La Neuropsichiatria Infantile oggi e l'integrazione con le Cure Primarie Pediatriche

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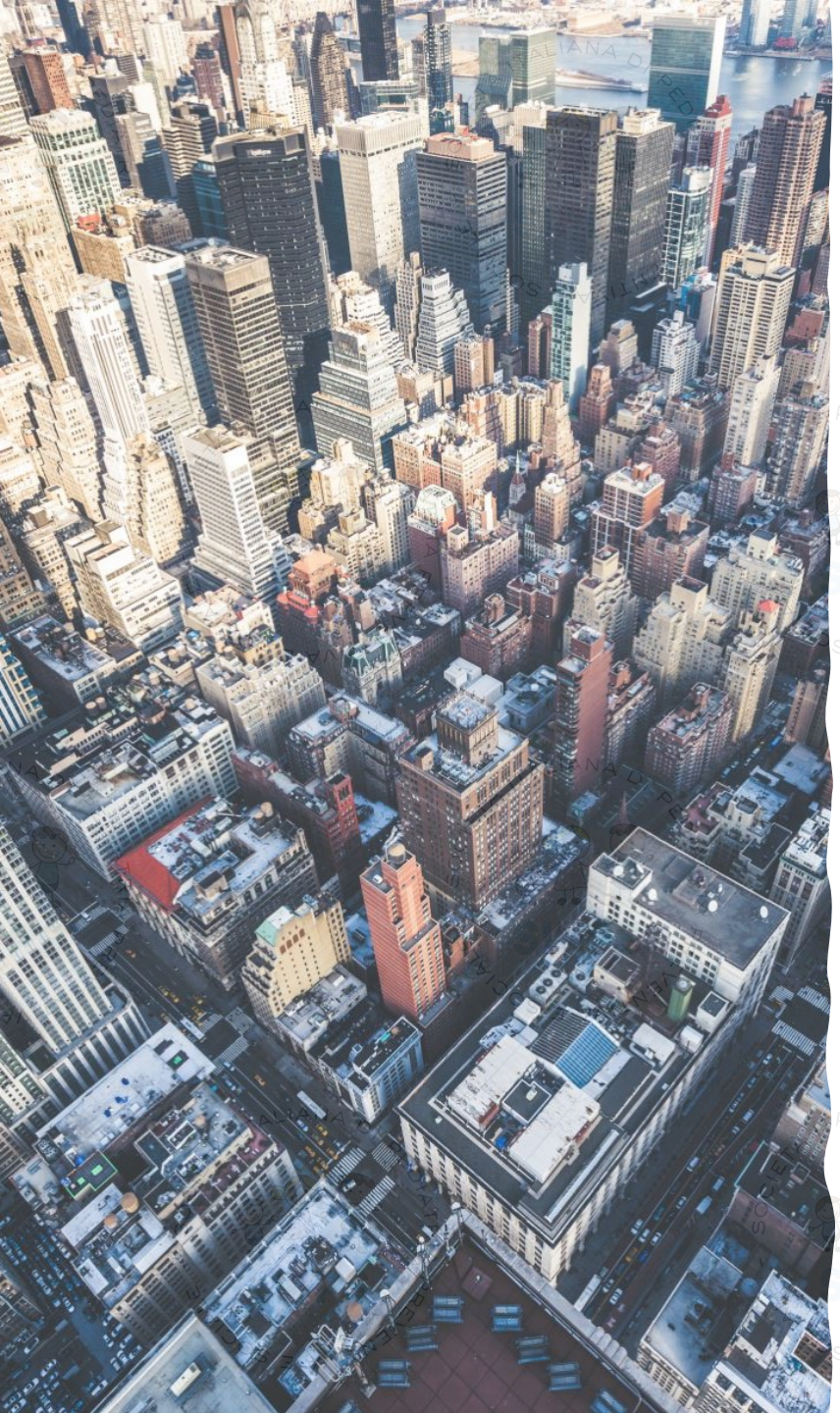
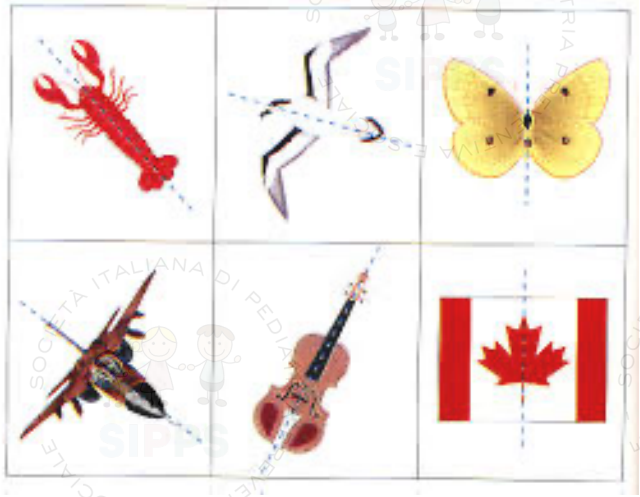
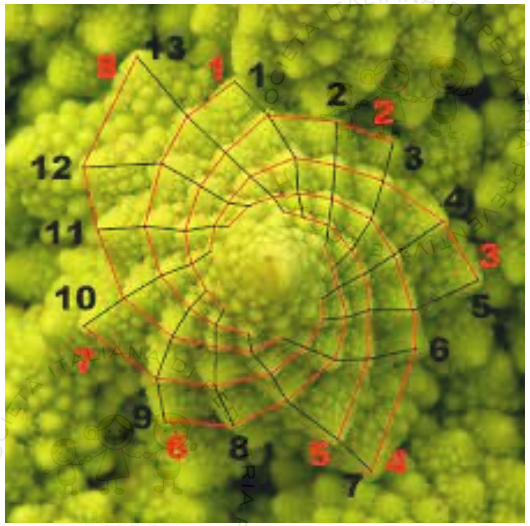


