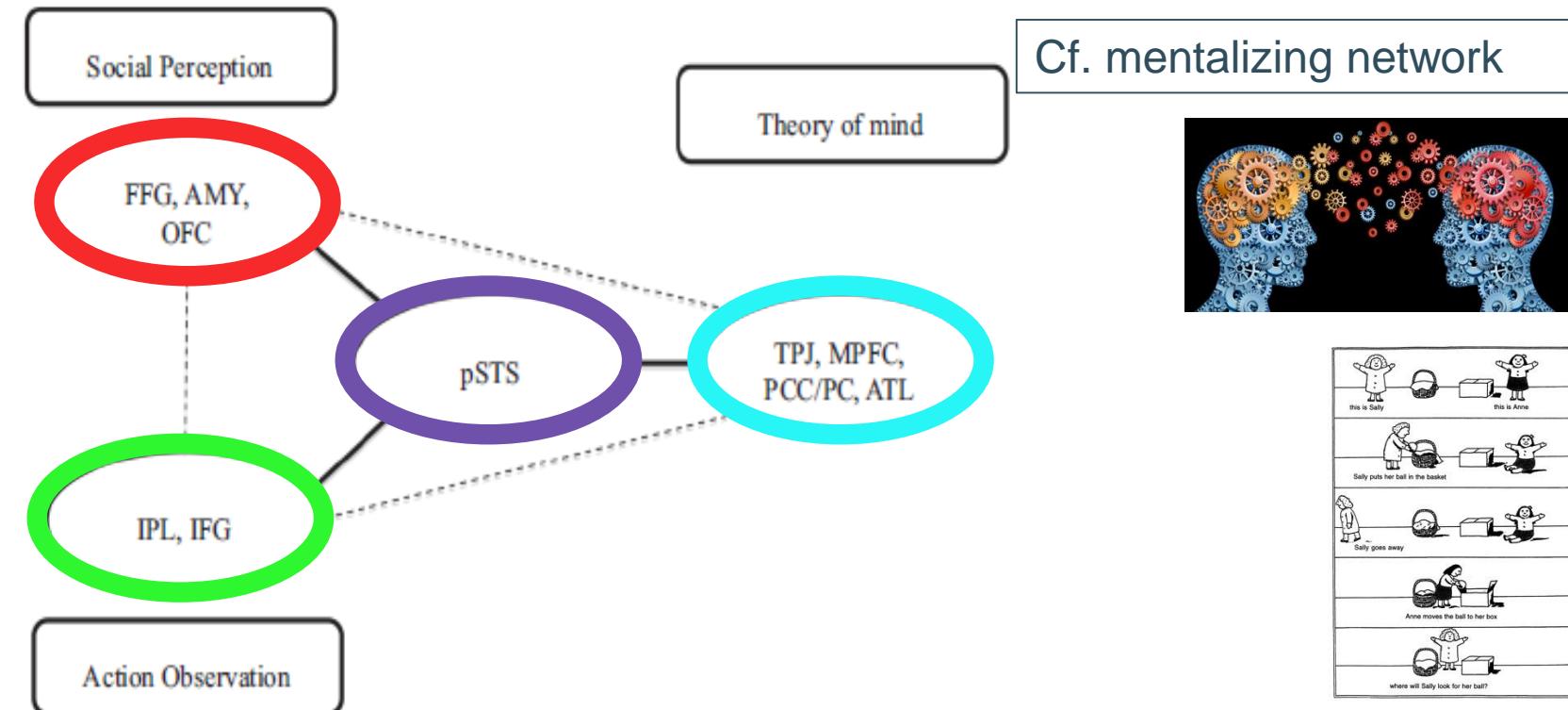
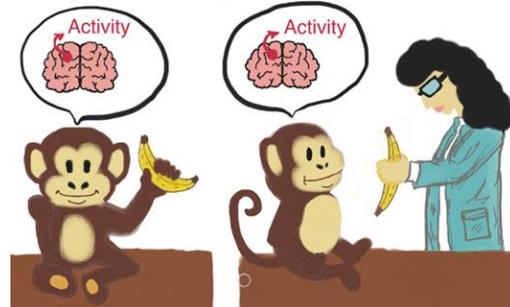


# Neural systems for social information processing

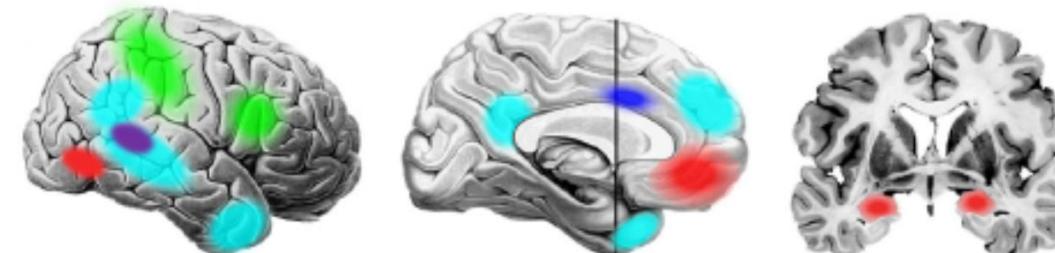
e.g. face, voice, body,  
biological motion



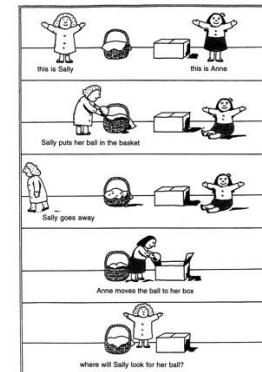
Cf. embodied simulation  
/ mirror mechanism



More Reflexive and Automatic      More Effortful and Controlled



Cf. mentalizing network



Yang et al. (2015).  
Neurosci Biobehav Rev

# Social touch observation in autism

Intact neural representations of affective meaning of touch but lack of embodied resonance in autism: a multi-voxel pattern analysis study

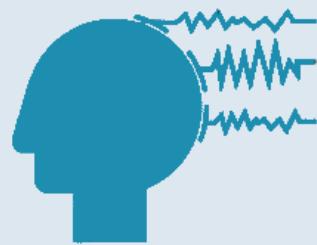
Haemy Lee Masson<sup>1,2,3\*</sup> , Ineke Pillet<sup>1</sup>, Steffie Amelynck<sup>2,3</sup>, Stien Van De Plas<sup>1</sup>, Michelle Hendriks<sup>1,2</sup>, Hans Op de Beeck<sup>1†</sup> and Bart Boets<sup>2,3†</sup>

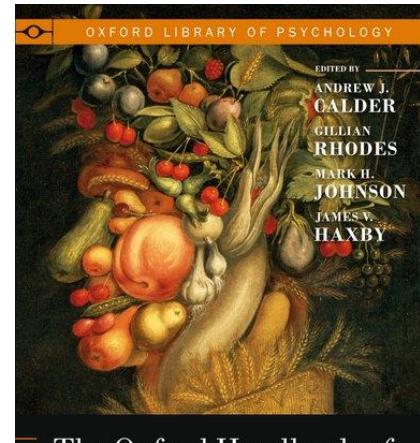




# Understanding face processing in autism using fast periodic visual stimulation (FPVS) frequency-tagging EEG

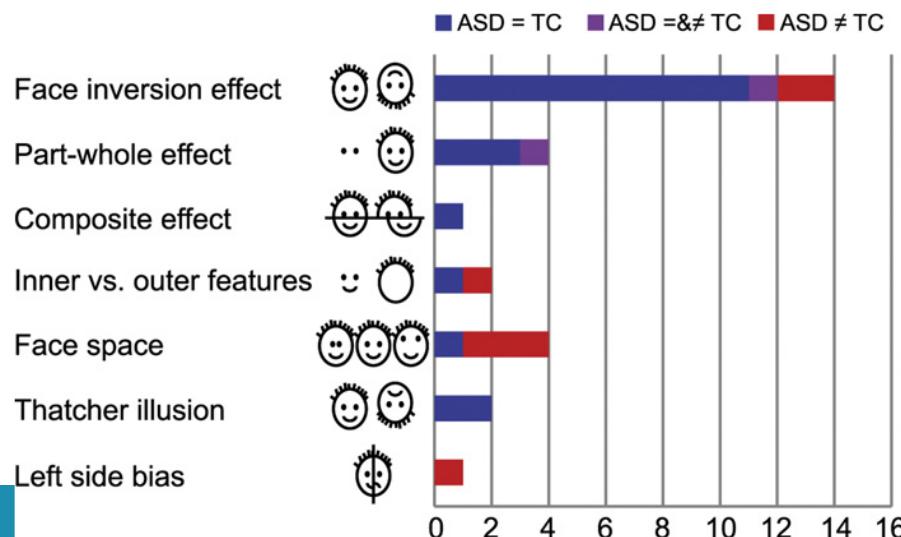
Sofie Vettori, Stephanie Van der Donck  
(in collaboration with Bruno Rossion & Milena Dzhelyova)



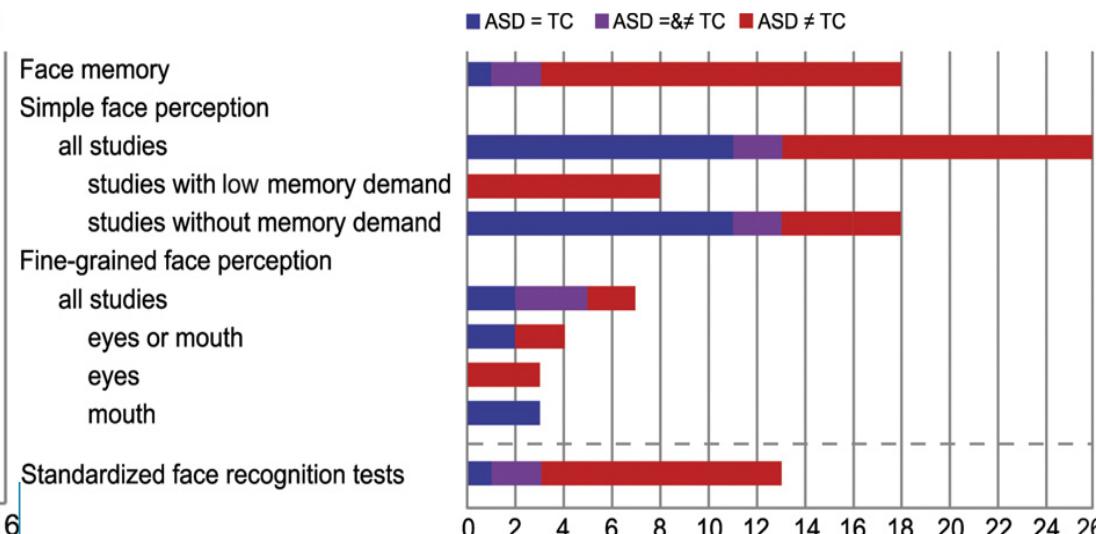


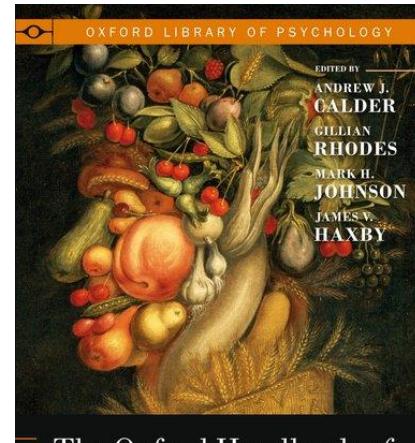
# Face processing in ASD

- DSM-5: A.2: Deficits in nonverbal communication (including eye contact, and use and understanding of facial expressions...)
- Exp studies: inconsistent and variable
  - Less attention for the eyes
  - Difficulties with facial expression
  - Less global/holistic face processing
  - Particular impairments with face memory



(e.g. meta-analysis Weigelt et al. 2012)





# Face processing in ASD

- DSM-5: A.2: Deficits in nonverbal communication (including eye contact and use and understanding of facial expressions...)
- Exp studies: inconsistent and variable
  - Less attention for the eyes
  - Difficulties with facial expression
  - Less global/holistic face processing
  - Particular impairments with face memory
- Implicit/indirect measures (neuroimaging, eye-tracking) may reveal differences

# Participants

- 8-12 year old boys with ASD (N=23)
- Matched typically developing control group (N=23)



# No group differences on behavioral face processing tasks

- Benton Facial Recognition Test (Benton et al. 1983)
- Cambridge Face Memory Test (Duchaine & Nakayama, 2006)
- Emotion Recognition Task (Kessels et al. 2014)
- Emotion Matching Task (Palermo et al. 2013)



7



1



2



3



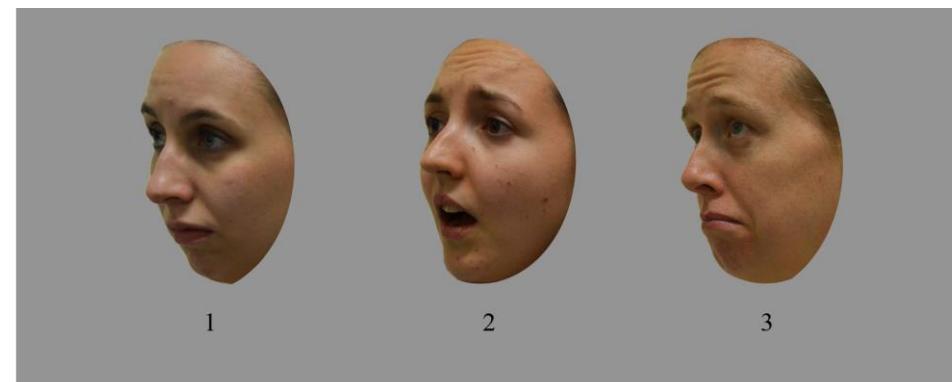
4



5

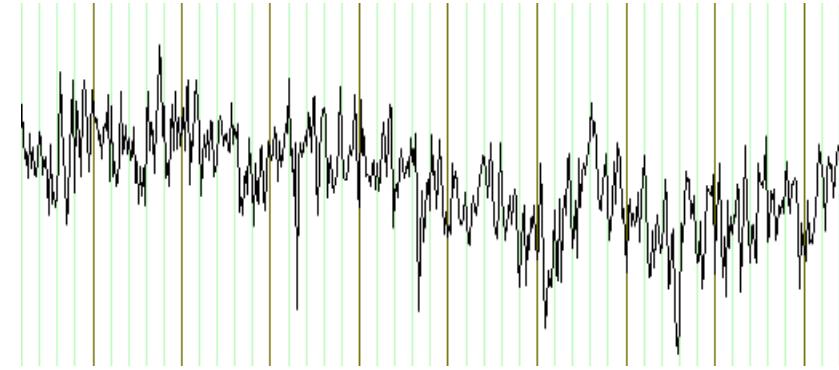


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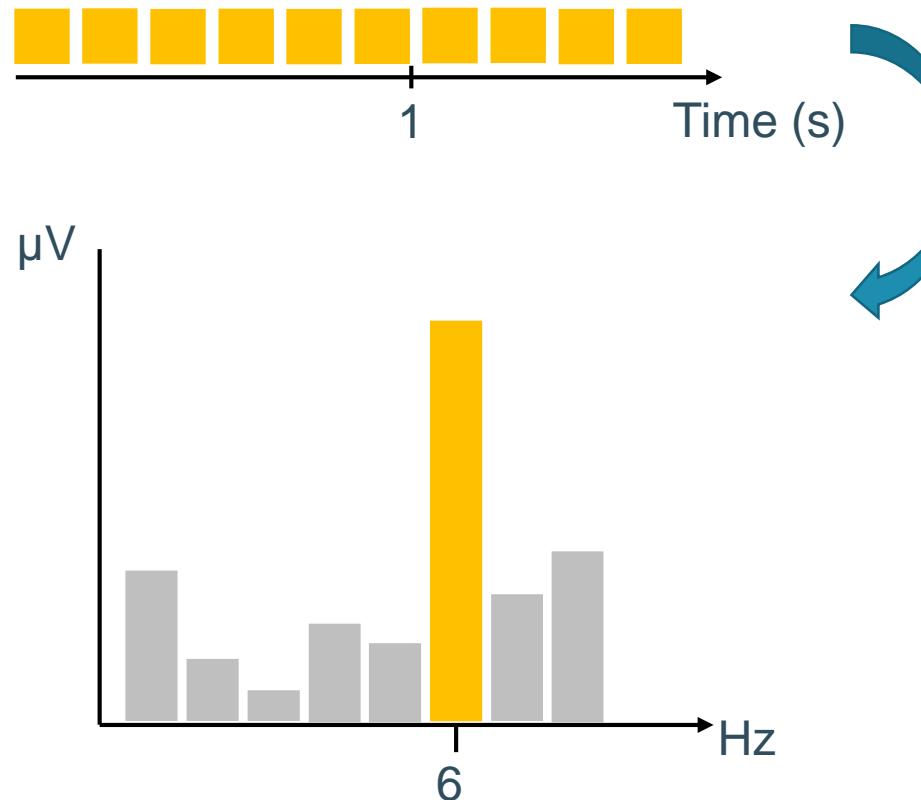
# Fast Periodic Visual Stimulation frequency-tagging EEG (FPVS EEG)

- If you stimulate the brain periodically :
  - Periodical EEG response
  - Exactly at the frequency of stimulation

