INTERNATIONAL WORKSHOP ON

FRAGILE X SYNDROME

PADUA, ITALY - JUNE 20th 2025

MOTORE SANITÀ Cure the Future

THE PADUA MODEL FOR FRAGILE X SYNDROME

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Developmental Neuropsychologist, Padova Fragile X Center– Pediatric Unit

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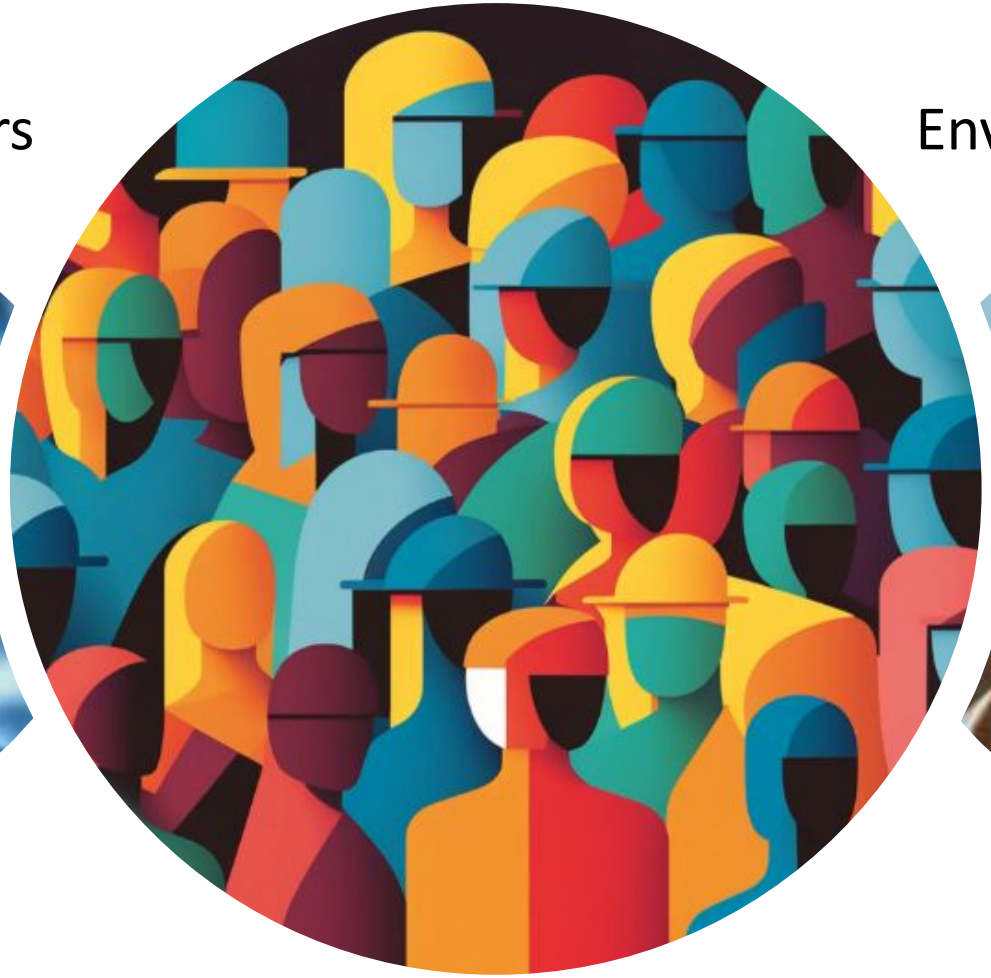
The starting point: Fragile X Syndrome is complex

