DOMINO

Development of cortical multisensory integration mechanisms at micro- and macro-scales during normal and pathophysiologival conditions

HBP Partnering Projects Meeting: Status quo & outlook
5-7 September 2022 | Nijmegen, The Netherlands
Impaired ability to properly integrate multiple sensory modalities has been hypothesized to underlie many of the symptoms in autism spectrum disorders (ASD).

However, how multisensory integration develops and how it is expressed in ASD is poorly understood.
Multisensory integration in autism spectrum disorders

The temporal window for multisensory integration (MI) is extended in ASD.

Understanding how MI develops, and its disruptions in ASD is key to improve diagnosis and develop new treatments.

Foss-Feig et al., 2010
The DOMINO paradigm

Mouse experiments
- Multi-area microcircuit-level characterization of MI development
- WT and ASD mice
- From birth to adulthood

Human experiments
- EEG and psychophysics experiments
- TD and ASD subjects
- From childhood to adulthood

Modeling experiments
- Spiking neural networks with biologically plausible plasticity
- A model of MI development
Project structure and interactions with HBP/EBRAINS

WP1: Mouse experiments
UNIVERSITY OF AMSTERDAM

WP2: Human experiments
Università Cattolica del Sacro Cuore
Panteion

WP3: Modeling
CerCo

WP4: Management & Dissemination
UNIVERSITY OF AMSTERDAM
Our team

Project Coordination
WP1: Animal experiments

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WP2: Human experiments

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WP3: Modeling

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EBRAINS
WP1: Mouse experiments

- WT PV-Cre
- WT VIP-Cre
- WT SST-Cre
- Fmr1--/- PV-Cre
- Fmr1--/- VIP-Cre
- Fmr1--/- SST-Cre
Response to flash (L: low, M: medium, H: high intensity)

Response to sound (white noise)

Sound-flash overlap as a function of SOA (in ms, black: visual response)

Example V1 responses

How do the temporal aspects of multisensory integration vary across development and in ASD?

WP1: Mouse experiments
Abnormal hippocampal hypersynchrony in the Frmp-KO mouse model of FRX

The hypersynchronization of Fmr1-KO oscillations and spike timing might reflect functional deficits in local networks.

Arbab et al. 2018
Is mouse posterior parietal cortex (PPC) involved in perception?

Cortical surface

Head-fixed awake mouse

V1

S1

PPC

A1

Multisensory integration

Decision

Action

Crochet et al., Trends Neurosci, 2019
Audio-visual change detection task

NE cohort (no response)

MST cohort

Amount of change (saliency)

Oude Lohuis et al., Nat. Commun., 2022
Oude Lohuis et al., J Neurosci, 2022
Audio-visual change detection is cortex-dependent

Oude Lohuis et al., Nat. Commun., 2022
Oude Lohuis et al., J Neurosci, 2022
Neural correlates of everything in PPC

Neuronal activity in PPC reflects sensory information and predicts task performance

Oude Lohuis et al., J. Neurosci., 2022
...but no causal role for anything

Oude Lohuis et al., J. Neurosci., 2022

****: BF > 100
#: BF < 1/3

**Oude Lohuis et al., J. Neurosci., 2022**
Current Activities WP1

- Data Recording during specific neurodevelopmental milestones
- Comparing with Dark rearing
- Recordings with combined genotypes
- LFP-Spike data analyses (TD mice – Frmp-1 KO)
WP2: Development of MI in TD and ASD individuals

- Aim: Uncover the rules governing data integration in the visual system
WP2: Development of MI in TD and ASD individuals

- **Aim:** Observe how MI processes arise in TD and ASD children and adolescents by combining psychophysics and EEG.

![Diagram showing visual and auditory input with McGurk illusion](image)

Keil, 2020
WP2: Development of MI in TD and ASD individuals

Development of a McGurk task for the Greek language → A potential new test for ASD

Example tha va AV combinations
- Multiple choice responses
- Response options
  - tha, fa, va, da, ba, ga, nta, pa, ka, other
- N = 90 participants, aged between 13-79 years of age, 88 native Greek speakers
- Significant relationship between stimuli and responses
McGurk preliminary behavioral results

**Congruence Vs. Fusion**

**Congruence Vs. Combination**

SOA: -550, -250, 0, 250, 550

Accuracy: 0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2

ASD, TD
WP2: Current Activities

- Data collection for McGurk & SIFI experiments
- Linguistic aspects of the McGurk effect: aim to explore the influence of place and manner of articulation in the McGurk illusion
- Pairs of mismatching AV components with:
  - the same place and different manner of articulation
  - the same manner and different place of articulation
  - different manner and different place of articulation
WP3: Computational model of MI development

Visual inputs

Retina simulator

Spikes

V1 model

Cochlea simulator

Spikes

A1 model

Auditory inputs

PPC model
WP3: Processing dynamics visual stimuli with SNNs

Motion-direction selective neurons

Chauhan et al., J. Neuroscience 2018; Frontiers in Neuroscience 2021

Retinal input  ---  LGN  ---  V1

Spatiotemporal convolutional processing

Asynchronous retinotopic spike-trains

Dense, plastic synapses

Biphasic  ---  Monophasic

STDPLearning

Co-funded by the European Union
WP3: Processing realistic auditory stimuli with SNNs

Frequency selective neurons

Next: audio-visual integration, normal and abnormal development
Progress and next steps

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Future Developments using EBRAINS

- Data sharing and curation
- Implementation of Large Scale Models
- Data Integration (mouse – human)
Thank you!

[Links]
www.humanbrainproject.eu  www.ebrains.eu