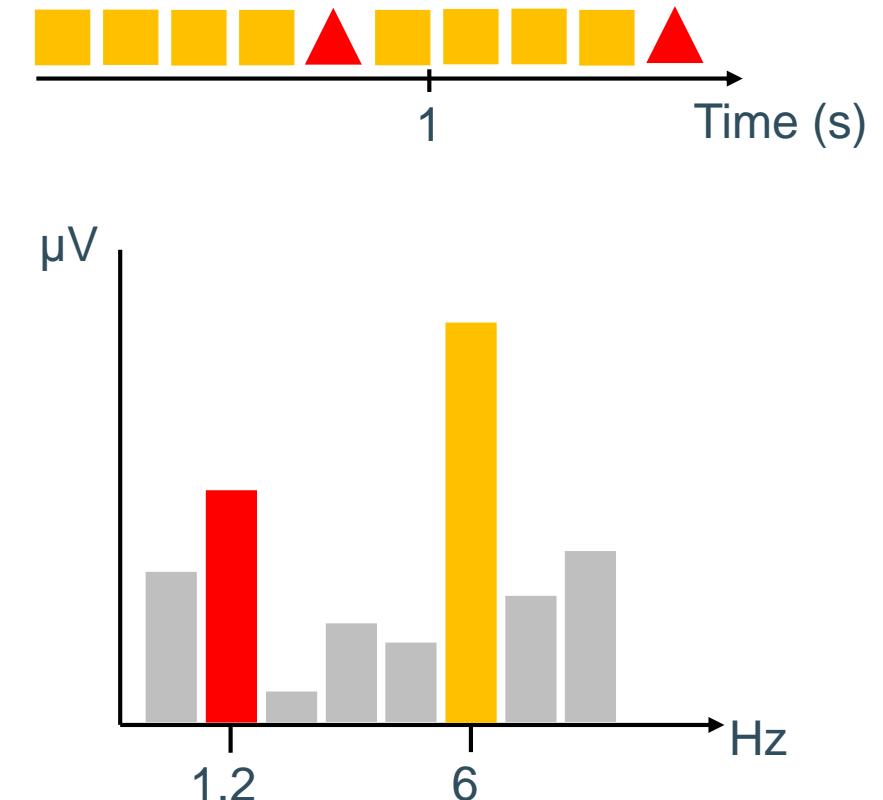


# Fast Periodic Visual Stimulation EEG

FPVS paradigm

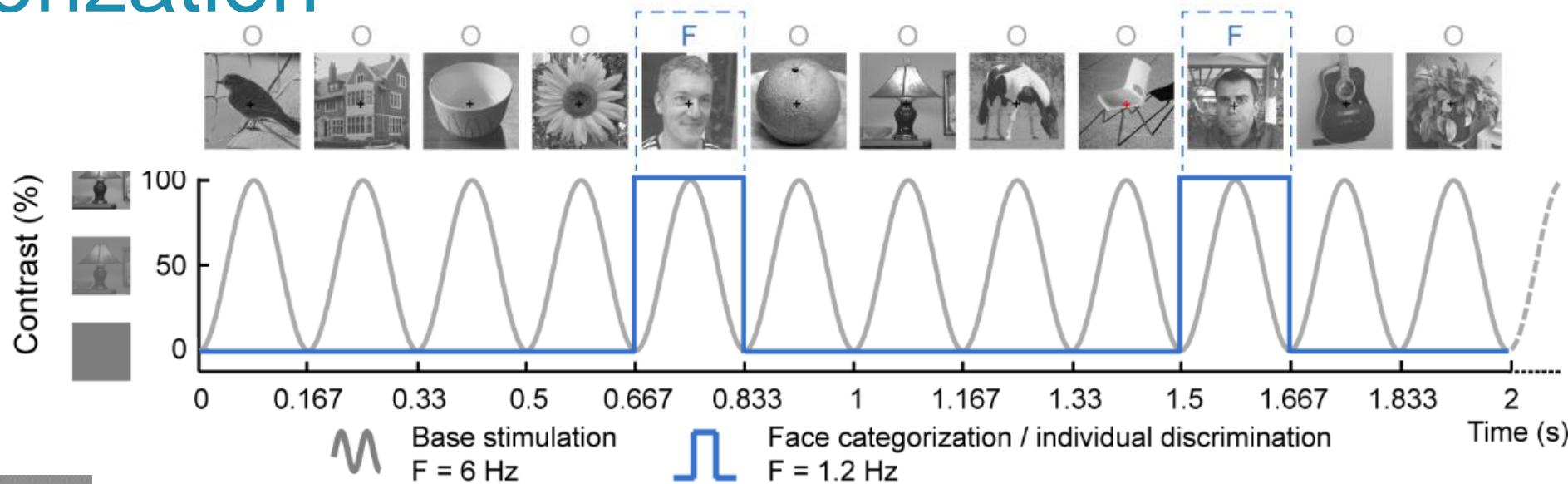


FPVS oddball paradigm



# Face categorization

(Rossion et al. 2015)

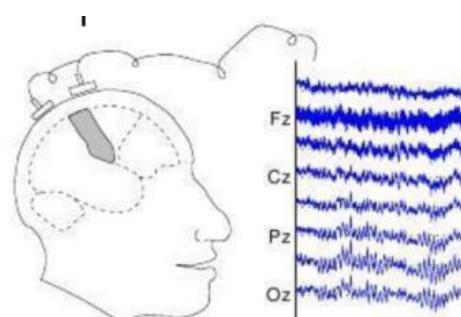
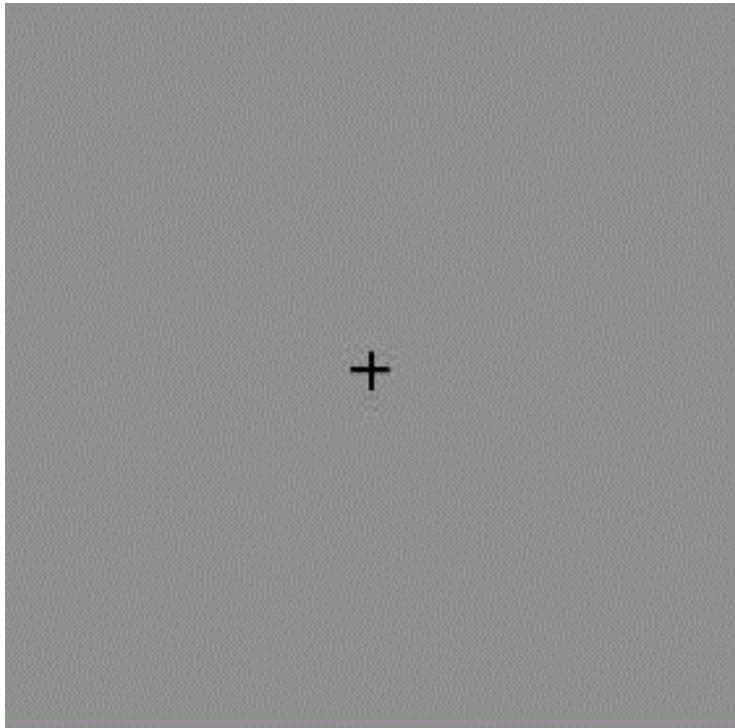
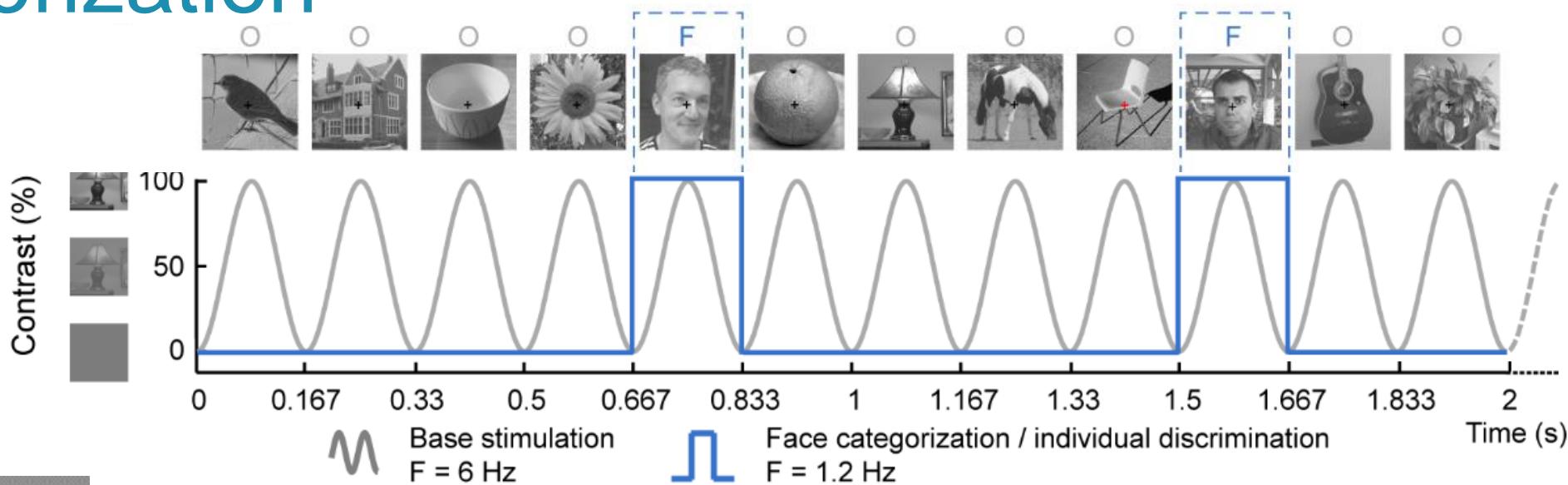


+

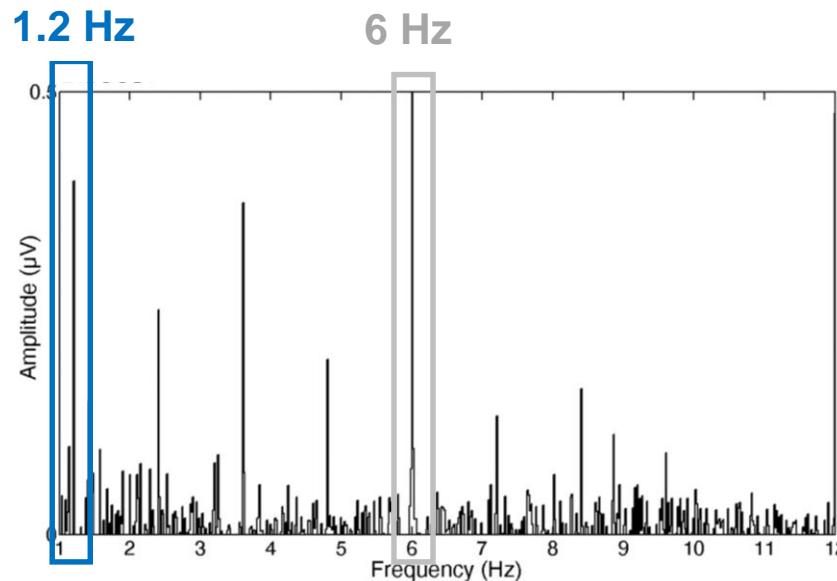
# Face categorization

(Rossion et al. 2015)

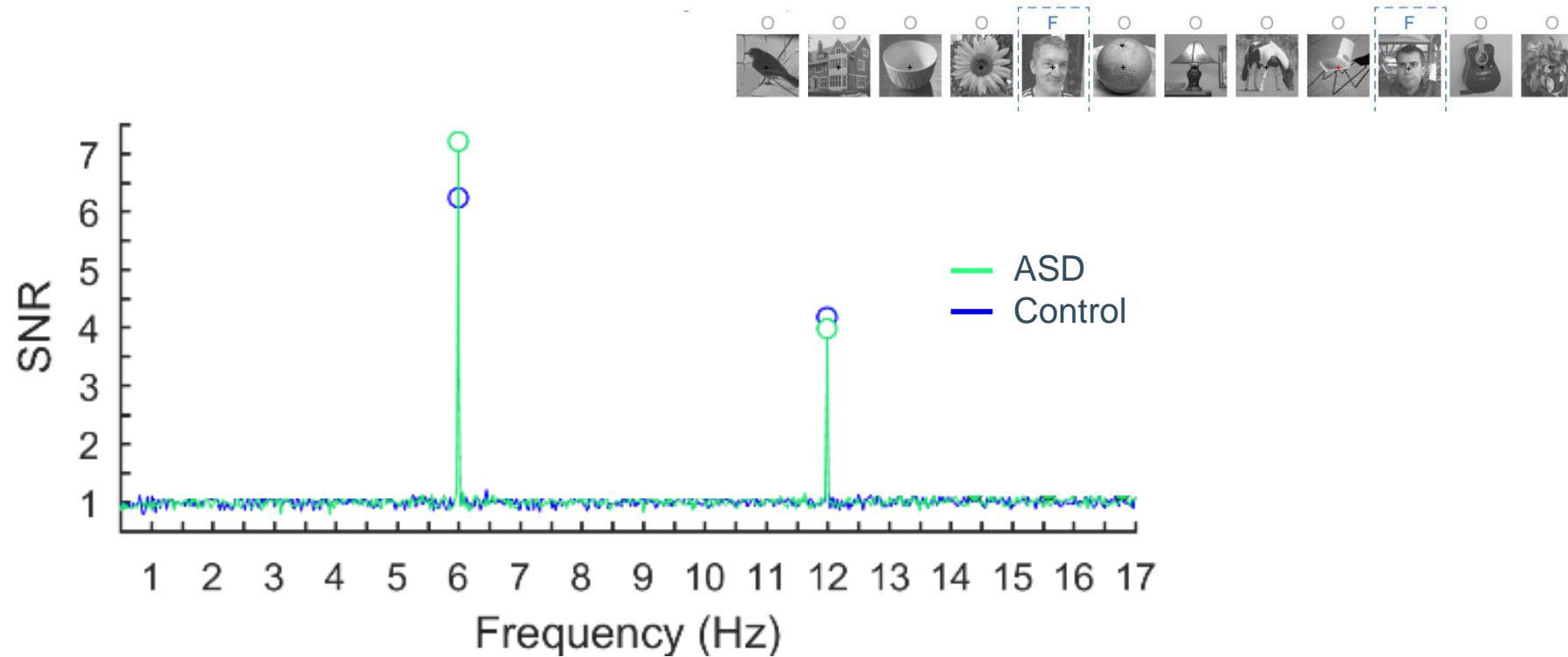
- 4 x 40 seconds
- **Implicit:** orthogonal task



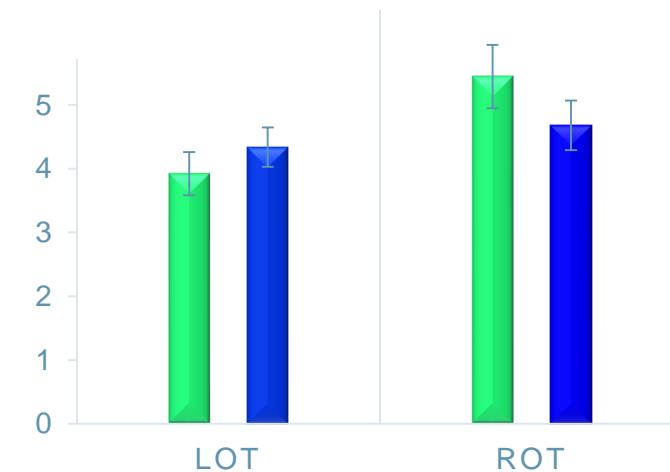
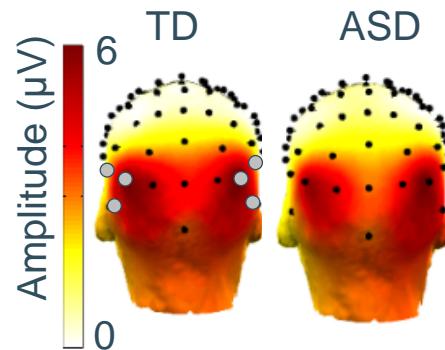
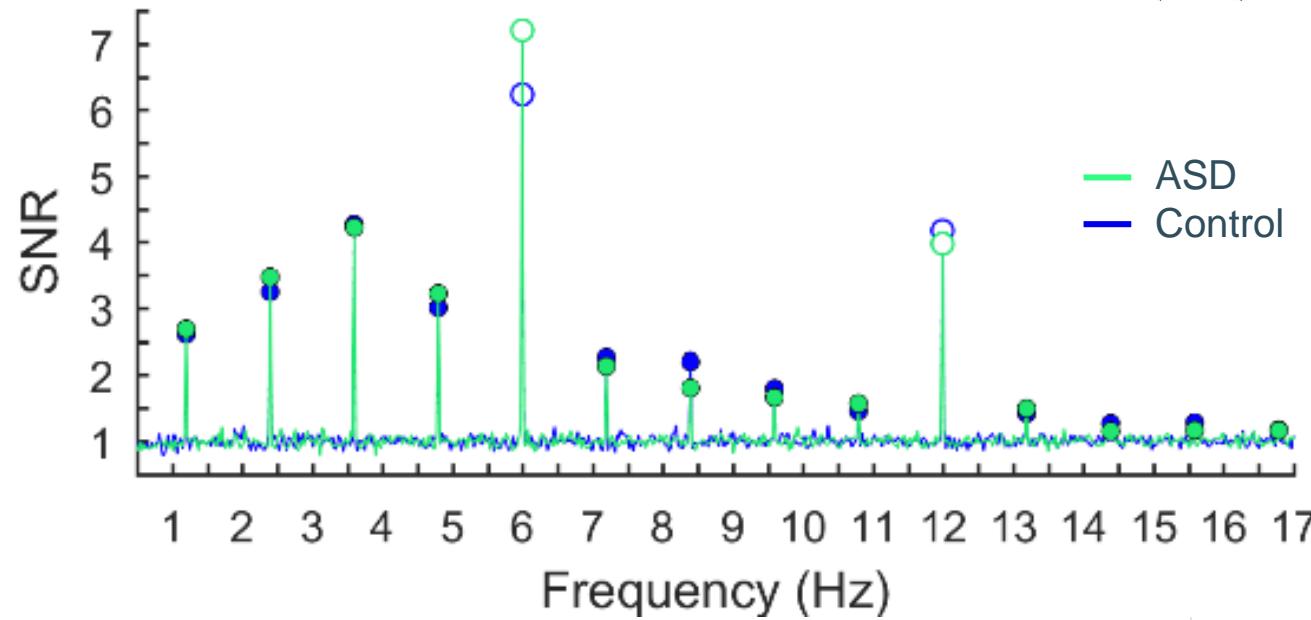
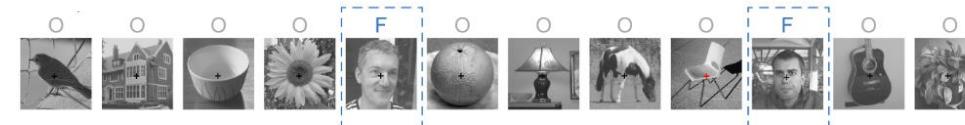
Fourier  
transformation