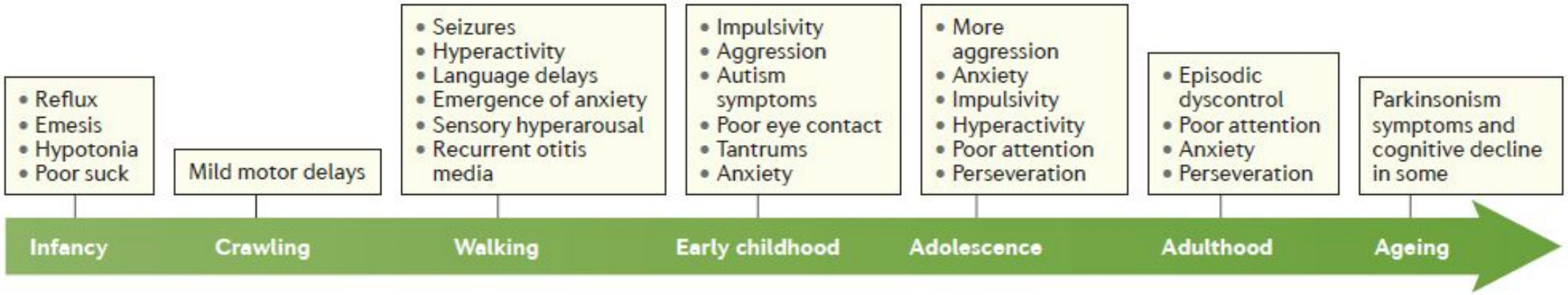
Molecular parameters



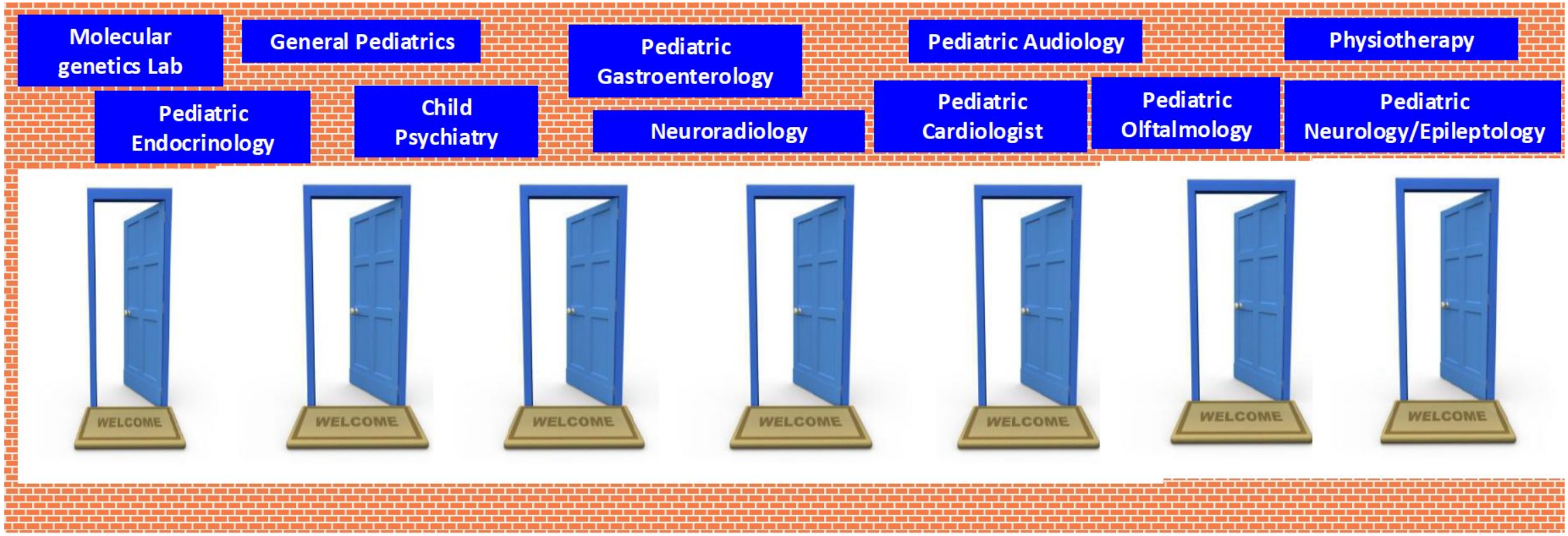
Environmental factors

Phenotypical heterogeneity
and severity

A life-span approach to Fragile X



A Fragile X diagnosis: many different clinical questions



Multidisciplinary FX network

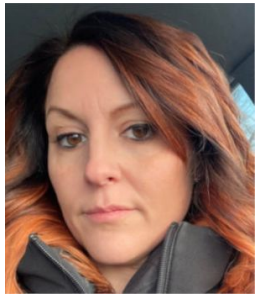
A unitary, multidisciplinary and integrated responses

- **Specific skills and clinical paths dedicated** to the “rare condition”
- **Children-centered care** with her/his family