Overview

- Storia
- Attualità
- Prospettive future

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1
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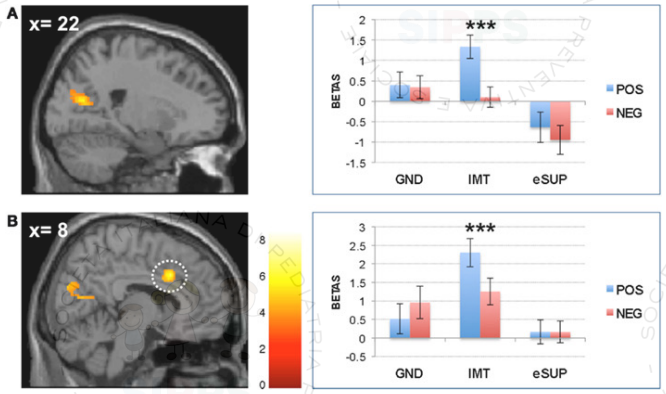
A
x= 22
B
x= 8
***
BETAS
GND
IMT
eSUP
POS
NEG
***
BETAS
GND
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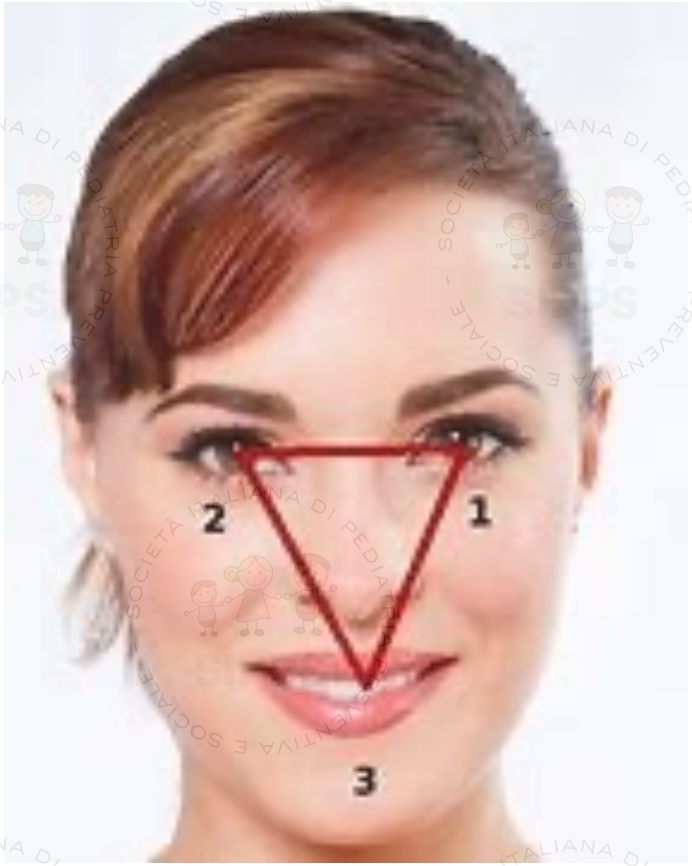
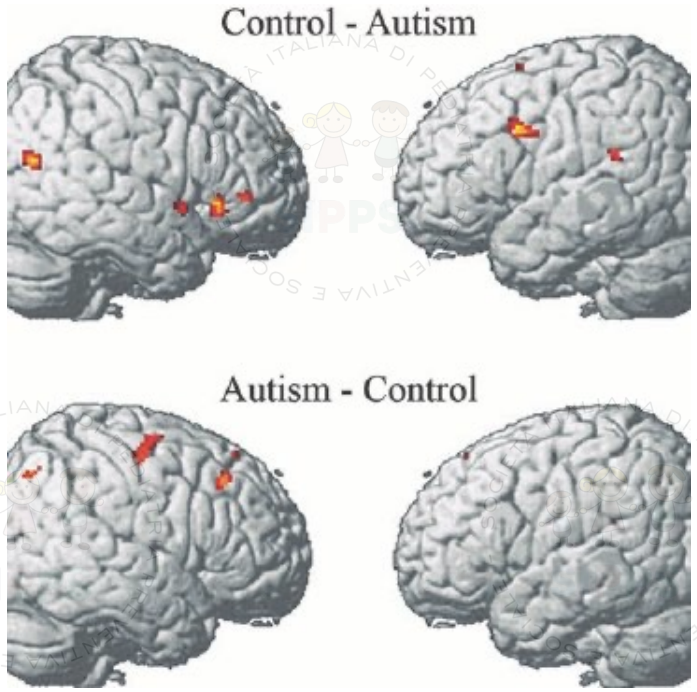
eSUP
POS
NEG