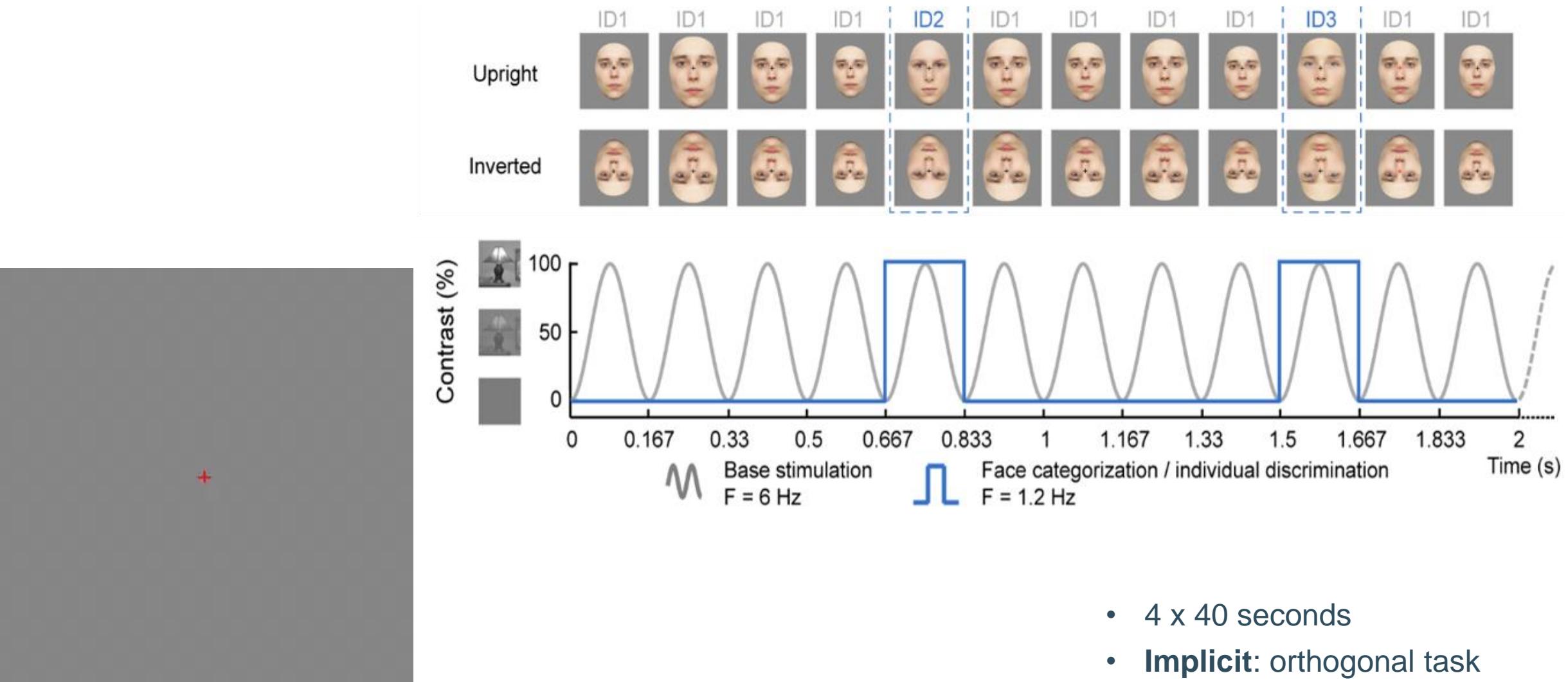
# No group differences in face categorization



# No group differences in face categorization

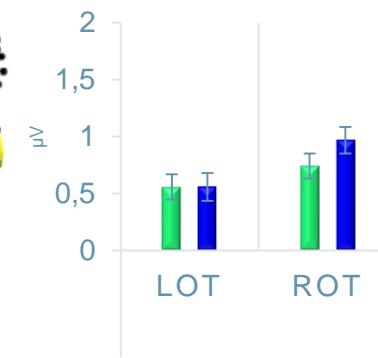
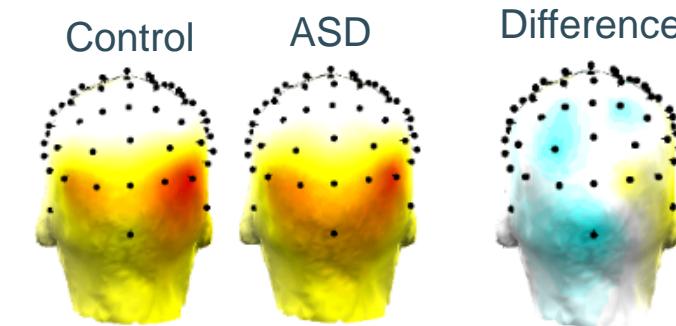
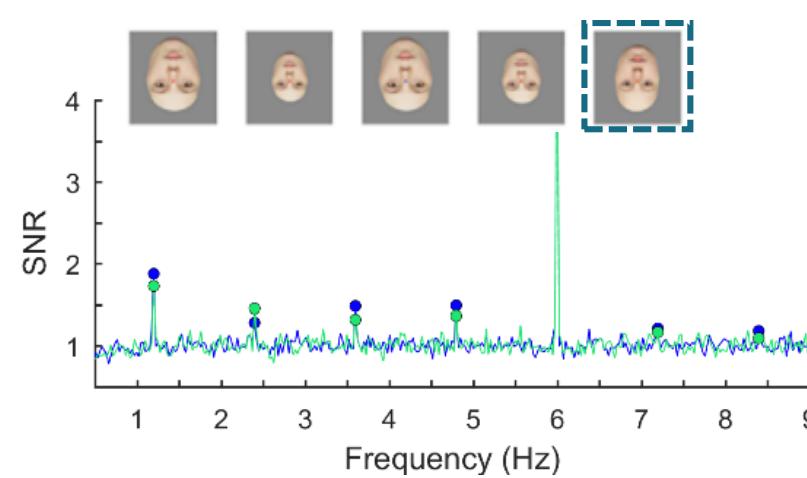


# Facial identity discrimination

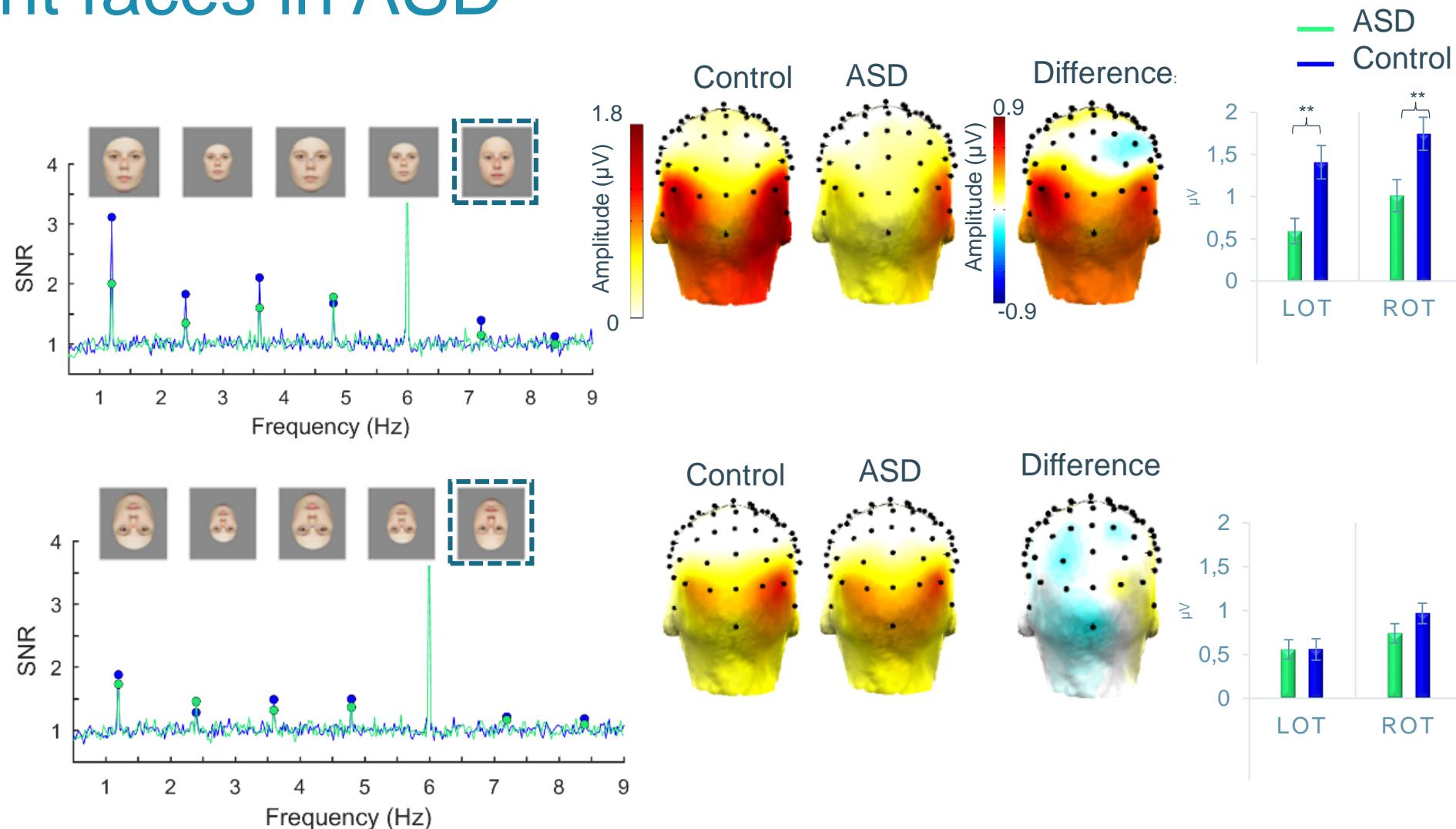


# Facial identity discrimination

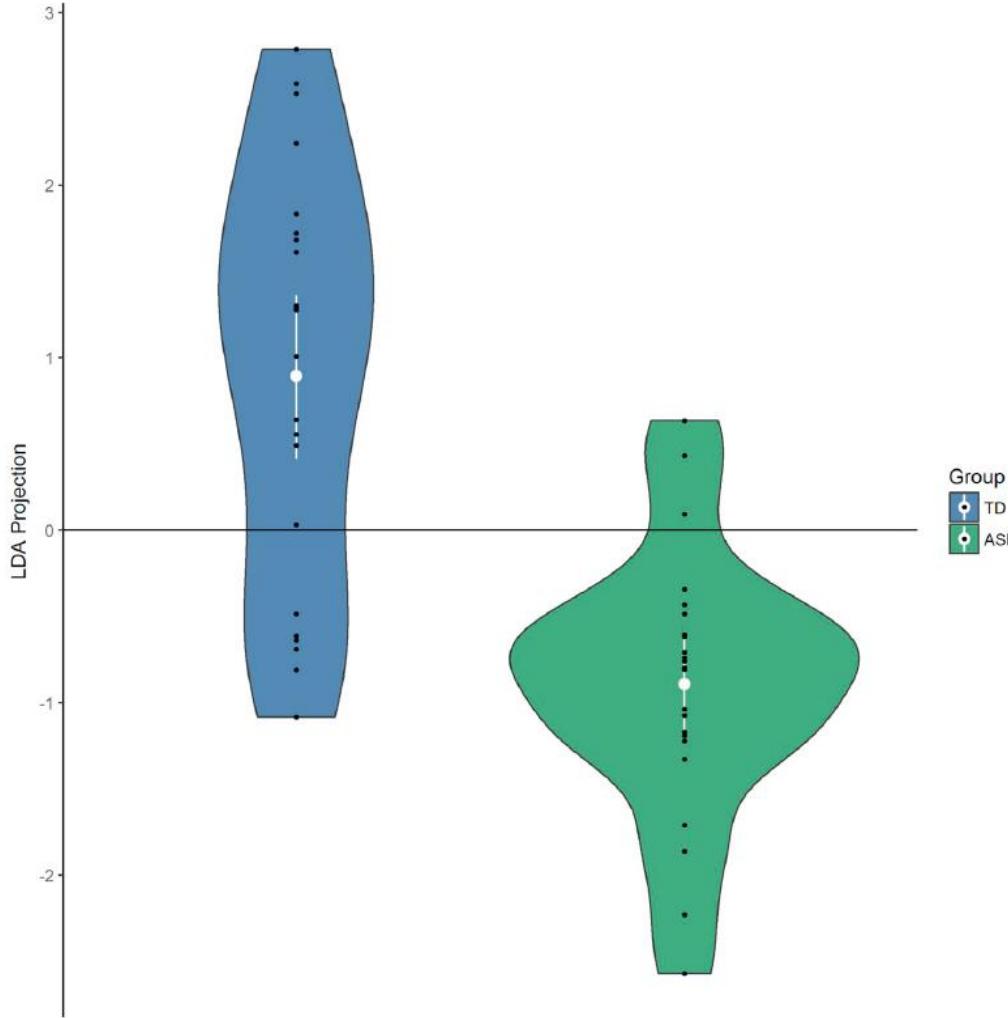
ASD  
Control



# Reduced individual face discrimination response to upright faces in ASD

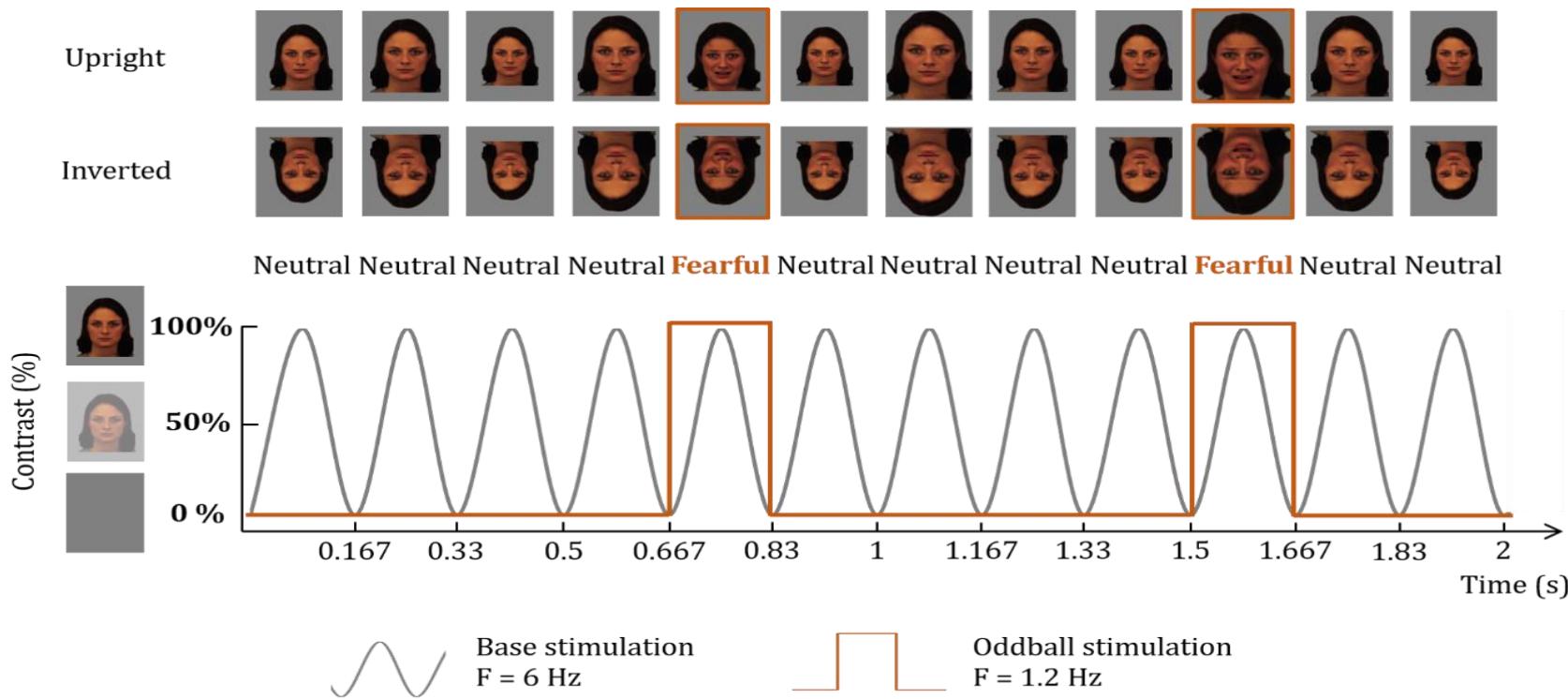
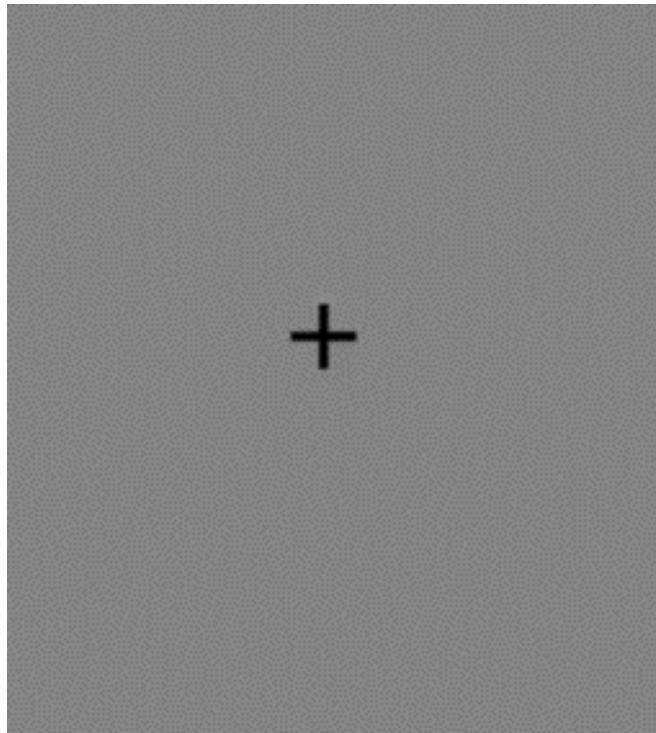


# Reduced individual face discrimination response to upright faces in ASD



- Accuracy of predicting clinical status at subject level = 78%

# Emotion discrimination: fear vs neutral

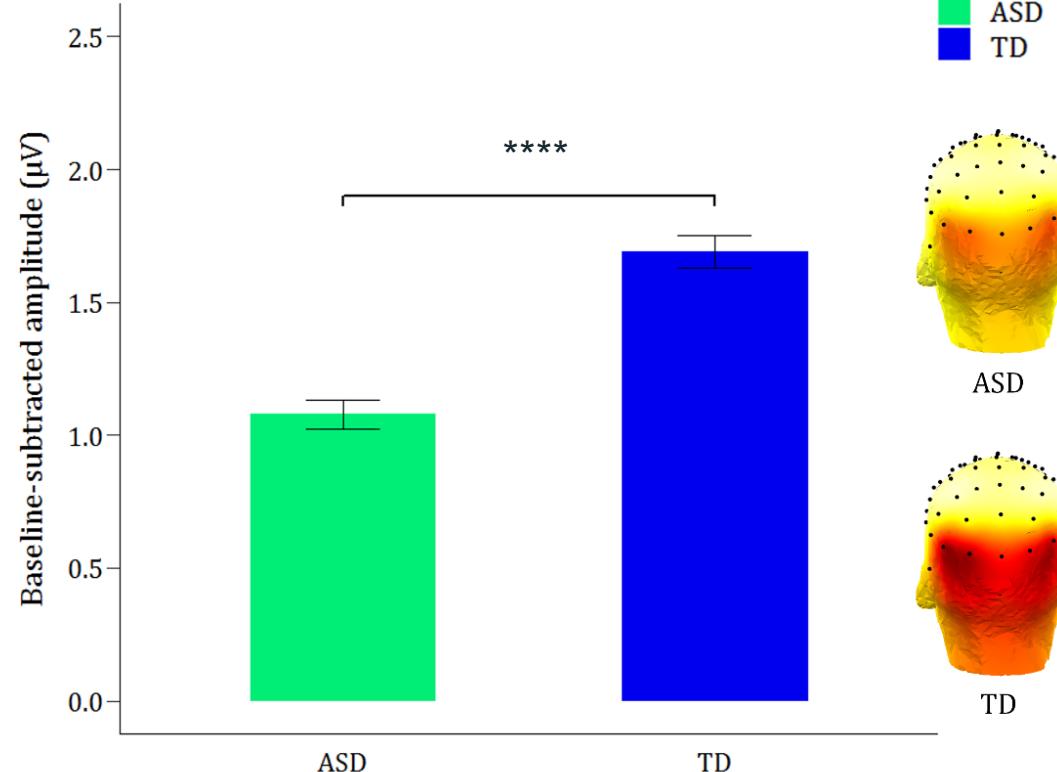


- **Fast:** 4 x 60 seconds
- **Implicit:** orthogonal task
- **Fixation on eyes vs mouth**

