



PROJECT

Supervisor: _____JACOPO_____LAMANNA_____

Title: Investigating defective social cognition and its neurophysiological correlates in an animal model of autism spectrum disorder

Curriculum: _____COGNITIVE AND BEHAVIORAL SCIENCES_____

Link to the personal page of the University or relevant hospital site website: <https://www.unisr.it/docenti/1/lamanna-jacopo>
<https://www.unisr.it/ricerca/centri/bnc>

Description of the Project (max 3,000 characters including spaces)

In neurodevelopmental disorders like Autism Spectrum Disorders (ASD), early diagnosis is crucial for effective intervention and improved child development. Diagnosis is based on behavioral observations, but recent research suggests that studying how children orient their attention towards social cues could serve as an early indicator of ASD¹. Indeed, social predispositions emerge very early in typical development, even in newborns². Early preference for social elements is not unique to humans but is also observed in species like newborn primates³ and domestic chicks⁴, suggesting it's highly conserved across evolution.

In this context, a popular approach to model ASD is based on the prenatal exposure to valproic acid (VPA), a drug known to induce developmental alterations related to autism also in humans. In chicks, VPA has already been shown to alter their preference for social stimuli^{5,6}.

Previous studies highlighted different morphological, molecular and synaptic alterations in the dopamine (DA) system of embryonically VPA-exposed chicks, both in the mesencephalon and in the septum⁷, as well as gene expression changes, thus supporting a prominent role of DA in social cognitive development. Taken together, such evidence indicates that ASD can be related to significant neurophysiological alterations during embryonic development.

Rationale and hypothesis

The rationale of our project is that focusing on social behaviors that manifest early in life and their possible prenatal neural underpinnings will provide valuable insights into ASD. The hypothesis is that VPA induces anomalies in embryos neurophysiology in terms of synaptic transmission and plasticity at the prenatal stage. The project will run at our laboratory of the Center for Behavioral Neuroscience and Communication (BNC) of UniSR, in collaboration with University of Trento.



Objectives and specific aims

Our research project aims to investigate prenatal neurophysiological correlates of early social preference alterations. We will perform a throughout characterization of neuronal excitability, synaptic transmission and plasticity, in acute brain slices^{8,9} from chicken embryos.

Specific aims:

1. Investigating the behavioral and cognitive anomalies in the animal model (chicken) of ASD based on embryonal VPA treatment. This will be achieved using natural and artificial stimulation of visual and auditory systems, evaluation of preference for biological motion, faces, natural and animal sounds.
2. Measuring AMPA and NMDA synaptic currents in D1/D2 MSNs in the striatum of VPA-treated and control embryos (II year, first half).
3. Investigating DA-dependent synaptic plasticity in the striatum of VPA-treated and control embryos, including: spike time-dependent plasticity (STDP) in D1/D2 MSNs and long-term potentiation/depression (LTP/LTD)^{8,9} (II year, second half, and III year, first half).

Last months will be devoted only to data analysis and thesis writing.

Expected outcomes

By focusing on early-life behaviors and their neural correlates during embryonic development, we aim to shed light on the origins of ASD and potentially identify targets for early intervention strategies. Our work may contribute to a deeper understanding of ASD developmental trajectory and pave the way for more effective interventions.

Skills that the student should acquire (max. 600 characters including spaces):

The PhD student will learn how to produce acute brain slice preparations from chicken embryos (prenatal) and to perform in vitro electrophysiological recordings, including whole-cell patch clamp and field recordings. After enough specific training, the student will conduct such experiments independently. Further activities will include brain tissue immunohistochemistry, molecular biology procedures, data analysis and paper writing. No previous specific training is required, albeit previous experimental experience (e.g. during Master's thesis) in neuroscience would be beneficial.



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**APPLICATION TO ACT AS SUPERVISOR AND
RESEARCH PROJECT PROPOSAL**

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References (max. 15)

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