Fragile X Padua Network

Roberta Biffanti
Ped. Cardiology

Mara Cananzi
Ped Gastroenterology



Elisa Di Giorgio
Neuropsychology

Carla Scaroni Chiara Sabbadin
Adult Endocrinology

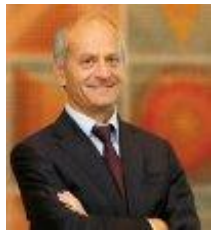
Marco Lunghi
Neuropsychology

Monica Polese
Nurse

Giulia Gatti
NPI

Elisa Zannin
Ped Ophtalmology

Valentina Liani
NPI



Angelo Antonini Miryam Carecchio
Adult Neurology

Stefano Sartori
Ped Neurology

Marina Giacon
Head Nurse

Silvia Zanato
Ped
Psychiatrist

Elena Cavaliere Ped Neurology

Alessandra Murgia
Pediatrics

Roberta Polli
Molecular Diagnostics

Eleonora
Lorenzon
Ped Neurology

Prof. Z. Sawacha

Marta
Magnolato
NPI

Federica
Beghetti

Marilena Cameran
Molecular Diagnostics

Elisa Bettella
Molecular Diagnostics

UNIL | Université de Lausanne
Département
des neurosciences
fondamentales

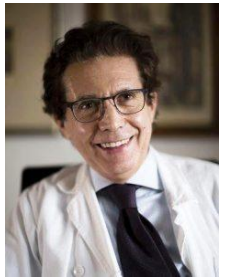
UC DAVIS HEALTH | SCHOOL OF MEDICINE

Prof. Flora Tassone

Prof. Claudia Bagni
Università di Roma
Tor Vergata

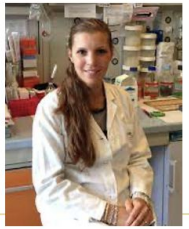
Università degli Studi di Padova

VENETO INSTITUTE OF MOLECULAR MEDICINE



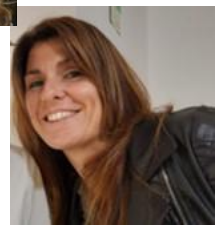
Prof. Cossu
Centro Medico di
Foniatria

Prof. Nicola Elvassore



Prof. Cecilia Laterza

AnnaMaria
Guiotto



Fabiola
Spolaor

Three core business

- Molecural Diagnostics
- Clinical Program
- Research activity

A Team effort

Organizing a multidisciplinary clinic for «fragile kids», within the schedule of a children's hospital

Monica Polese

Marina Giacon

Integrated clinical assessment

How to access:

- **Direct contact from the family** who received a diagnosis by our center or by another one.

- Before accessing the Clinics, we ask to study available clinical documents, and establish **online contacts in order to discuss with the family** the possible evaluation plan and explain the organization of our service.

- **We provide the family with the precise planning** of the organized clinical evaluations.

Integrated clinical assessment

The program, which take place from Mondays through Thursdays, is designed on the basis of age and individual needs

Evaluations:

- **Multidisciplinary** (Mon)
- ophtalmological
- gastroenterological
- audiological
- cardiological
- child psychiatric (*ADHD, ASD, anxiety, pharmacology*)
- neuropsychological
- gait analysis
- **Multidisciplinary** (Thu)

Fondazione
ISTITUTO DI RICERCA
PEDIATRICA

Laboratory
Molecular Genetics of Neurodevelopment

Department of Women's and Children's Health, University of Padova
Pediatric Research Institute, Città della Speranza, Padova