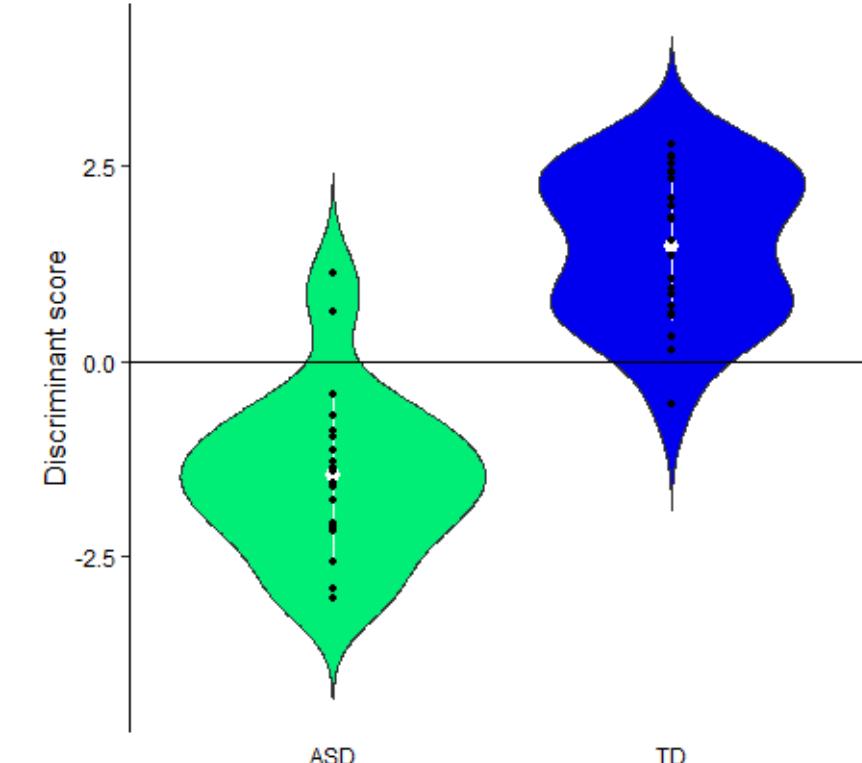
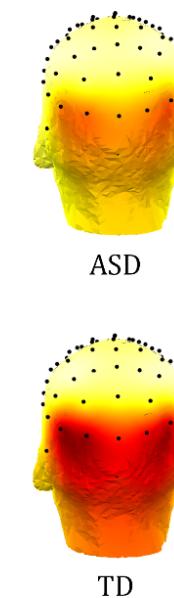
# Reduced fear discrimination response in ASD

A

Main effect of *Group* ( $p < .0001$ )



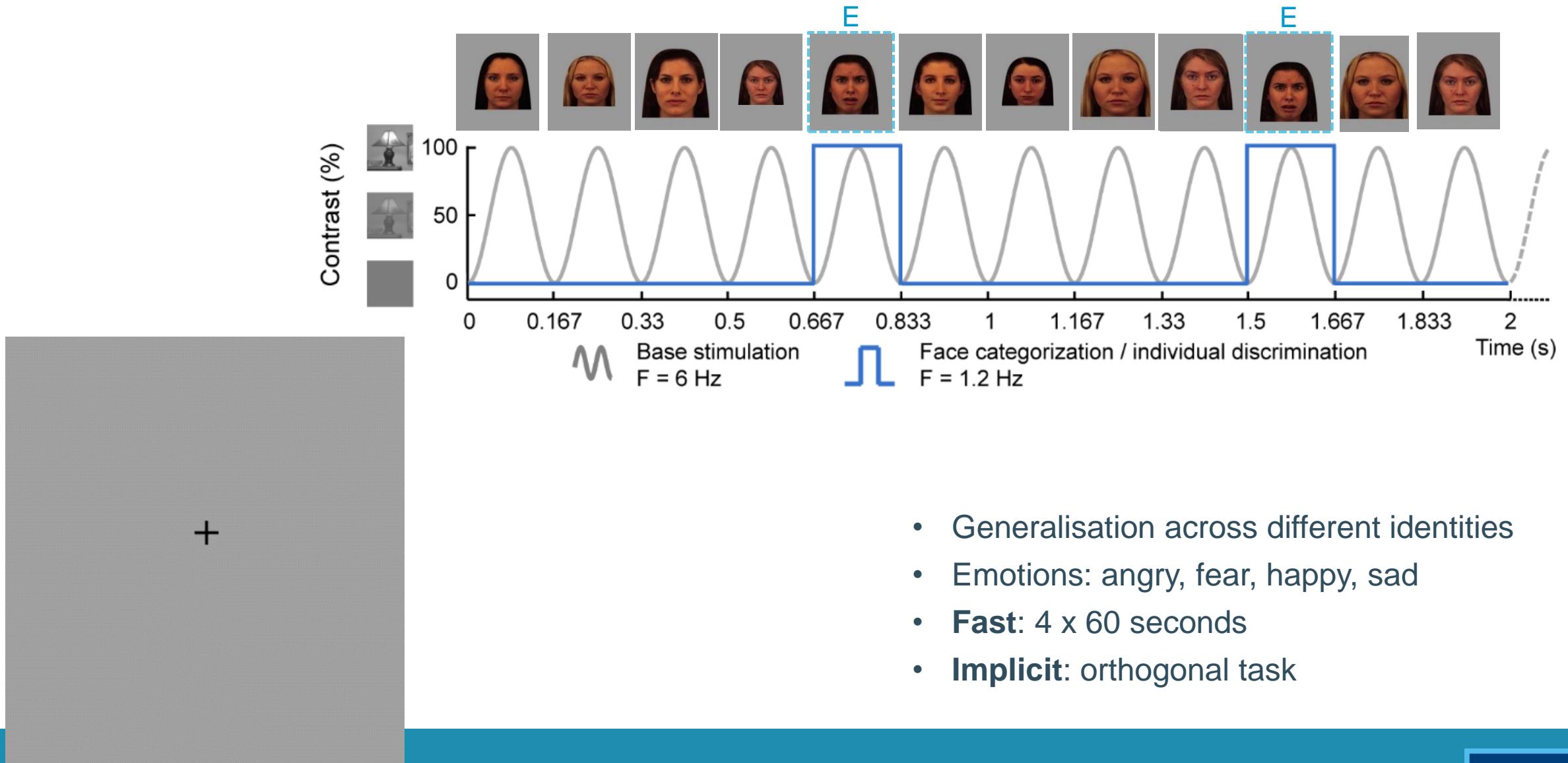
Group  
ASD  
TD



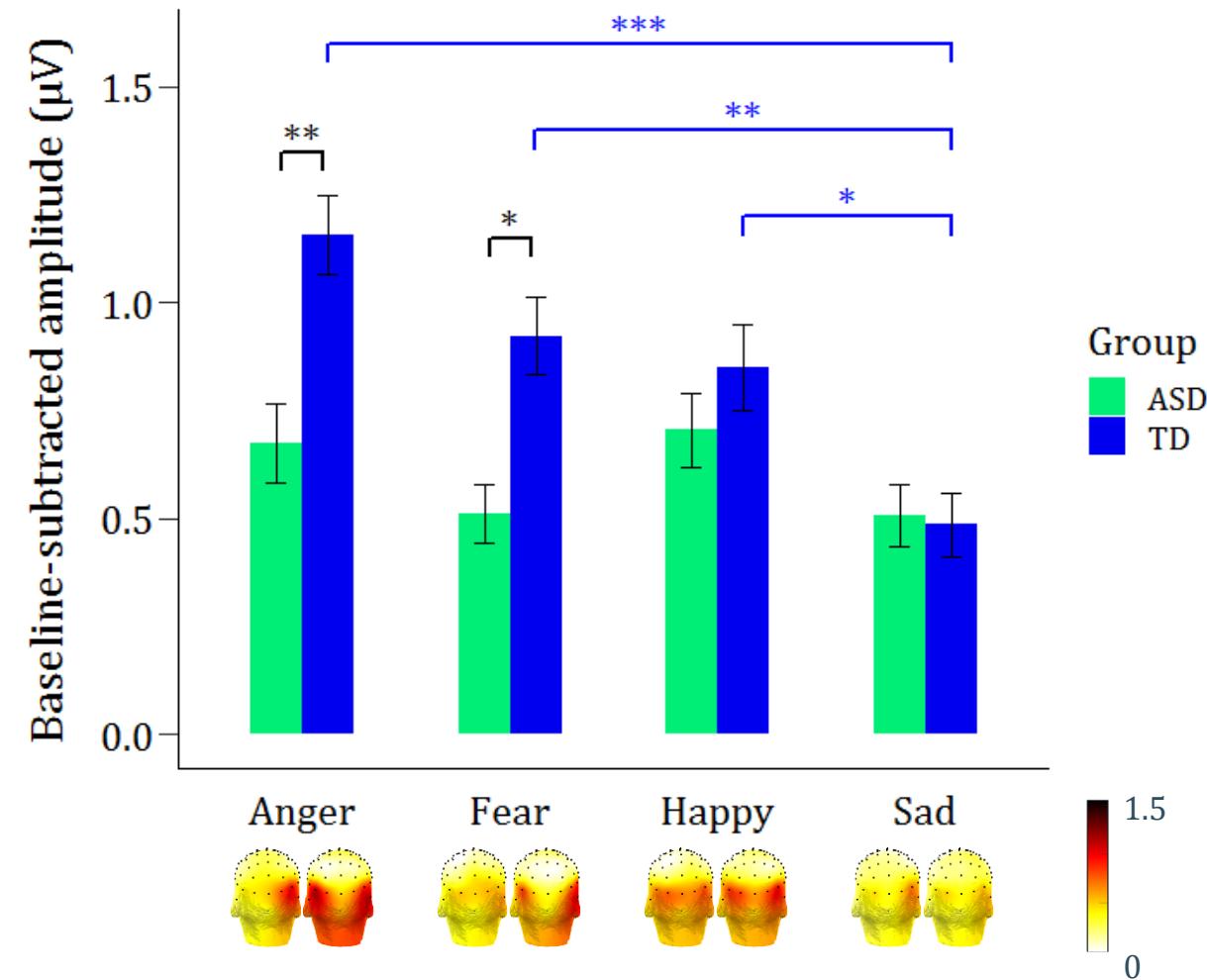
Group  
ASD  
TD

Accuracy of predicting clinical status at subject level = 83%

# Expression discrimination across different identities

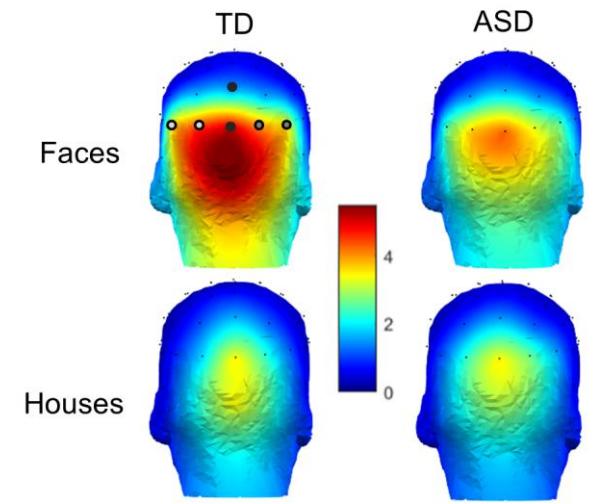
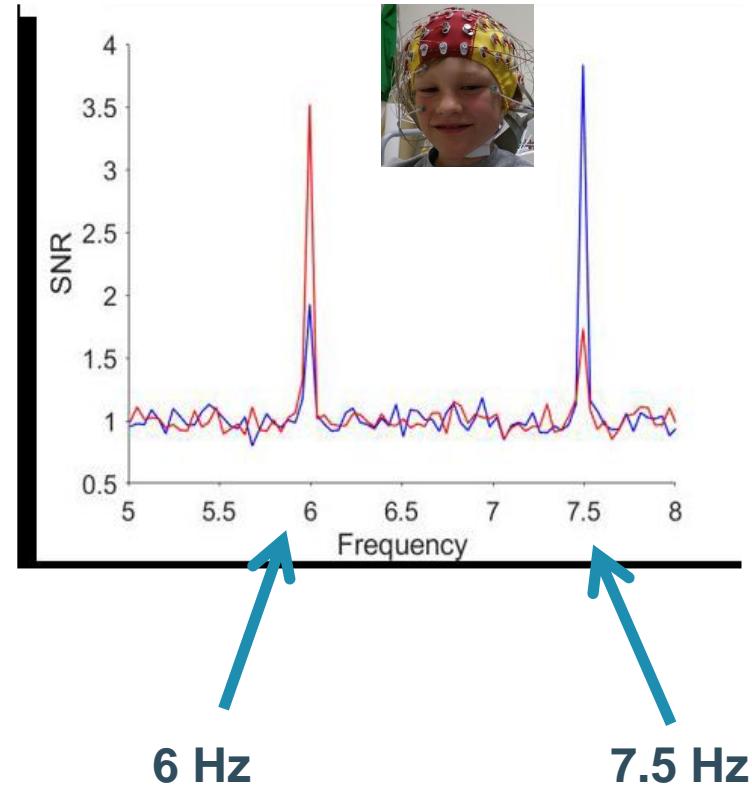
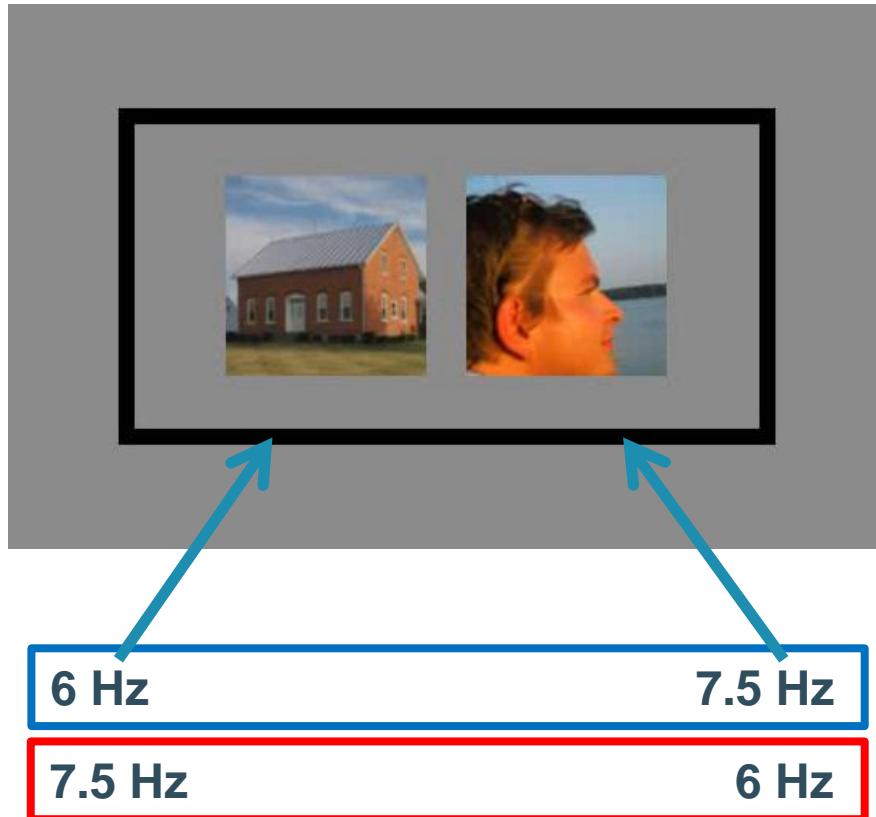


# Reduced expression discrimination in ASD



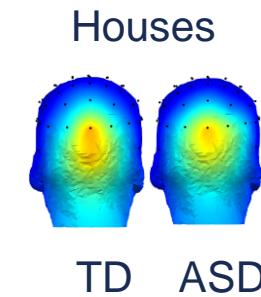
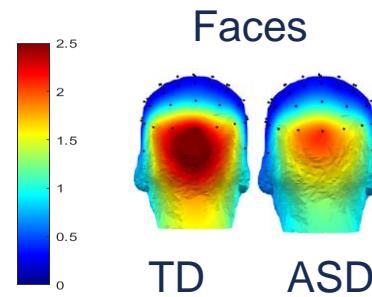
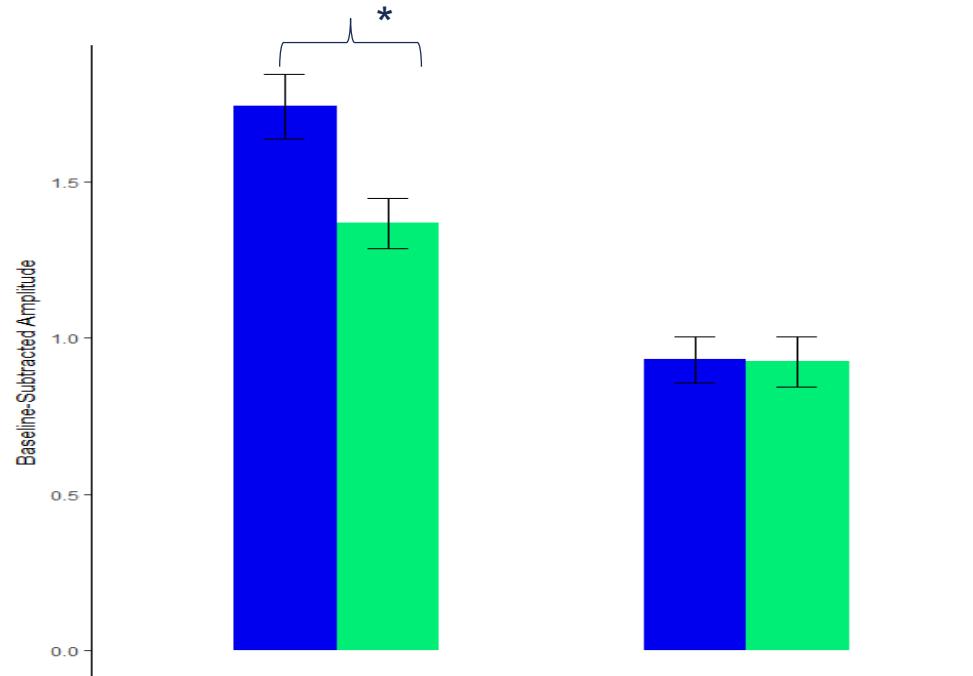
# Frequency-tagging EEG and eye-tracking