2
1
3


Control - Autism
Autism - Control

Il Signore disse ancora a Mosè:

«Parla ad Aronne e digli: nelle generazioni future nessuno dei tuoi discendenti che abbia qualche deformità si avvicinerà per offrire il pane del suo Dio; perché nessun uomo che abbia qualche deformità potrà accostarsi: né il cieco, né lo zoppo, né chi ha una deformità per difetto o per eccesso» *(Levitico, 21,16-20).*

- I Vangeli narrano l'incontro di Gesù con malati di ogni genere: ciechi, deformi e paralitici.

- In diversi passi del Nuovo Testamento vengono esplicitate le credenze popolari della Palestina di quei tempi: **l'handicap era considerato una conseguenza del peccato.**

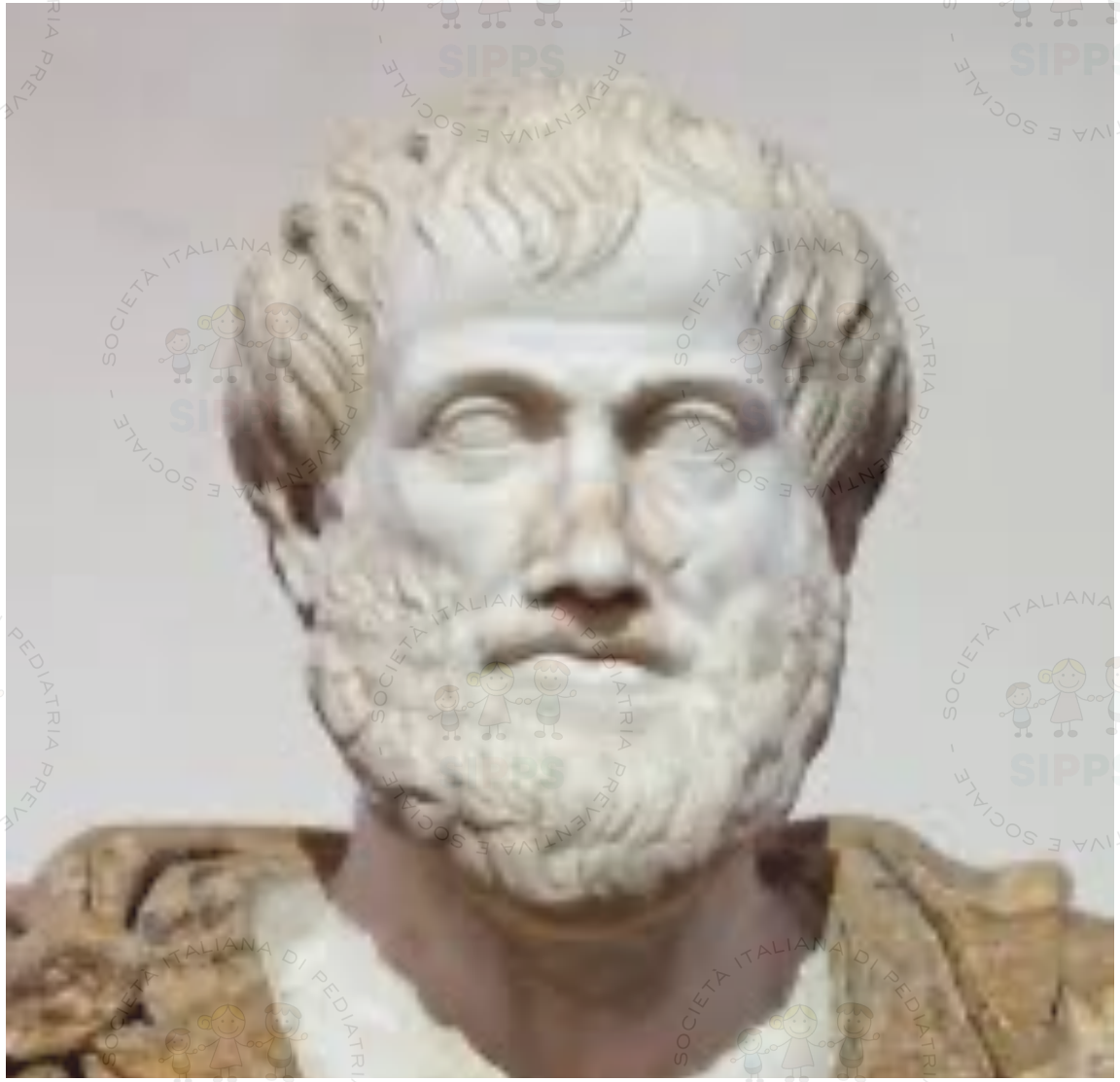
- Secondo quanto riportato dai vangeli, dopo la guarigione miracolosa di un cieco ad opera di Gesù, gli apostoli gli chiesero: «Rabbi chi ha peccato, lui o i suoi genitori perché egli nascesse cieco? Rispose Gesù: né lui ha peccato né i suoi genitori, ma è nato cieco perché si manifestassero in lui le opere di Dio» *(Giovanni 9,1-3)*.

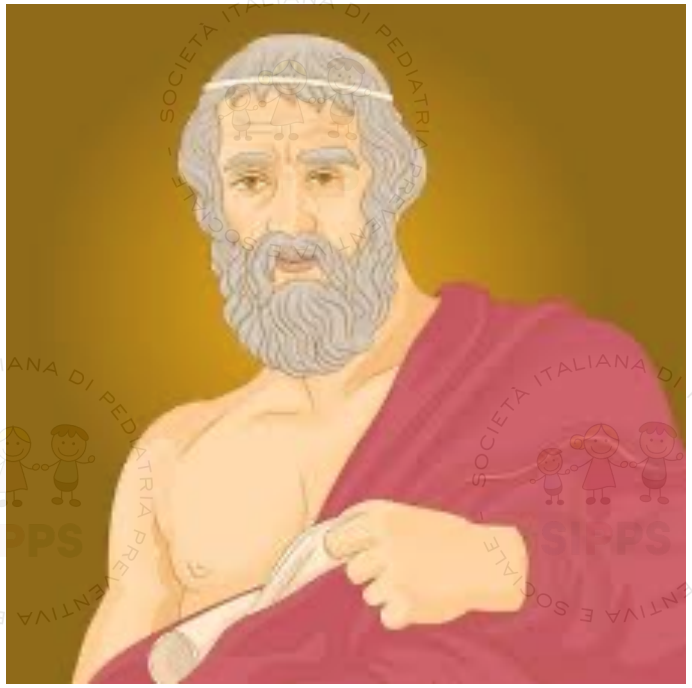
La chiesa del V e VI secolo ricorda ai fedeli che il peccato originale accompagna le loro vite e coloro i quali non sapranno conservarsi casti nei giorni proibiti e nelle festività avranno figli malati di lebbra o epilettici per punizione.