Alessandra Murgia
MD PhD

Roberta Polli
PhD

Elisa Bettella
PhD

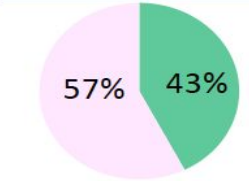
Marilena Cameran
Lab Technician

FMR1 molecular analysis: our cohort from 1992 to March 2024

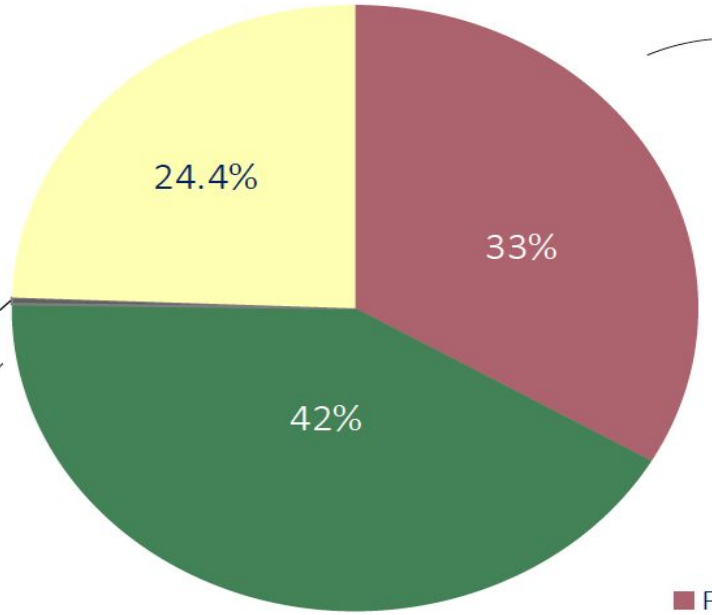
224 index individuals with *FMR1* repeat expansions,

FMR1 cascade testing: **835** index individuals and family members

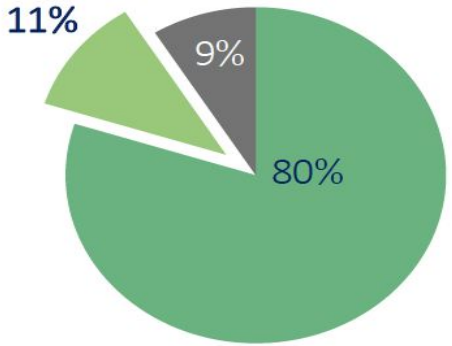
Males vs Females



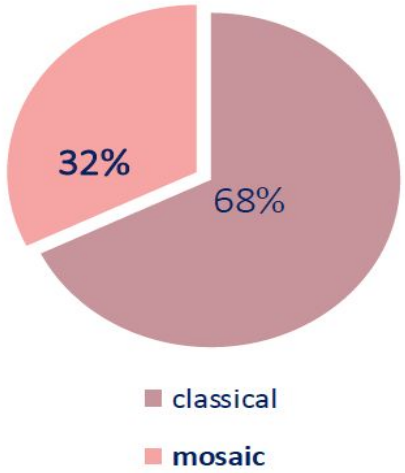
categories of FMR1 repeats in 835 subjects



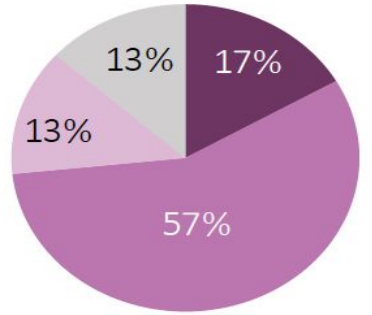
Premutation



Full mutation



Full mutation mosaicism



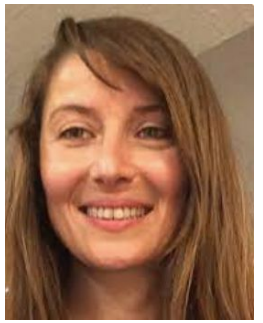
What are the questions that the Fragile X test should address?

- Number of CGG repeats
- State of Methylation of the mutation
- AGG interruptions
- FMR1 Activation Ratio (AR)

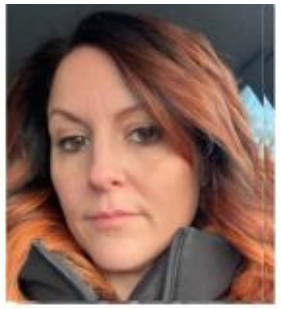
Cognitive, Behavioral and Adaptive Assessment

- **Cognitive domains**
  - *IQ*
  - *Visual and Auditory Attention*
  - *Visual and Auditory Memory*
  - *Executive Functions*
  - *Speed of Processing*
  - *…*

- **Adaptive Profile** (VABS-II)
- **Behavioral profile** (CBCL, CONNERS)
- **Sensory Profile**