## Social versus non-social sensitivity



After 5s: Sign group x condition interaction

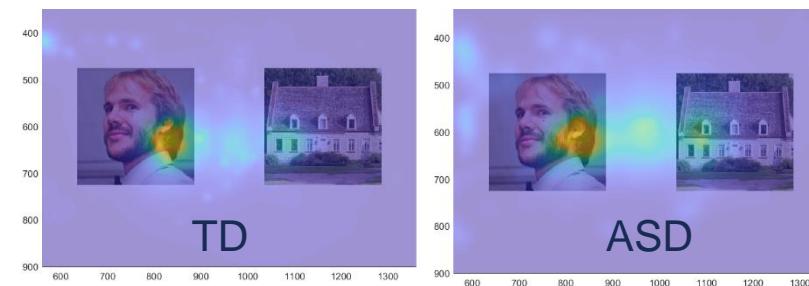
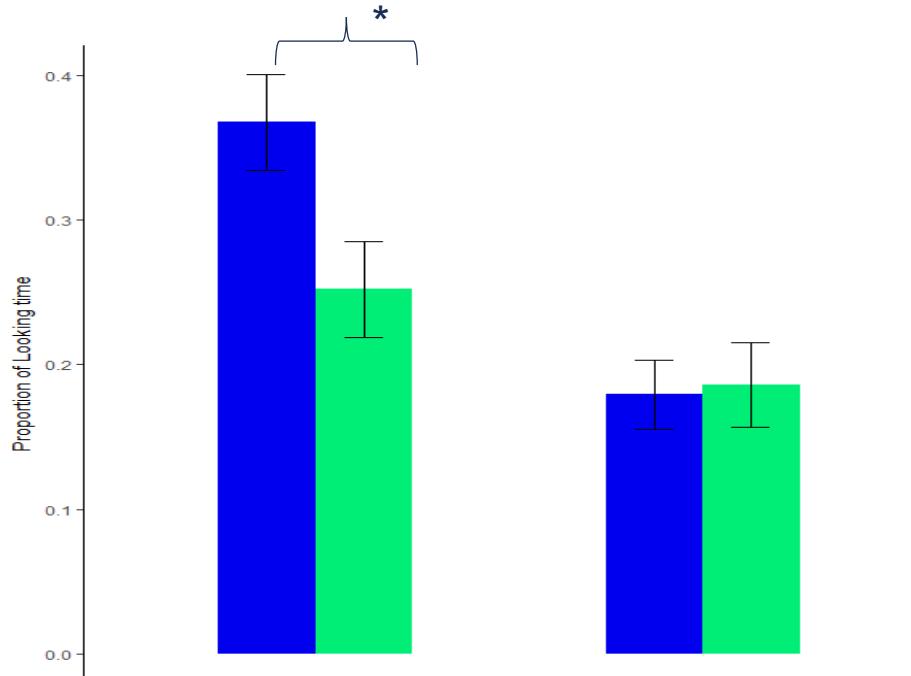
# Reduced sensitivity/preference for faces vs houses in ASD



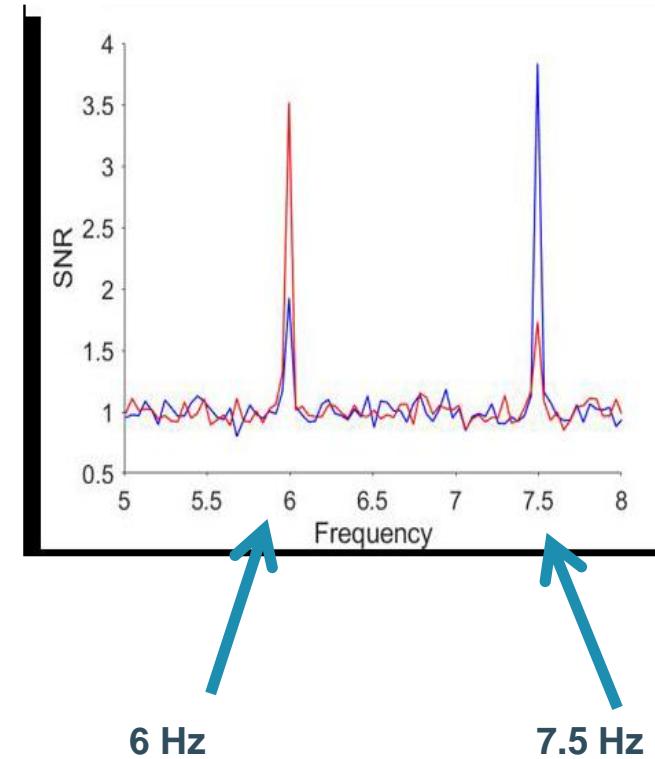
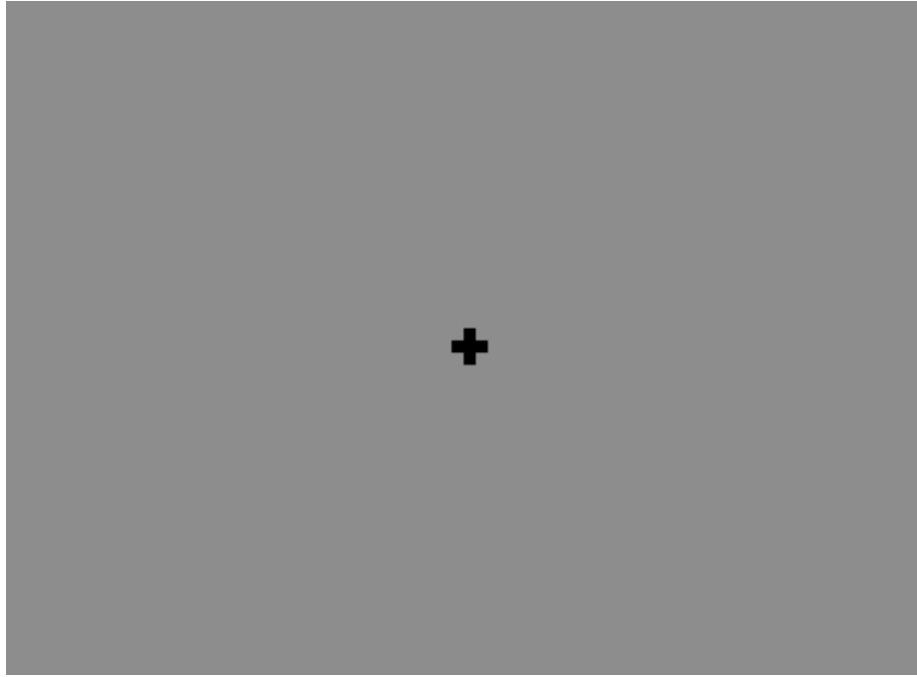
NEURAL SALIENCE

CORR = .75

PREFERENTIAL LOOKING



# Social vs non-social neural sensitivity: Overlay paradigm



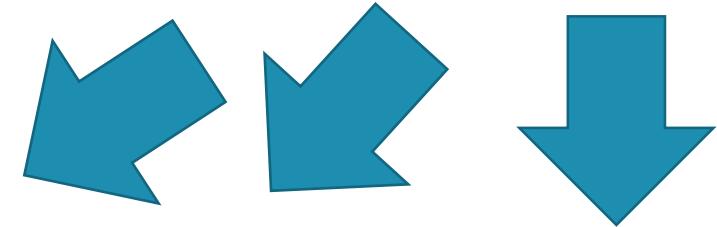
Group x Stimulus type interaction

- TD: Brains are tuned towards social information
- ASD: reduced modulation of the neural response by social content

# Potential of frequency-tagging EEG

- Clear response with high SNR in individual subjects
- Fast, implicit, double-objective
- High test-retest reliability
- Straightforward, cheap
- Differentiates clearly between clinical populations

children/adults with ASD



Preterm children



Preterm toddlers at risk



Infants at risk



# Exploring the potential of frequency-tagging EEG as an early biomarker in high-risk infant populations?



KU LEUVEN

# Infants at increased risk for socio-emotional disturbances and ASD

## 1. ASD siblings

- genetic load



- Steffie Amelynck
- Lyssa de Vries

## 2. Prematurely born infants

- altered maturation of the brain
- exposure to prenatal/perinatal stress & pain
- altered early parent-infant interactions
- Monitoring of socio-communicative sensitivity and attachment
  - At 5 – 10 - 14 months + follow-up



# Infant applications

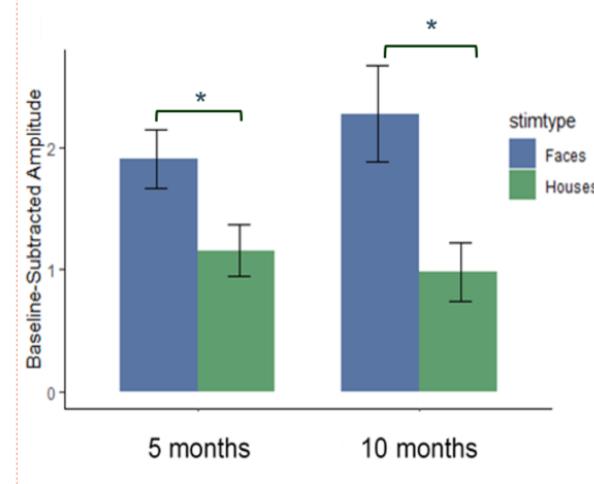
- Infants naturally orient towards faces
    - Especially, mother's face and faces with smile or direct eye gaze
- Atypicalities in (neural) sensitivity towards these social stimuli might index deviant socio-emotional development



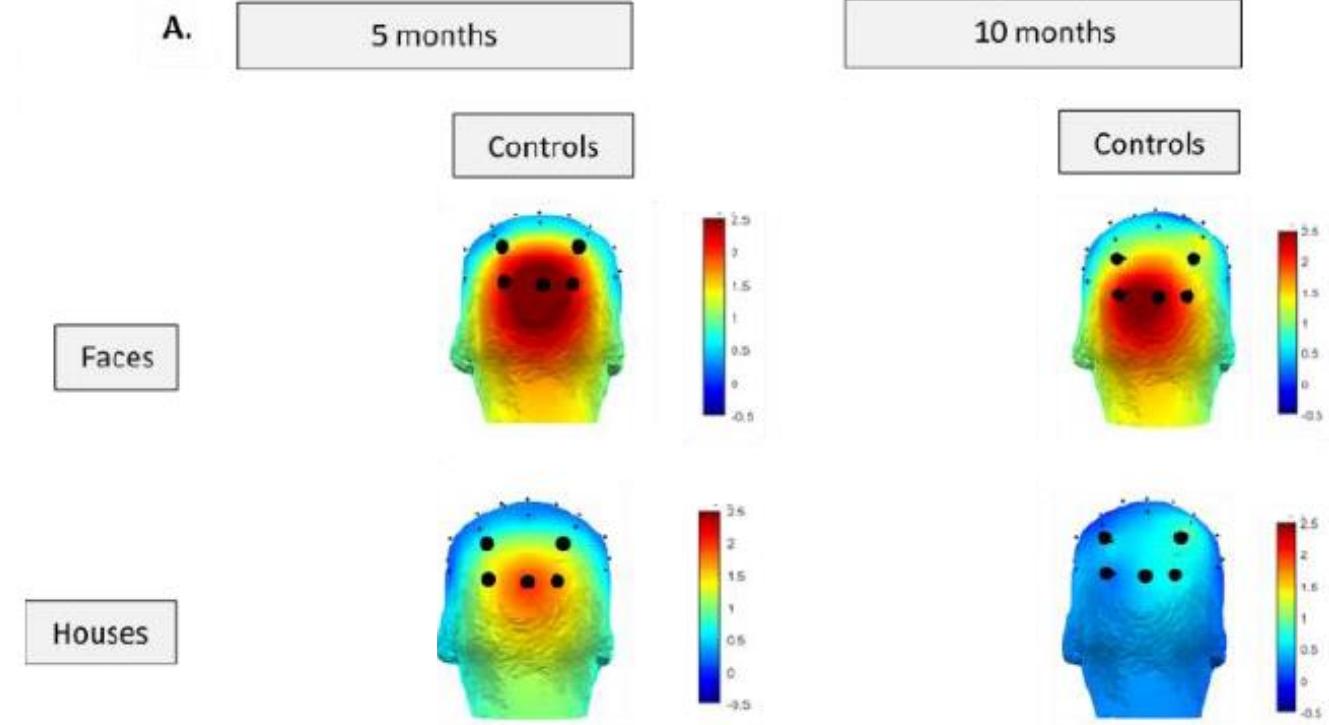
# ... tuned towards faces



4 x 30s (5 Hz vs 6 Hz)



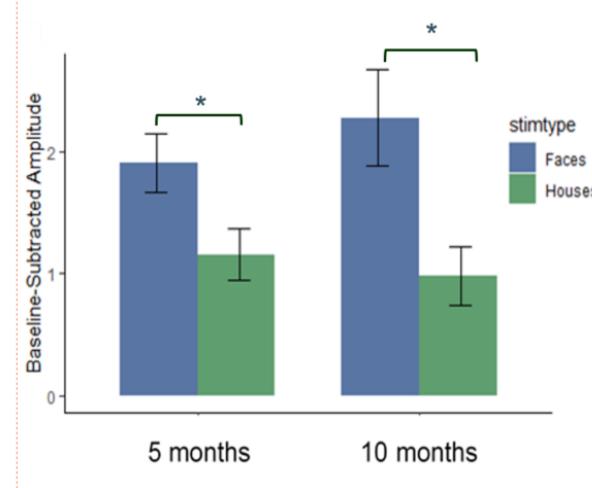
Preterms: N=23 (data points)  
Term-born controls: N=41 (data points)