- “Soffochiamo i nati mostruosi, anche se fossero nostri figli. Se sono venuti al mondo deformi o minorati dovremo annegarli. Ma non per cattiveria. Ma perché è ragionevole separare esseri umani sani da quelli inutili…”.

• Nell’opera *Politica*, si sosteneva la necessità di una legge che impedisse ai bambini deformi di sopravvivere perché inutili allo Stato, affermando:

«Quanto all’esposizione e all’allevamento dei piccoli nati sia legge di non allevare nessun bimbo deforme»





Nella *Repubblica* Platone affermava che il compito della giustizia e della medicina era curare i cittadini sani nel corpo e nello spirito: «Quanto a quelli che non lo siano, i medici lasceranno morire chi è fisicamente malato

«Conviene che gli uomini migliori si accoppino con le donne migliori il più spesso possibile e che, al contrario, i peggiori si uniscano con le peggiori, meno che si può; e se si vuole che il gregge sia veramente di razza occorre che i nati dai primi vengano allevati; non invece quelli degli altri»

Con la diffusione del **Cristianesimo** si fa strada il concetto di **tolleranza**, ma la disabilità è percepita sempre come **malattia**.

“Una anima sana non trova albergo in un corpo tumefatto”

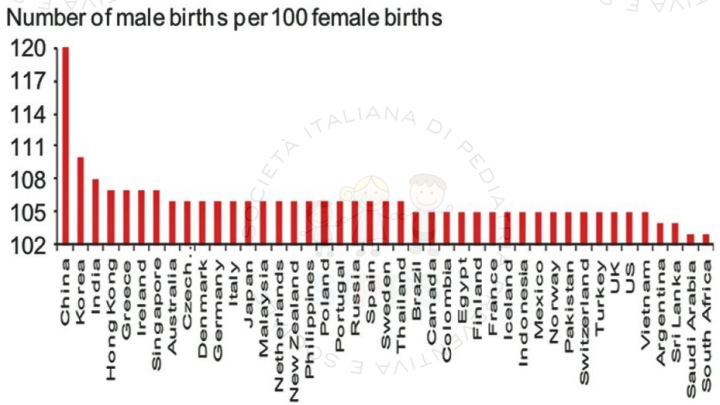
- A Londra l’ospedale di St. Mary Bethlehem, noto alla storia come Bed-lem, rappresenta uno dei primi manicomi, famoso per i trattamenti brutali e disumani riservati ai pazienti.

- Simili strutture nascono anche a Parigi, dove disabili fisici e mentali sono rinchiusi nei due ospedali più famosi di tutta la Francia: Salpêtrière e Bicêtre.

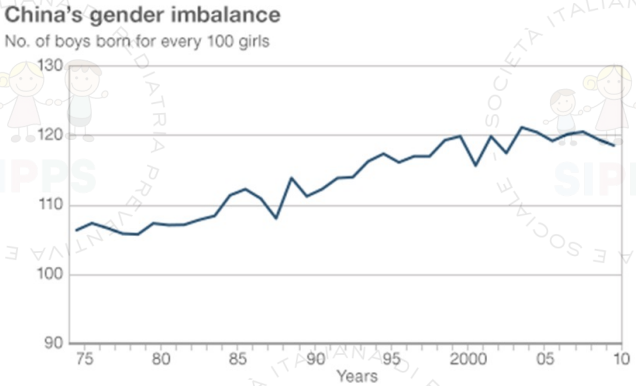
- Negli stessi anni, gran parte della popolazione europea sviluppa una crescente curiosità nei confronti della malattia mentale, tanto che alcune strutture diventano teatro della «mostruosità»: come raccontato nel film Bedlam di Mark Robson (1946), al costo di pochi penny, i londinesi potevano visitare l’ospedale Bedlam e osservare i comportamenti bizzarri dei pazienti rinchiusi nelle gabbie come animali da circo