Prof. Paola Rigo



Prof. Elisa Di Giorgio

Dott. Marco Lunghi

Gait analysis

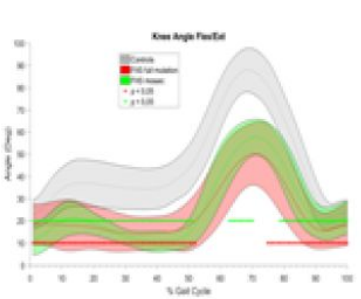
BioMovLab

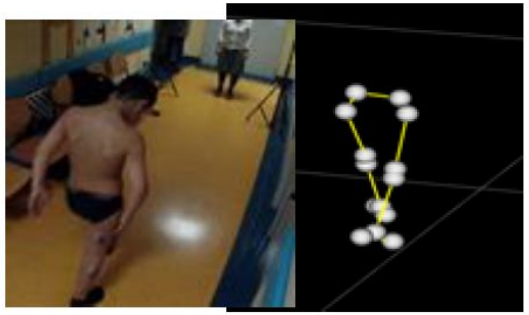
FRAXA Research Foundation

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

Joint kinematics

Sagittal plane kinamatics
Hip, knee and ankle flexion-extension joints rotations
Spatio-temporal parameters





Zimi Sawacha

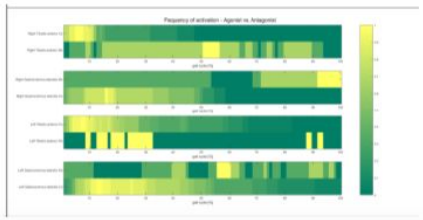
Annamaria Guiotto

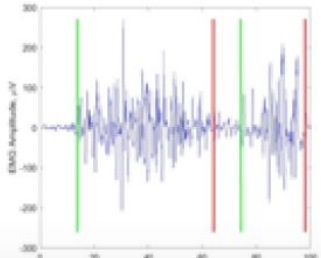
sEMG

Duration of contraction
Onset and offset activation timing
Peak of the envelope
Cocontractions