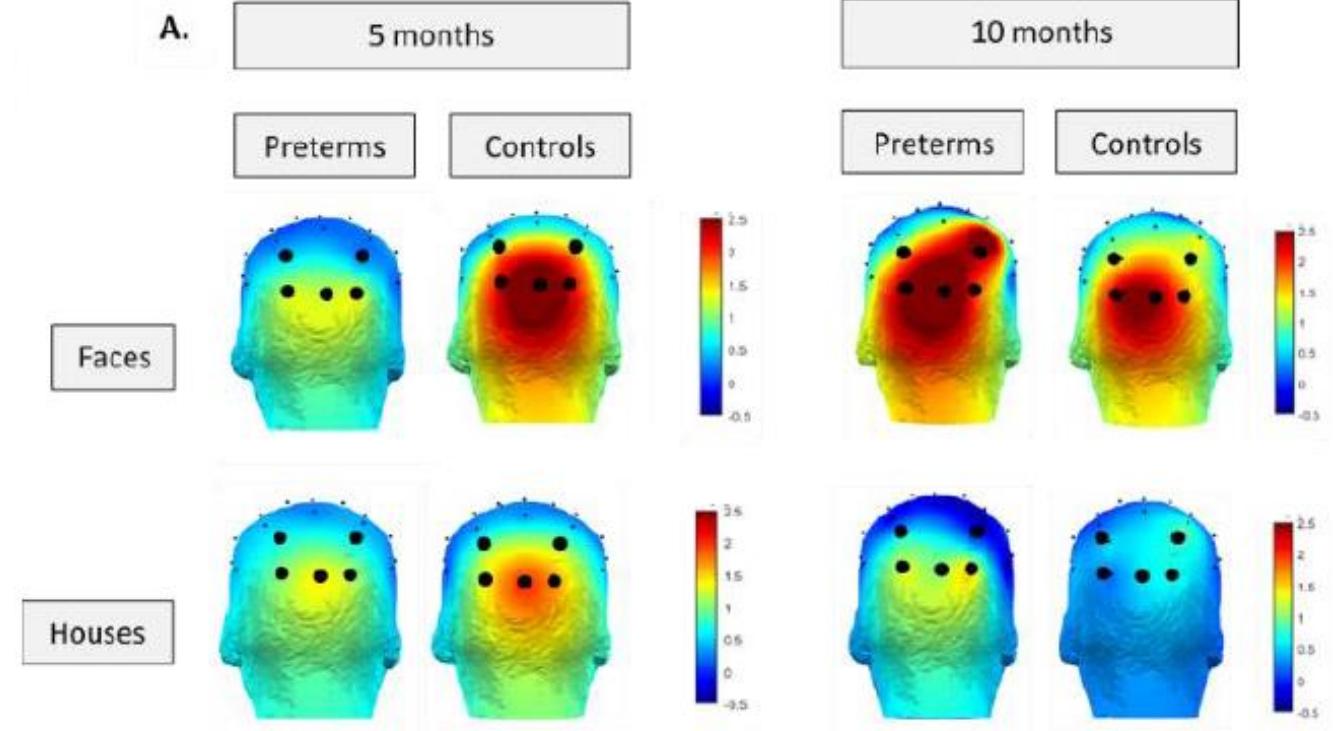
# ... tuned towards faces



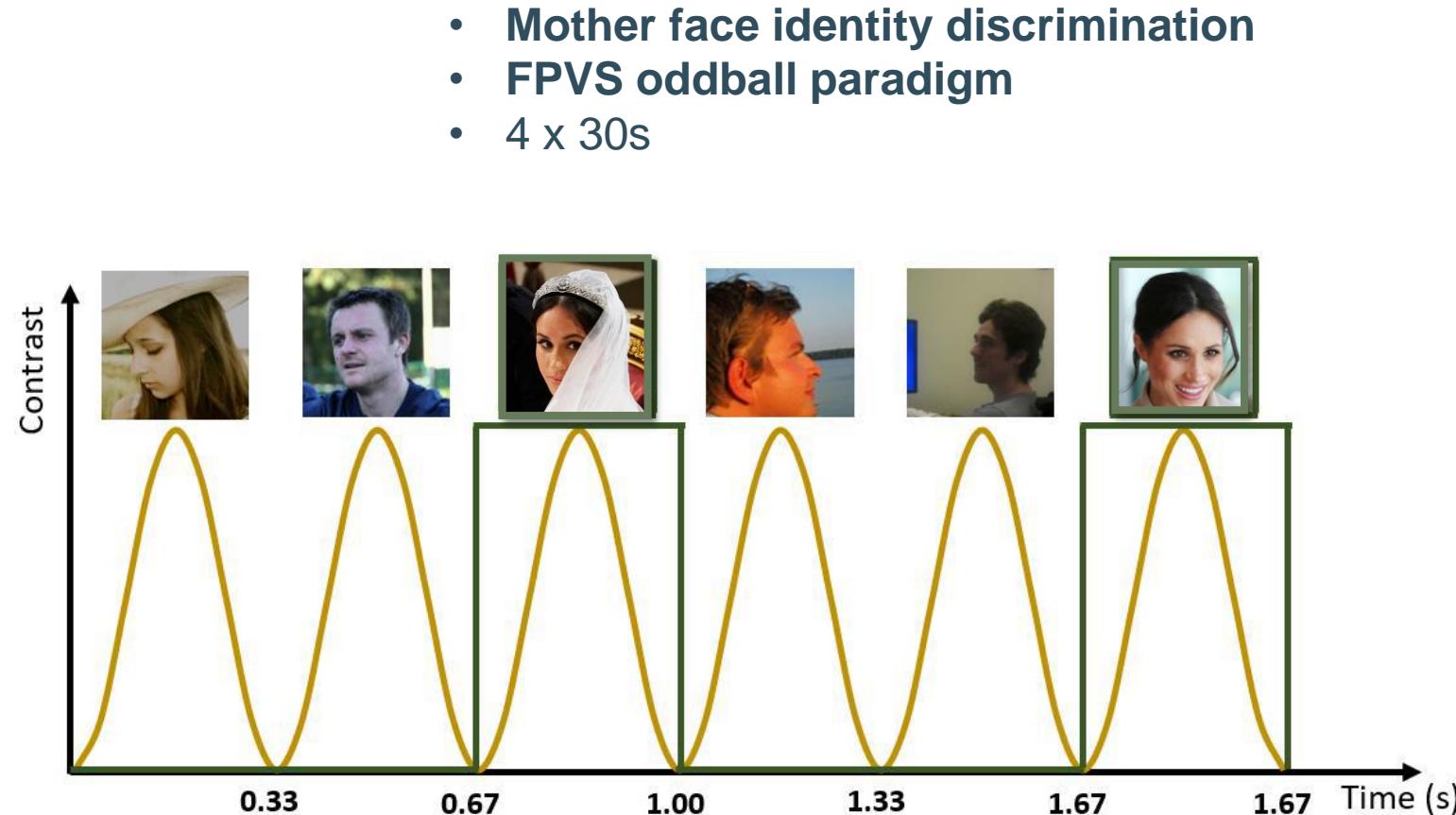
4 x 30s



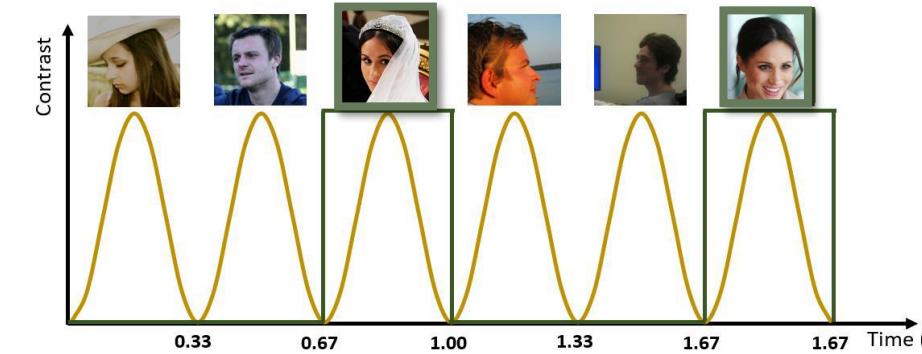
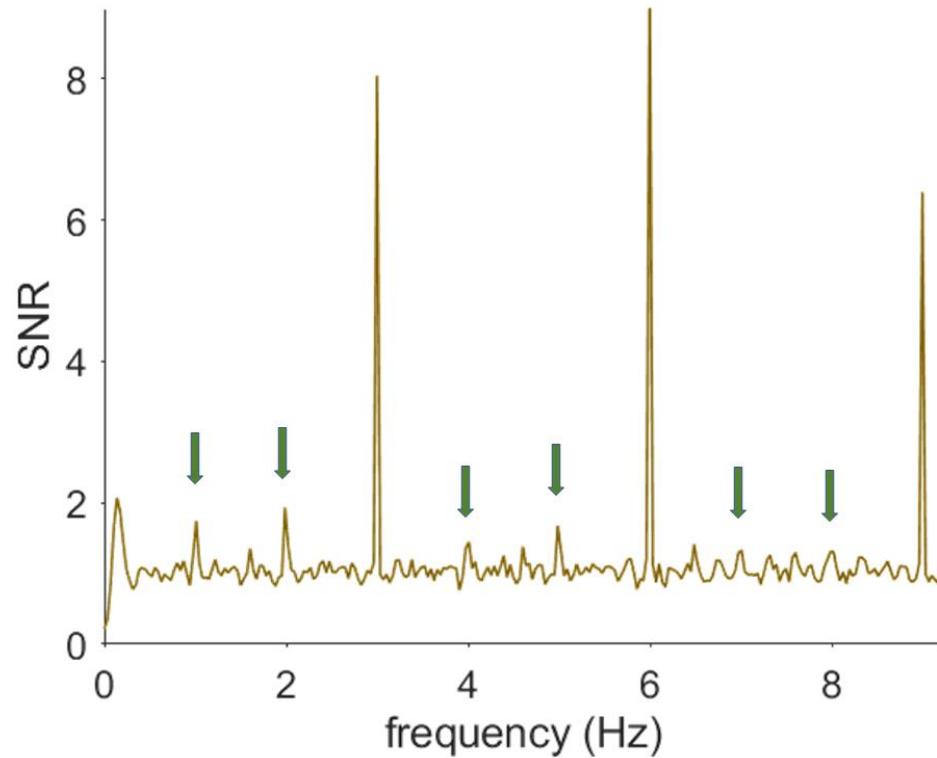
Preterms: N=23 (data points)  
Term-born controls: N=41 (data points)



# ... tuned towards mother's face

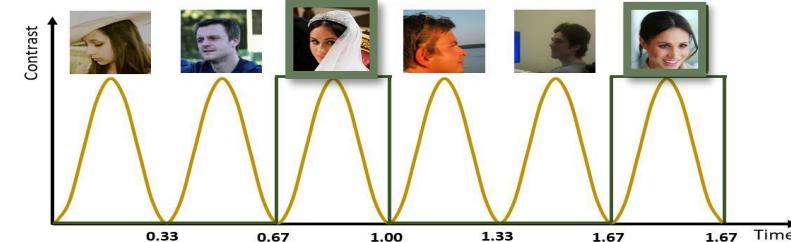


# ... tuned towards mother's face

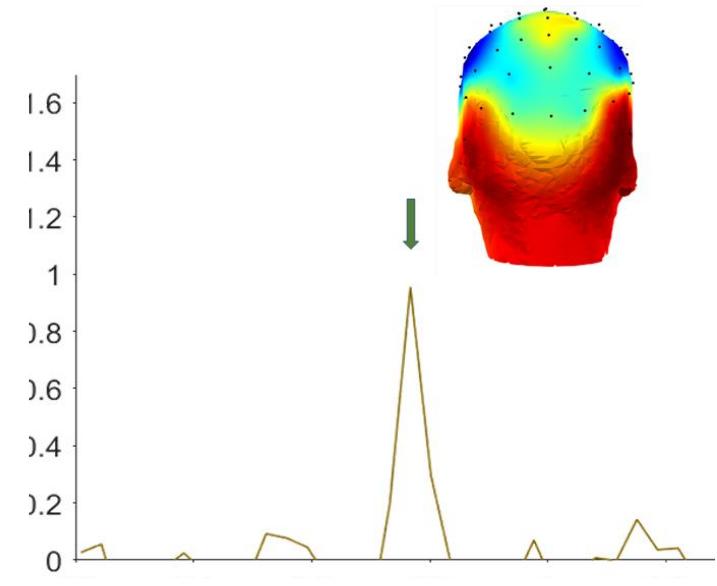


- Familiar face identity discrimination
- N = 25 adults
- Target face = familiar other
  - Romantic lover
  - Friend
  - Experimenter

# ... tuned towards mother's face



## Summed baseline-subtracted oddball amplitudes

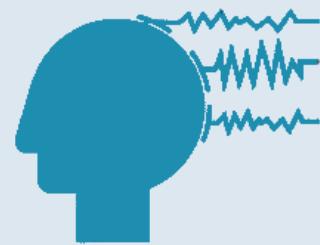


- 25 Adults
- 24 significant ( $p < .01$ )

# Quantifying socio-communicative sensitivity using periodic AUDITORY stimulation EEG

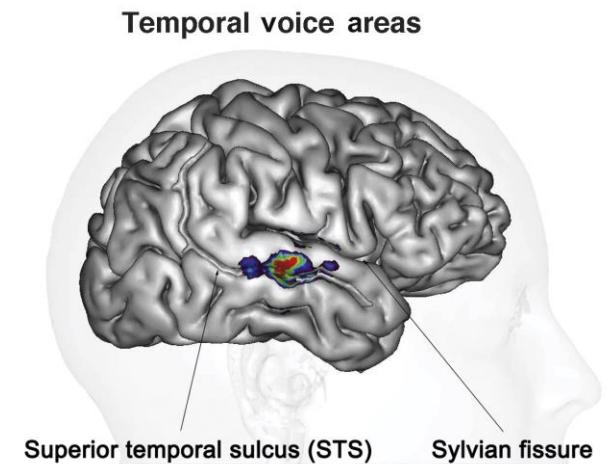


Silke Vos

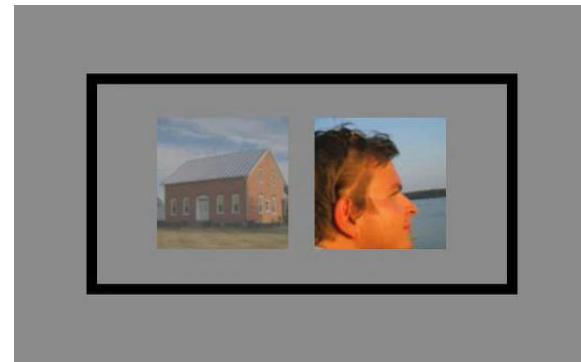


# Atypical voice processing in ASD?

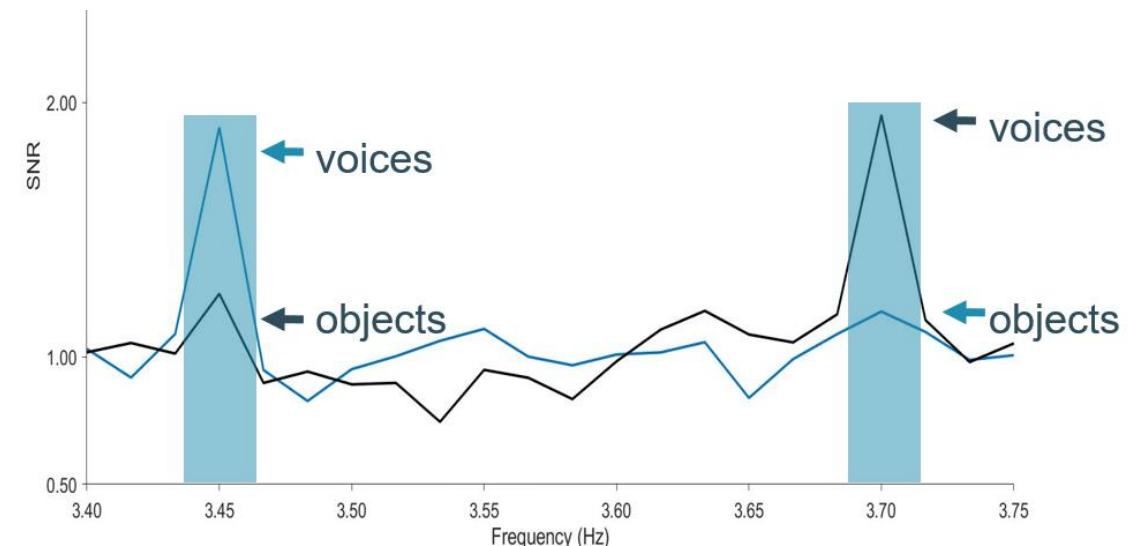
- Face // voice → social information on age, gender, identity, emotion ... (+ speech)
- Dedicated neural circuitry, including Temporal Voice Area
- Atypical voice processing in ASD?
  - No automatic orienting to vocal stimuli
  - No / reduced activity in TVA in response to human voices
  - Difficulties with speech processing (e.g. speech-in-noise; competing speech)
  - Difficulties with speaker identity and emotion identification
    - mixed evidence



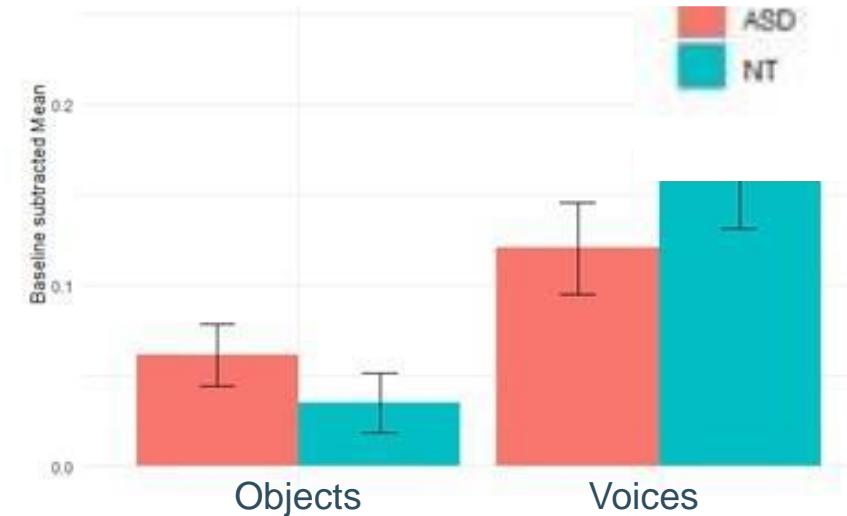
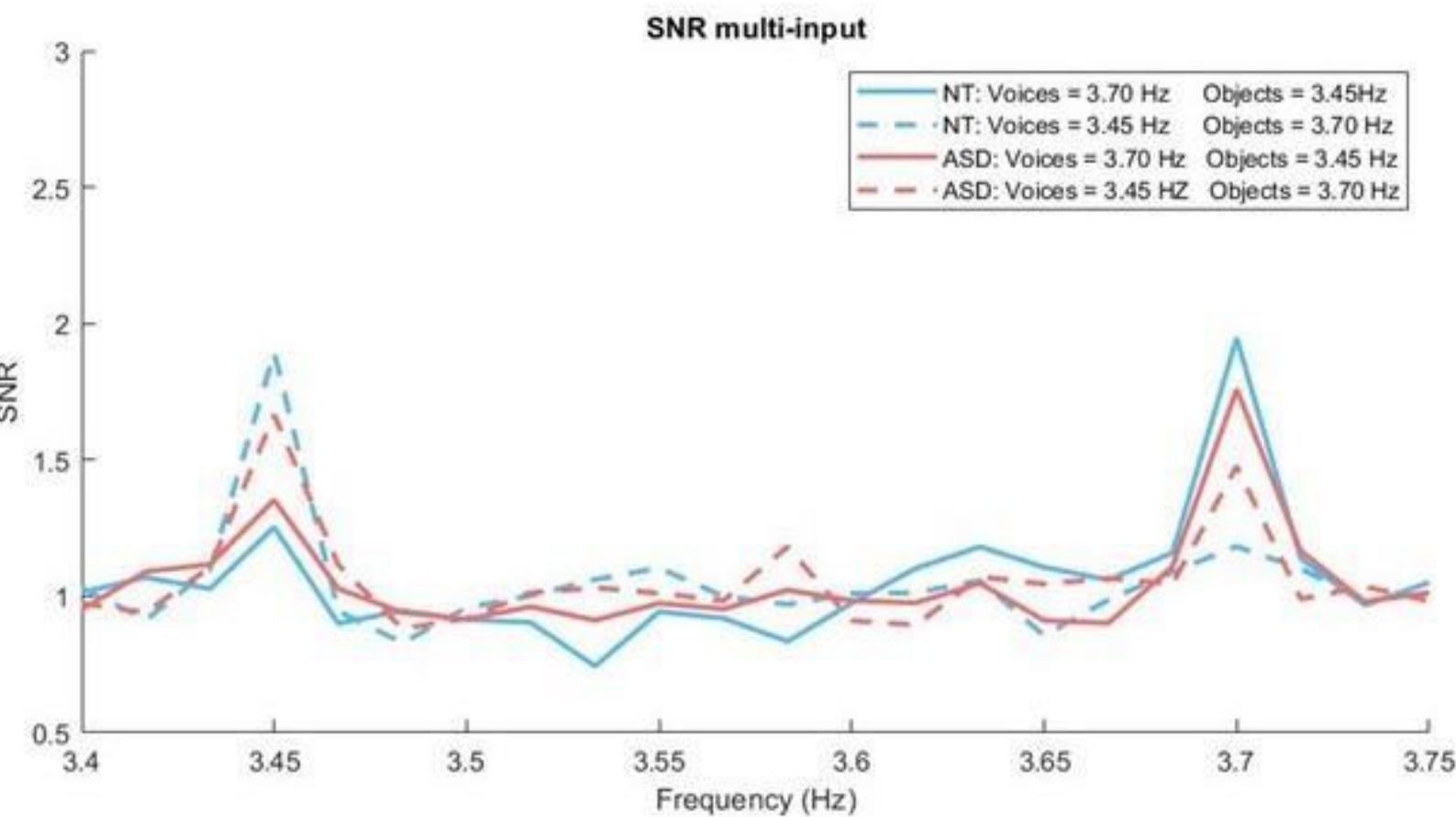
# Social preference / sensitivity for voices versus objects



3.45 Hz	3.70 Hz
3.70 Hz	3.45 Hz



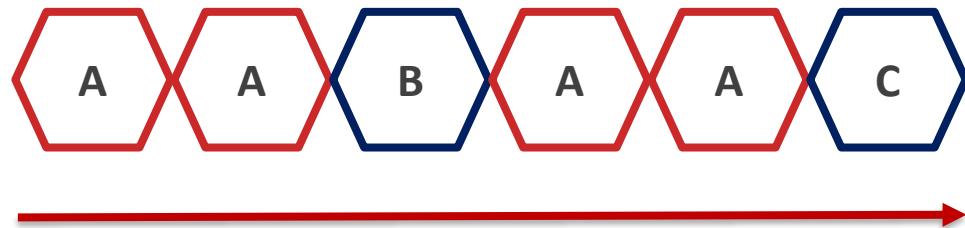
# Reduced neural tuning to voices in ASD