Bertram

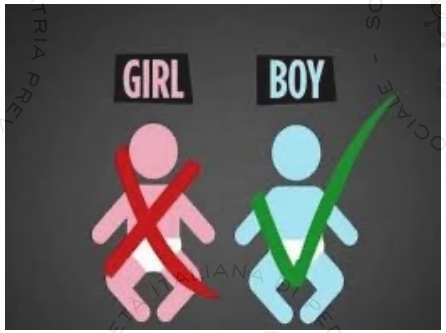
Fig. 39: Country rankings of sex ratio at birth

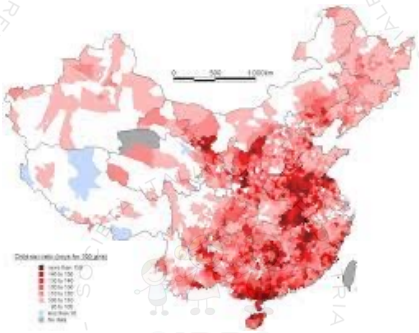


Source: United Nations and Nomura Global Economics.



Source: Jiang, Quanbao, Shuzhuo Li, and Marcus W. Feldman. 2013. China's population policy at the crossroads

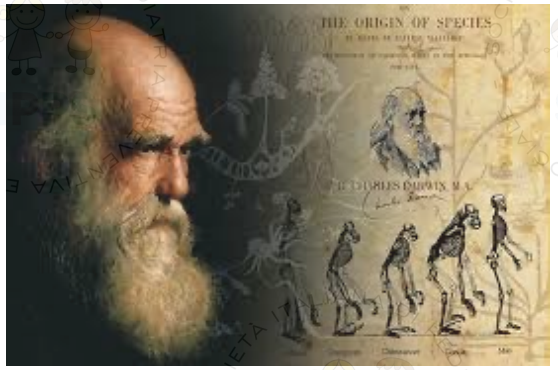


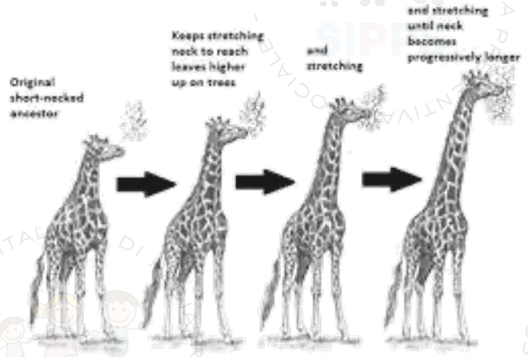


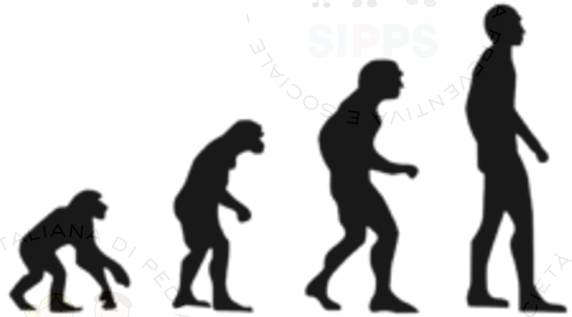
- Nel Rinascimento si fa strada l'idea dell'**antropocentrismo** e dell'**homo mensura**, la disabilità, la menomazione e la diversità sono percepite ancor più sminuite che nelle epoche passate.

«Scimmie, elefanti e negri.
Tra tutti questi esseri, quello
ragionevole è l'elefante»

Voltaire

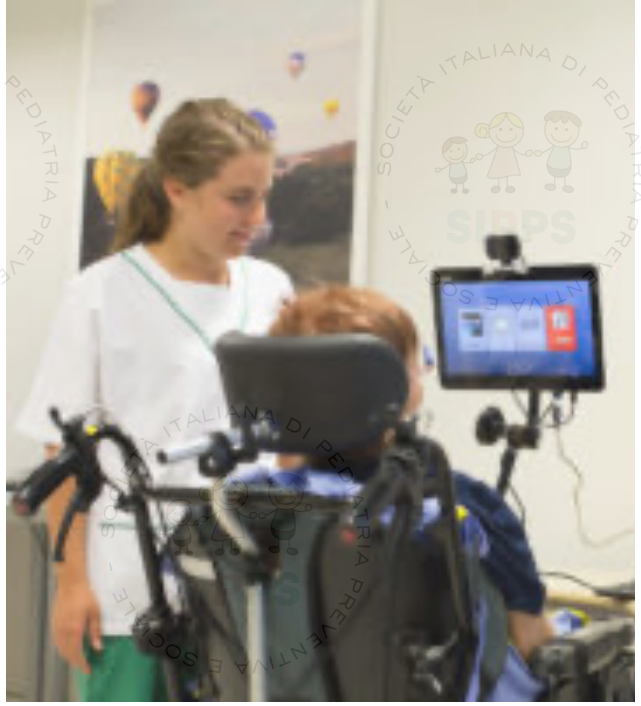






Il disabile considerato l'anello debole della catena evoluzionistica e destinato a soccombere nella **selezione naturale**.