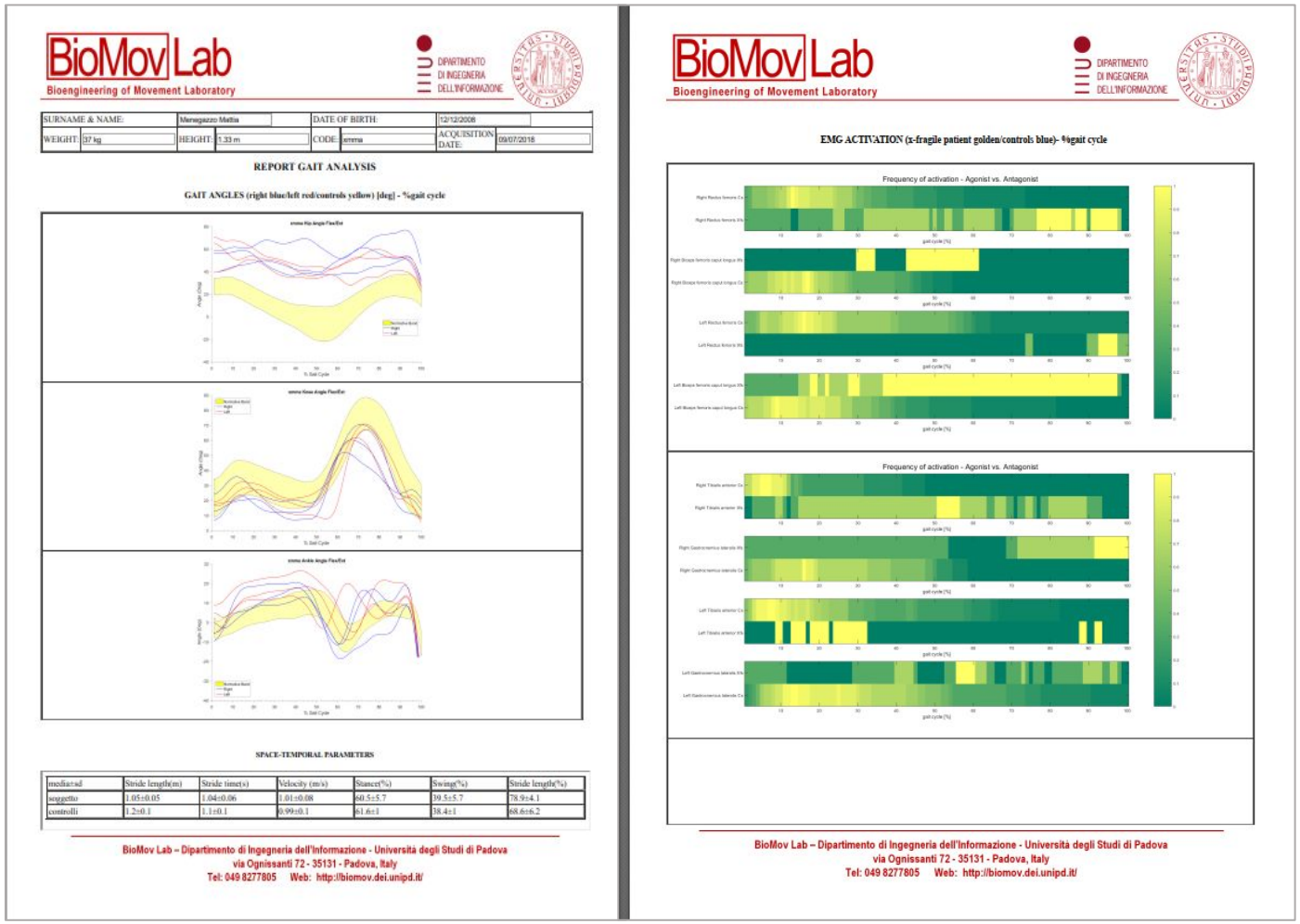
Fabiola Spolaor

Federica Beghetti





Gait analysis



BioMovLab
Bioengineering of Movement Laboratory

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

SURNAME & NAME:	Meneguzzo Mattia		DATE OF BIRTH:	12/12/2008	
WEIGHT:	37 kg	HEIGHT: 1.33 m	CODE: emma	ACQUISITION DATE:	09/07/2018

REPORT GAIT ANALYSIS

GAIT ANGLES (right blue/left red/controls yellow) [deg] - %gait cycle

SPACE-TEMPORAL PARAMETERS

media±sd	Stride length(m)	Stride time(s)	Velocity (m/s)	Stance(%)	Swing(%)	Stride length(%)
soggetto	1.05±0.05	1.04±0.06	1.01±0.08	60.5±5.7	39.5±5.7	78.9±4.1
controlli	1.2±0.1	1.1±0.1	0.99±0.1	61.6±1	38.4±1	68.6±6.2

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BioMovLab
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EMG ACTIVATION (x-fragile patient golden/controls blue)- %gait cycle

Frequency of activation - Agonist vs. Antagonist

Frequency of activation - Agonist vs. Antagonist

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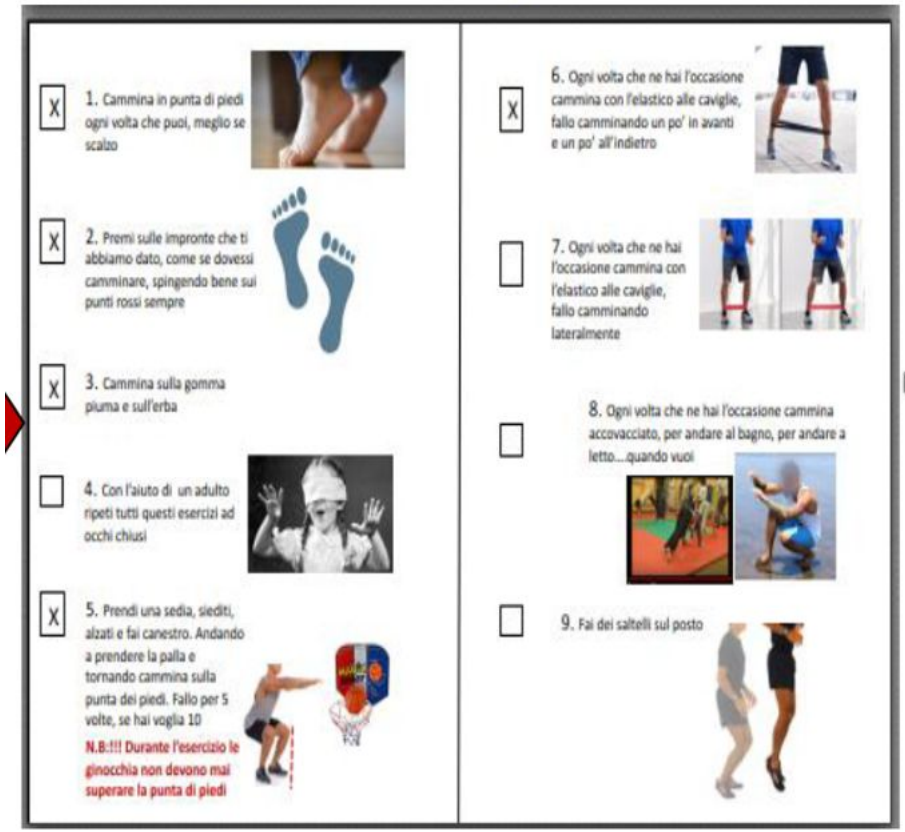