**Group x condition interaction ( $p < .01$ )**

- Both groups are tuned towards voices
- Reduced neural social tuning in ASD

# Vocal identity discrimination via oddball frequency-tagging EEG

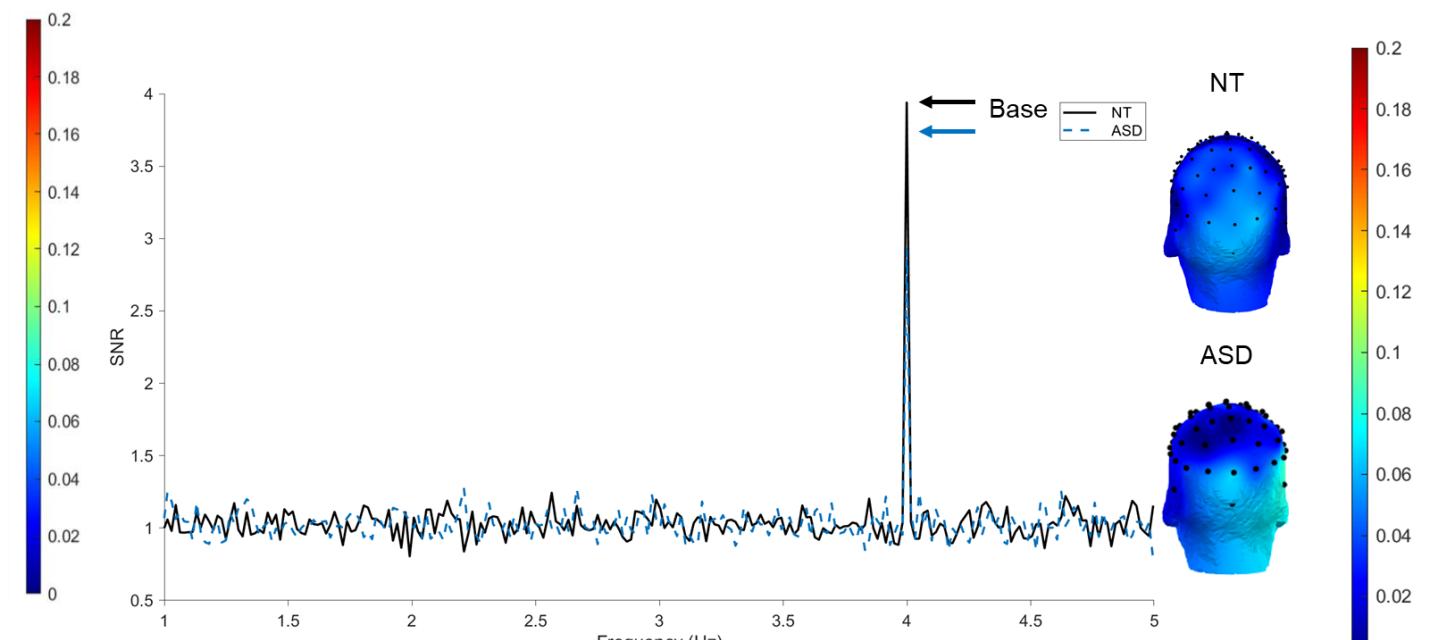
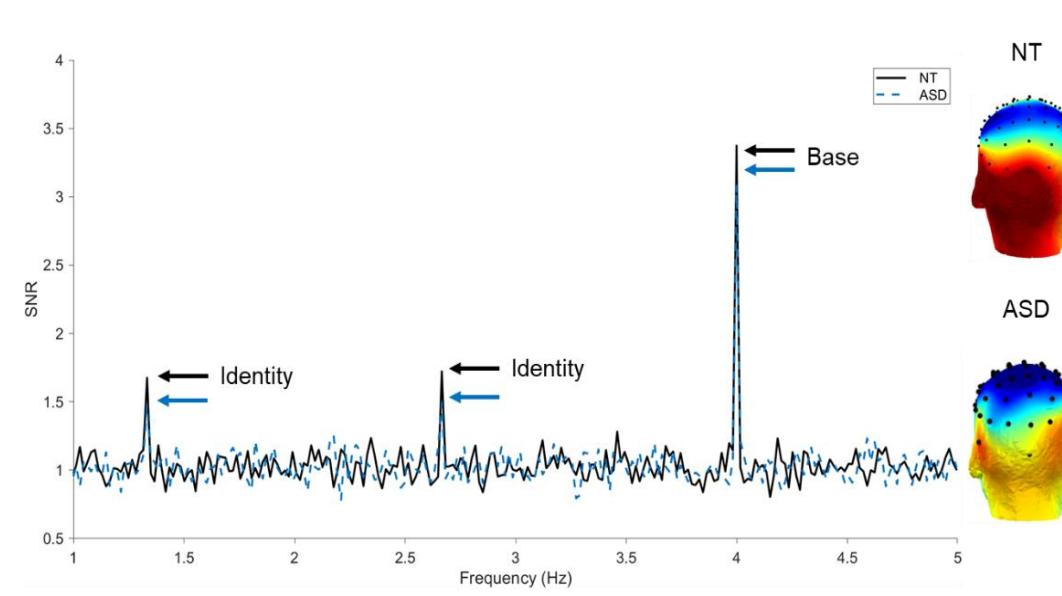


- 4 Hz base rate identity A
- 1.33 Hz oddball identity B-C-D

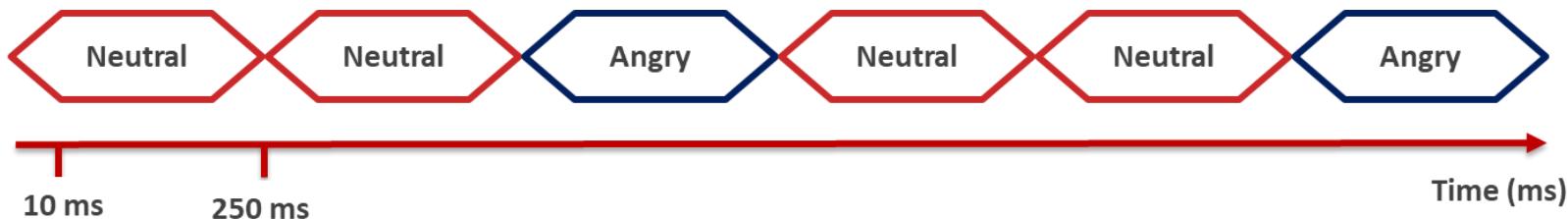
Identity oddball - Original



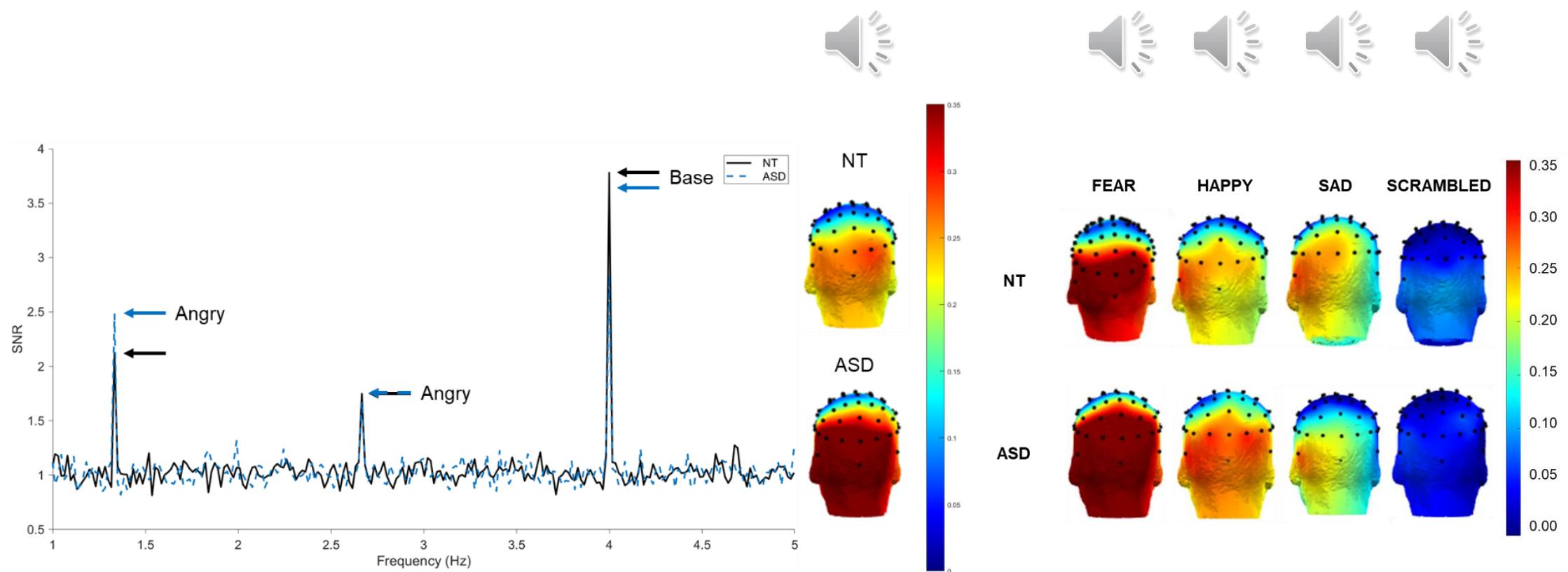
Identity oddball - Scrambled



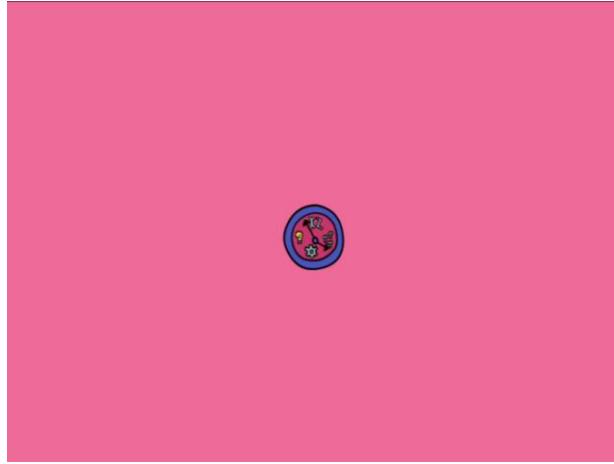
# Vocal emotion discrimination using frequency-tagging EEG



- 4 Hz base rate neutral voice
- 1.33 Hz oddball emotional voice



# Eye-tracking as implicit measure of cognitive functioning, social processing, ANS functioning



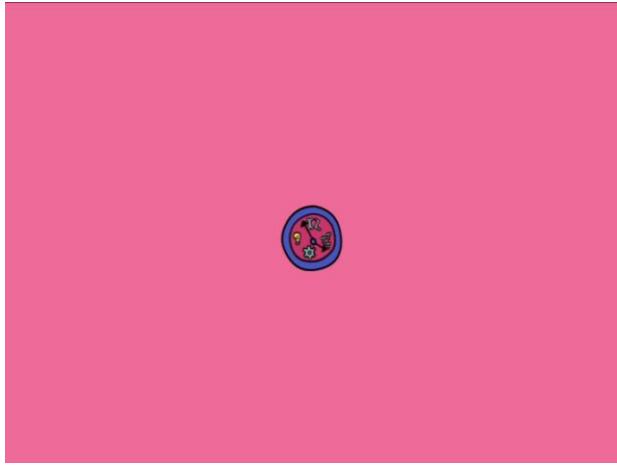
Disengagement



Face pop out



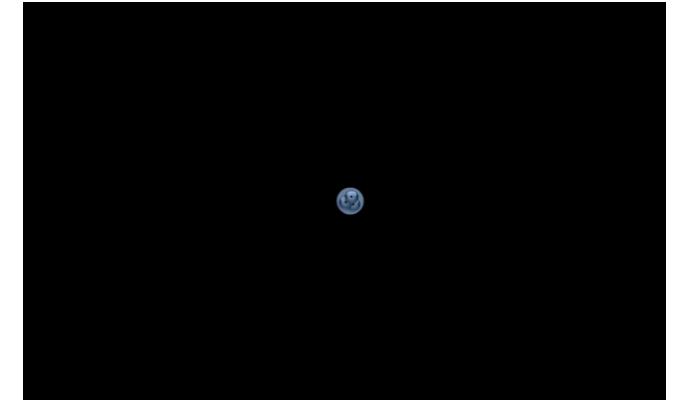
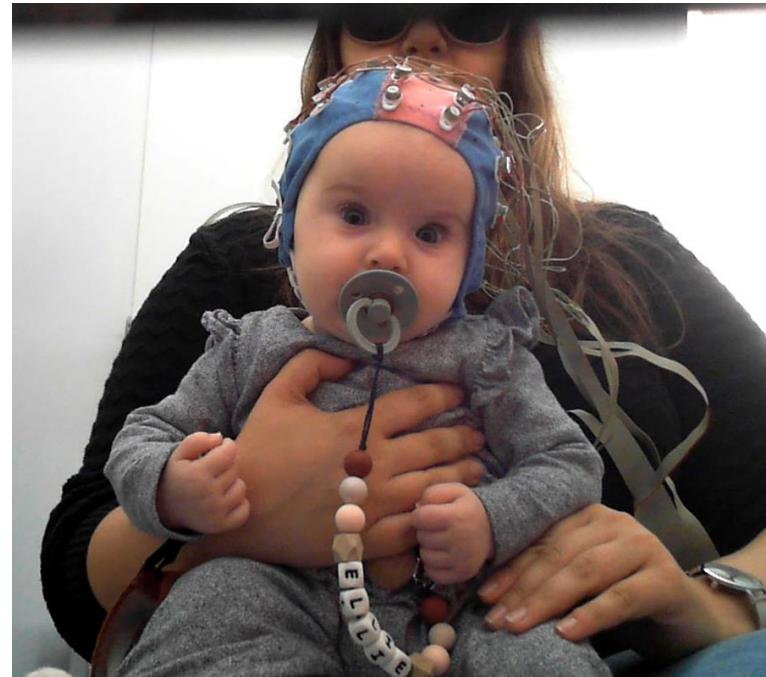
# Eye-tracking as implicit measure of disengagement, social processing, ANS functioning



Disengagement

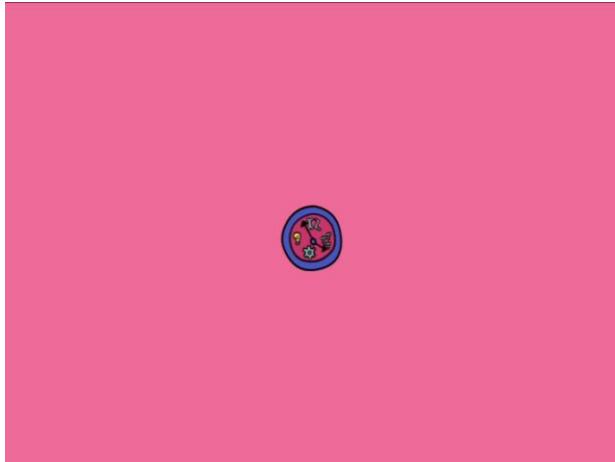


Face pop out



Pupillary light reflex

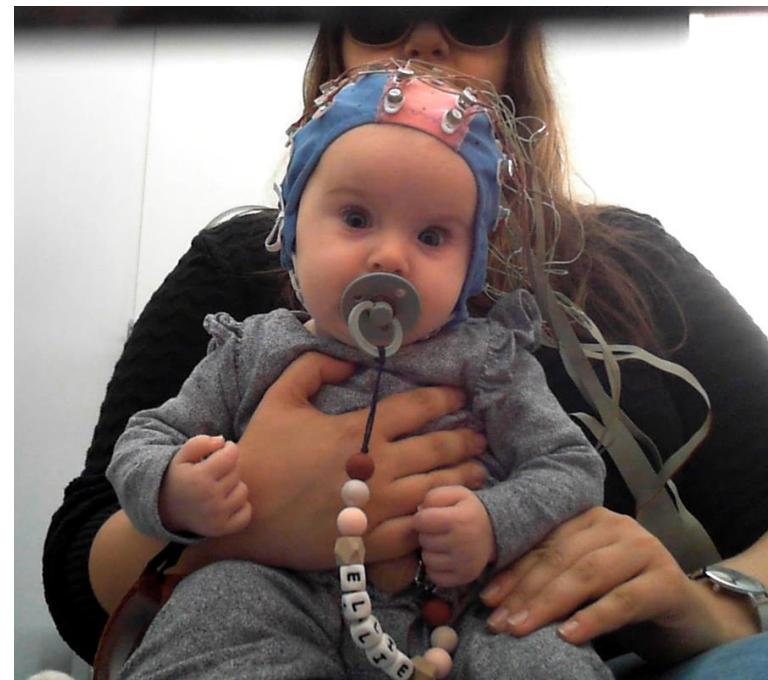
# Eye-tracking as implicit measure of disengagement, social processing, ANS functioning