- La disabilità fisica è percepita come menomazione, quella mentale addirittura come subumanità.

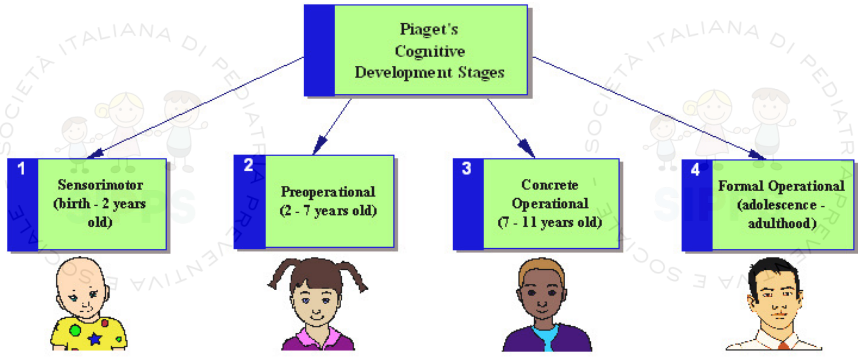


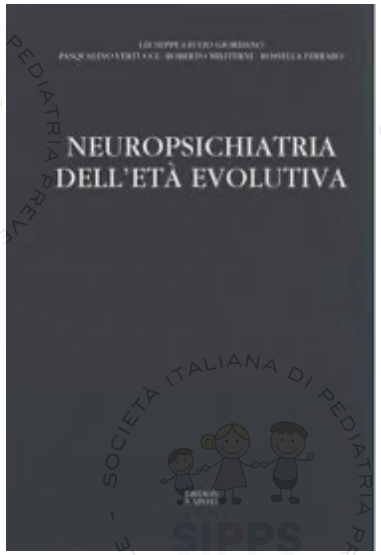
- Per quasi tutto il XX secolo la disabilità resta una vergogna da celare in famiglia, per evitare che sia scoperta da amici e vicini.

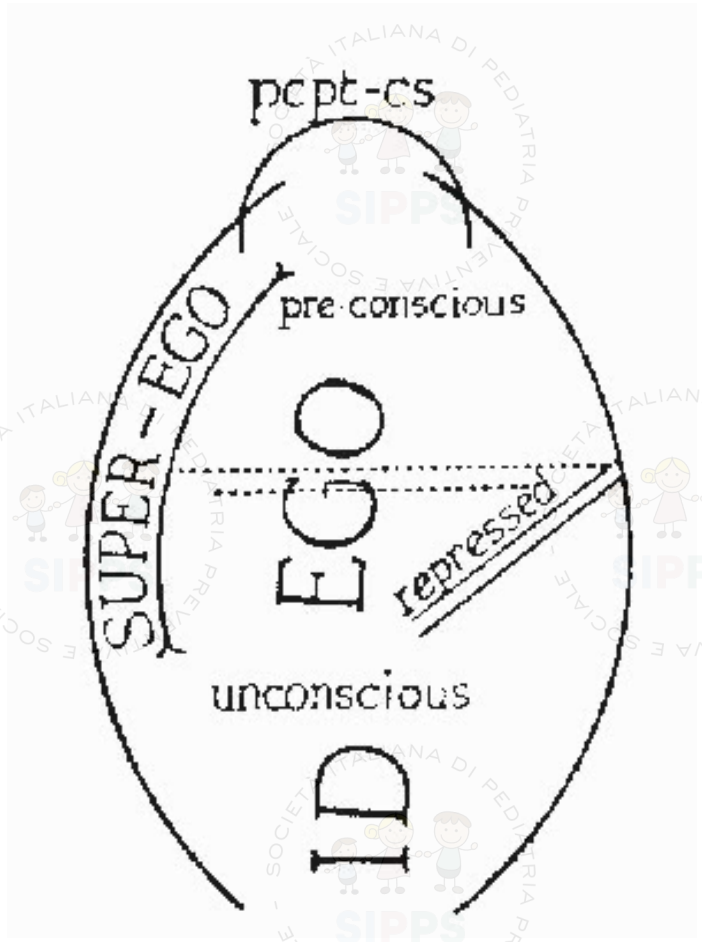
- L'esistenza del disabile è tollerata, purché non arrechi danno al buon nome e alla buona reputazione.