1. Cammina in punta di piedi ogni volta che puoi, meglio se scalzo

2. Premi sulle impronte che ti abbiamo dato, come se dovessi camminare, spingendo bene sui punti rossi sempre

3. Cammina sulla gomma piuma e sull'erba

4. Con l'aiuto di un adulto ripeti tutti questi esercizi ad occhi chiusi

5. Prendi una sedia, siediti, alzati e fai canestro. Andando a prendere la palla e tornando cammina sulla punta dei piedi. Fallo per 5 volte, se hai voglia 10

N.B.!!! Durante l'esercizio le ginocchia non devono mai superare la punta di piedi

6. Ogni volta che ne hai l'occasione cammina con l'elastico alle caviglie, fallo camminando un po' in avanti e un po' all'indietro

7. Ogni volta che ne hai l'occasione cammina con l'elastico alle caviglie, fallo camminando lateralmente

8. Ogni volta che ne hai l'occasione cammina accovacciato, per andare al bagno, per andare a letto....quando vuoi

9. Fai dei saltelli sul posto

Exercise protocol as a result of gait analysis

Research

The Centre is promoting several research projects investigating different yet interrelated aspects of FMR1 gene mutation conditions.

The projects mainly focus on identifying and validating biomarkers that can be used to:

- characterize and stratify the different neurodevelopmental phenotypes in FXS and PM conditions; and
- reliably measure and monitor outcomes (even in potential clinical trials)

Research projects

- "**Identification of molecular and functional biomarkers** in Fragile X Disorders: improving knowledge about basic molecular mechanisms and measurable outcomes for clinical follow-up and evaluation of new treatments" (IRP Consolidator Project 2024-2026)
- "**Gait signature** in Fragile X Syndrome: an innovative translational approach" (PRIN 20227JA8R3)
- "Early identification and **cognitive outcome measure biomarkers** in Fragile X Syndrome: *a Proof of Concept* Investigation" (BIRD Project 2023-2025)
- "Developmental motor phenotype in Fragile X Syndrome: assessment of motor control through innovative **gait analysis and definition of new biomarkers**" (FRAXA Research Foundation Fellowship, 2022-2024).
- "Impact of the Fragile X Premutation on Neurodevelopment. Identification of **altered levels of FXTR1-mRNA and FXP as possible new biomarkers**" (BIRD Project 2022).

The elements that contribute to the success of a model

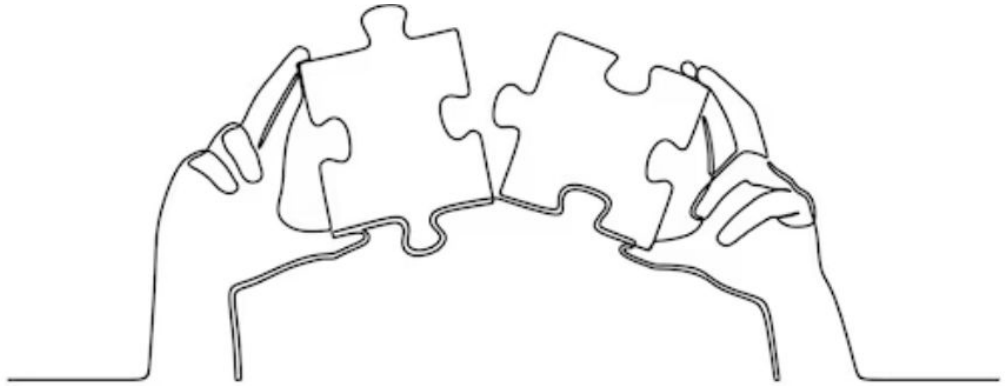
Specific skills, with high-level molecular and clinic expertise