Disengagement



Face pop out



Pupillary light reflex

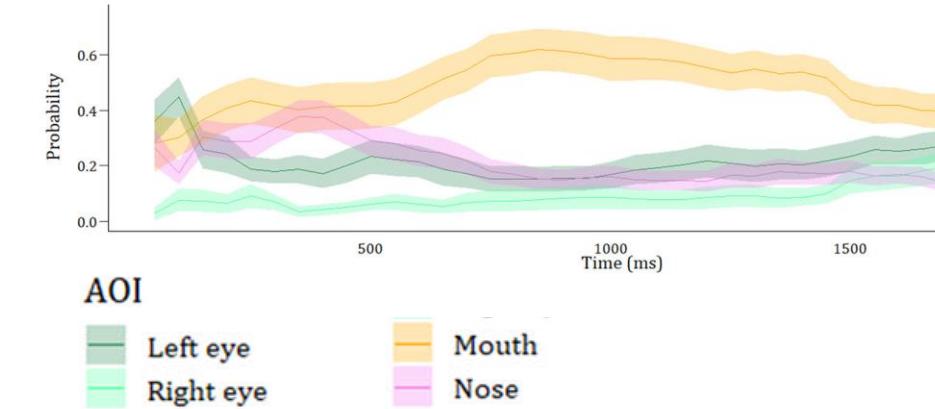
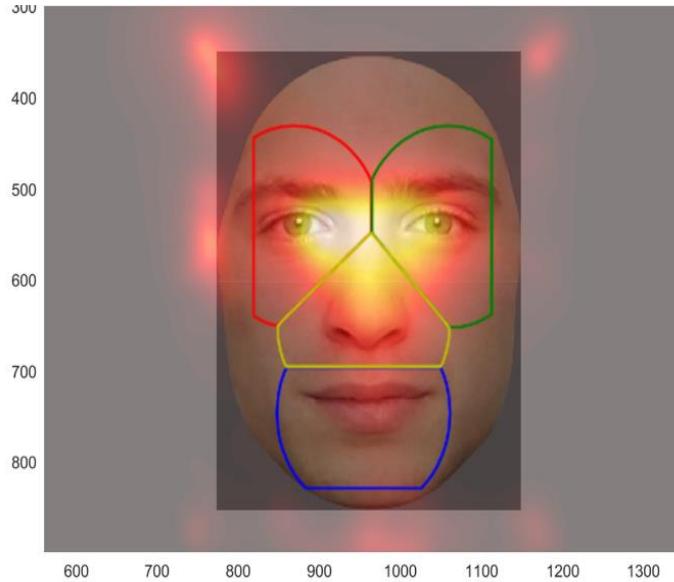
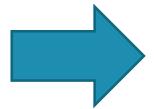
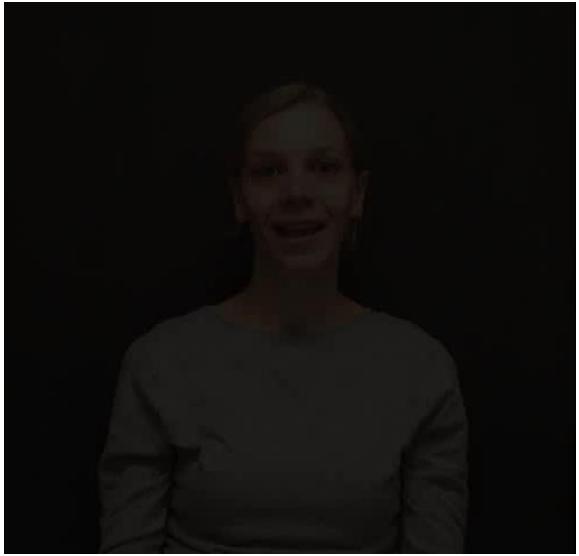


Face scanning patterns

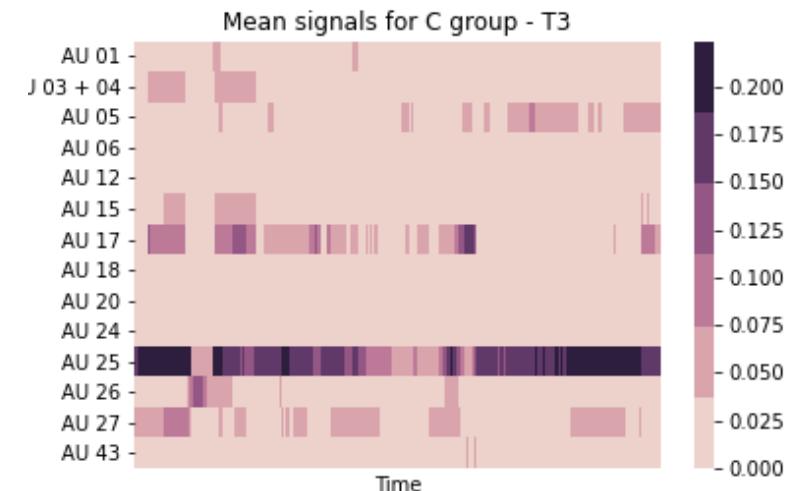
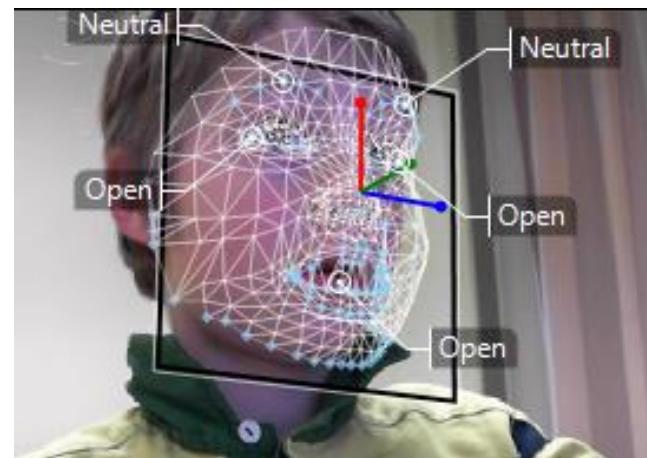
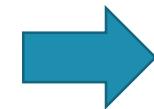
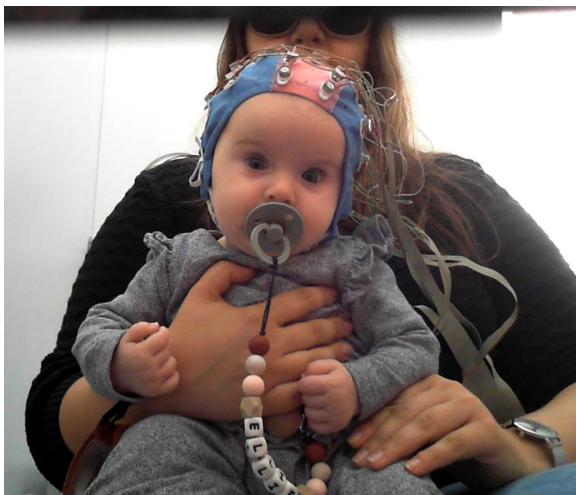
# Dynamic face scanning patterns

## Facial dynamics, facial mimicry

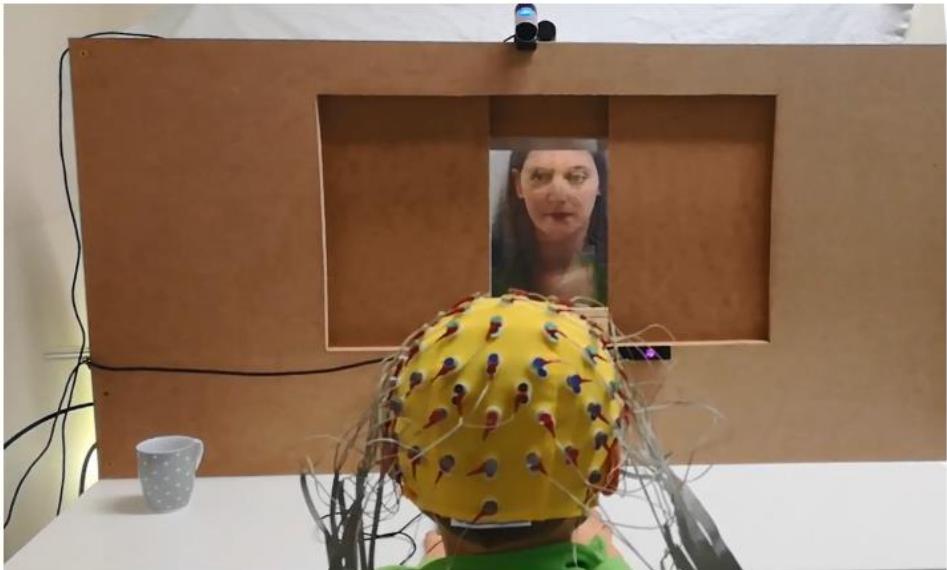
Eye-tracking



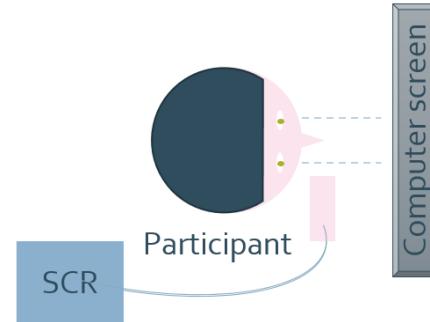
Facial dynamics



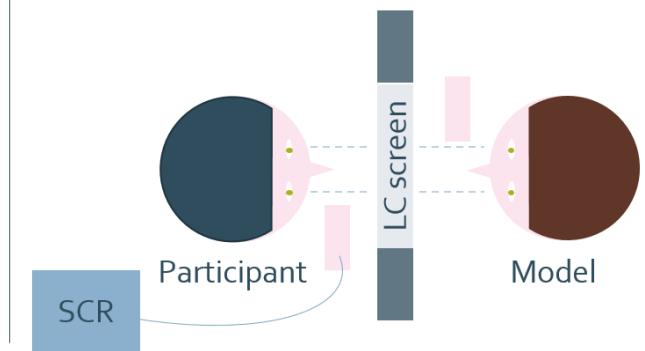
# Towards real-life dyadic measurements



Video presentation mode



Live presentation mode



Semi-structured dyadic interactions, combined with

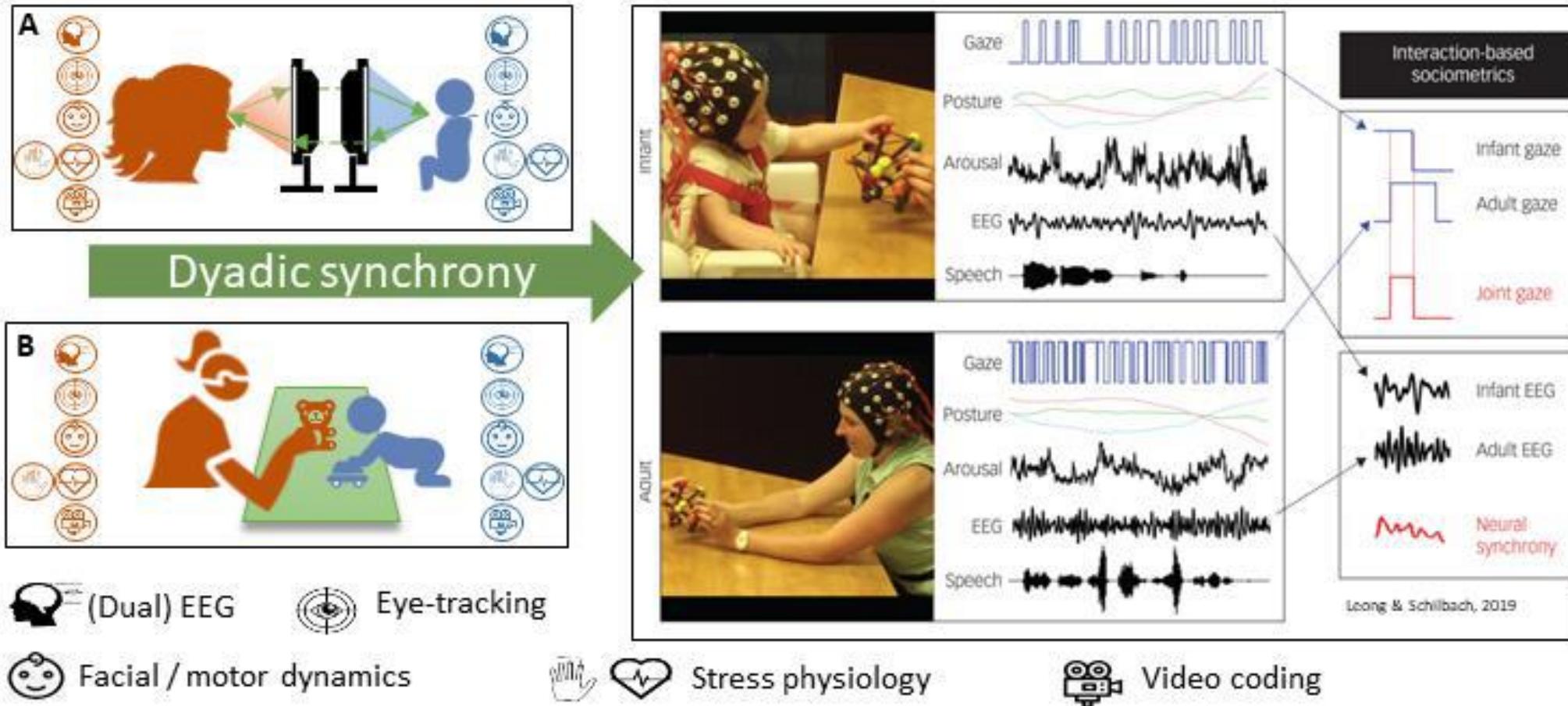
- Eye-tracking
- EEG
- Mimicry
- Stress physiology (heart rate, skin conductance, respiration, pupillometry)



# Towards *dual* real-life dyadic measurements



- Measure both partners simultaneously
- Focus on the dynamics of social interaction
- Investigate the interdependency between the biobehavioral signals of both partners



# Thank you!

## Developmental Psychiatry

- S. Amelynck
- L. De Vries
- N. Anarat
- L. Gistelinck
- R. Van den Broeck
- T. Tang
- S. Vos
- S. Vettori
- J. Steyaert
- B. Boets



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- C. Vanhole
- G. Naulaers

## COS

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- B. Itzhak
- E. Ortibus

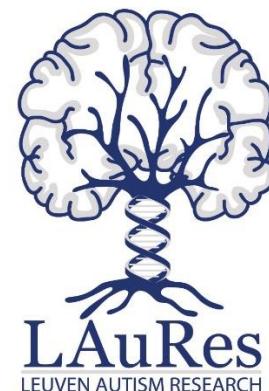
## PPW

- M. Schaap
- L. van Esch
- J. Segers
- GJ Vanaken
- I. Noens
- G. Bosmans

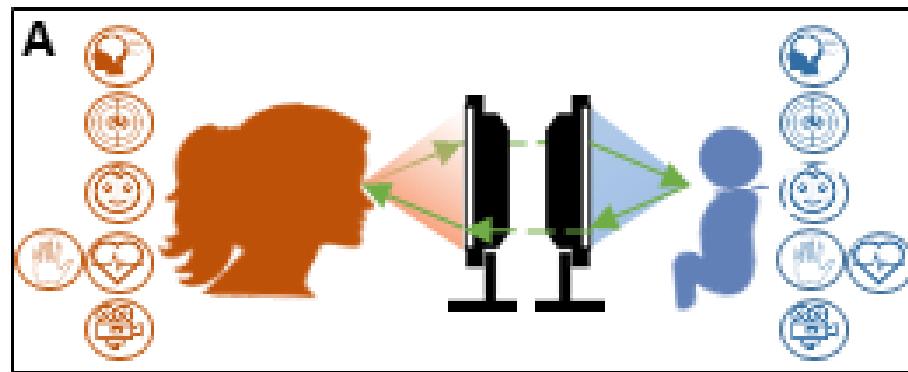
## ESAT

- L. Smets
- M. De Vos
- P. Claes

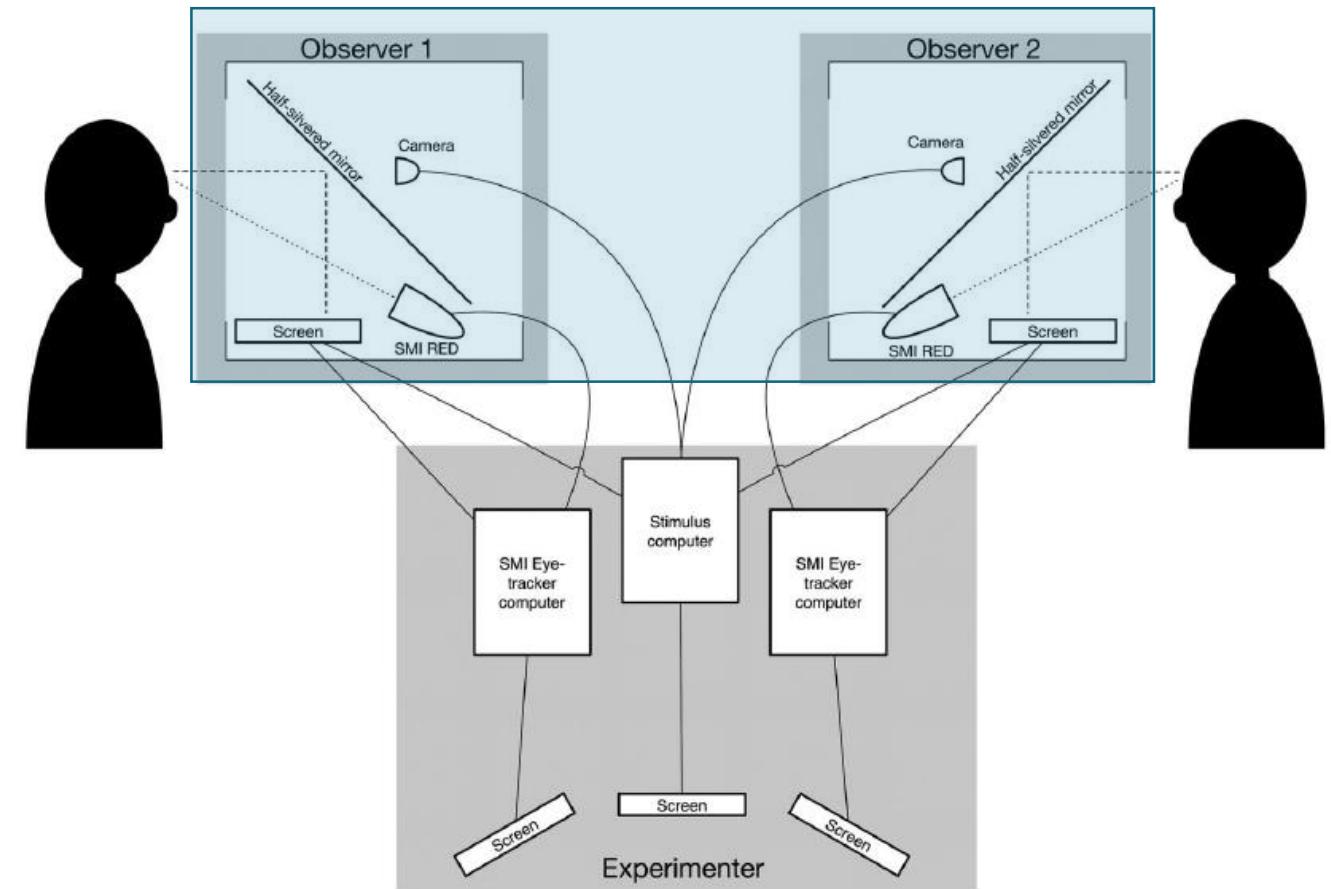
KU Leuven Babylab



# Methodologie Biobehavioural Synchrony



Eye-tracking   EEG   Stress physiology  
Facial / motor dynamics   Video coding



# Challenges of infant research

Characteristics of young participants ...

- Preverbal
- Non-cooperative
- Very short attention span
- Offer no direct responses
- Infant data are intrinsically noisy