Activities and dedicated personnel

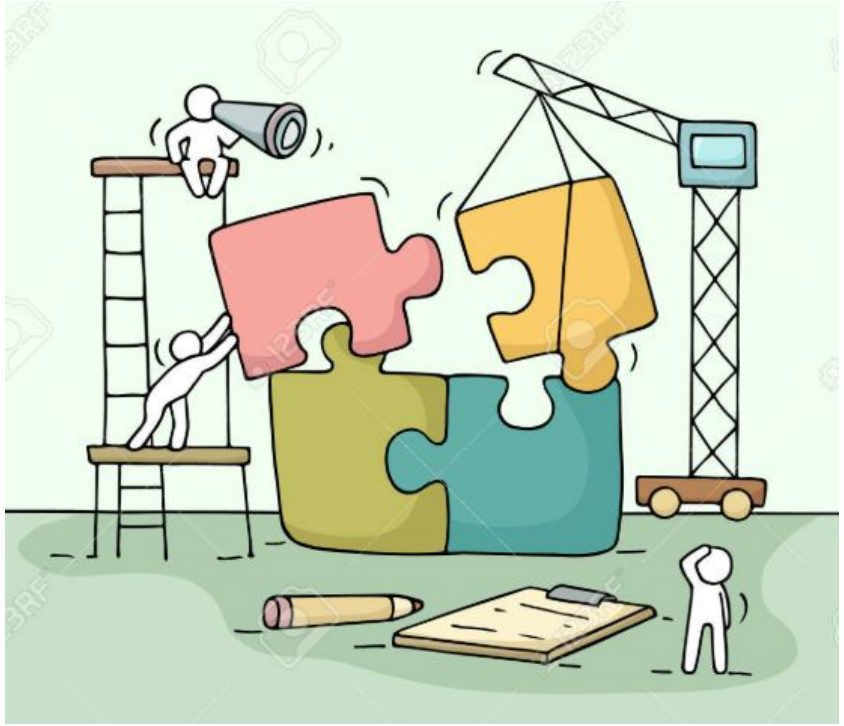
A Children's hospital that is part of a University

Infrastructure organisation

Integration of extensive multidisciplinarity



The whole is more than the sum of its parts



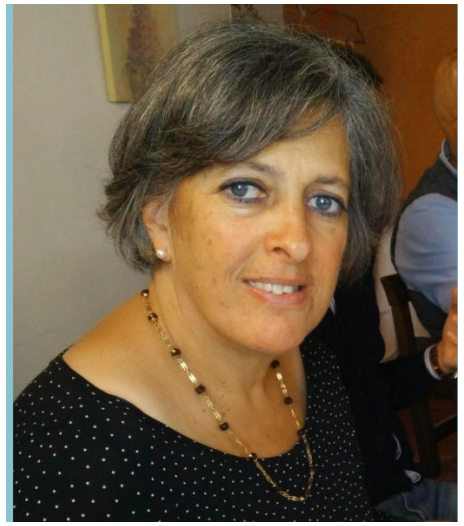
Multidisciplinarity is about integrating all the pieces of the puzzle together to provide a complete care plan for each child.

Still a lot of work to do

- Develop and foster clinical and molecular innovation
- Implement clinical based on the results of translational research
- Attract and train young professionals in the field of neurodevelopment
- Increase national and international research and study activity.
- Raise Awareness of Fragile X Syndrome
- Strengthen the relationship between the Centre and family associations

No one can reach families better like other families can do !

Acknowledgements



Grazie

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Azienda Ospedale Università Padova

SDB Dipartimento Salute Donna e Bambino

Fondazione Salus Pueri

Uniti per Crescere

Fondazione Istituto di Ricerca Pediatrica

Dipartimento di Ingegneria dell'Informazione

Dipartimento di Psicologia dello Sviluppo e della Socializzazione

Associazione Italiana Sindrome 'X-Fragile'