- E ancora oggi sono tanti i pregiudizi duri a morire

The Giants


Piaget's Cognitive Development Stages
1 Sensorimotor (birth - 2 years old)
2 Preoperational (2 - 7 years old)
3 Concrete Operational (7 - 11 years old)
4 Formal Operational (adolescence - adulthood)


NEUROPSICHIATRIA DELL'ETÀ EVOLUTIVA


pcpt-cs
SUPER-EGO
pre-conscious
EGO
repressed
unconscious
ID

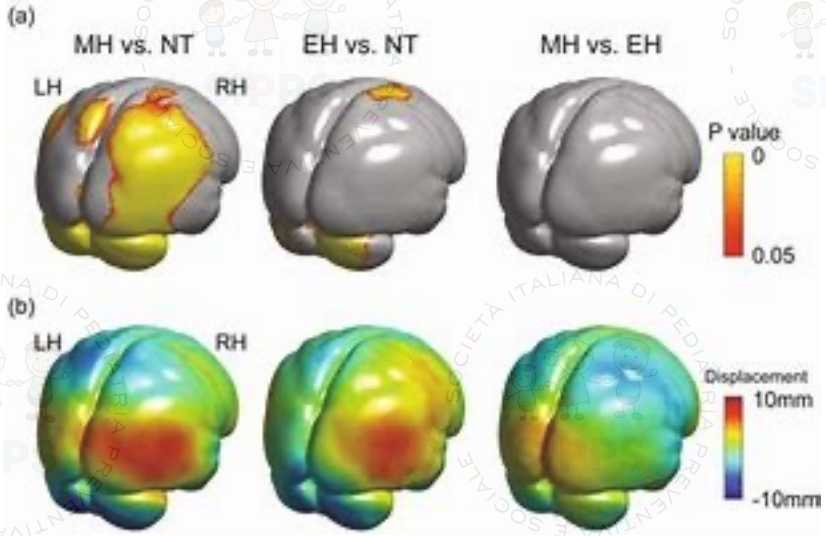
CAMPO DELLA NEUROPSICHIATRIA

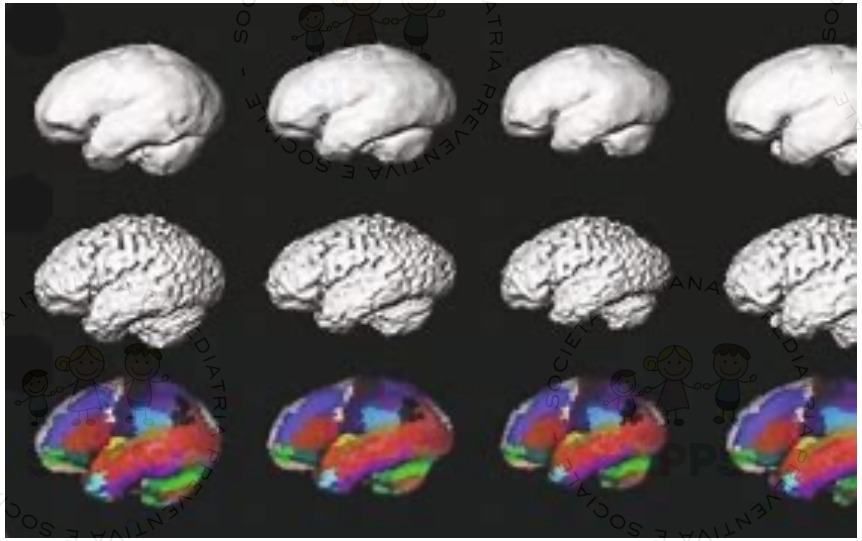
- Sindromi genetiche
- Disturbi neurologici
- Disturbi cognitivi
- Disturbi neuropsicologici
- Disturbi comportamentali

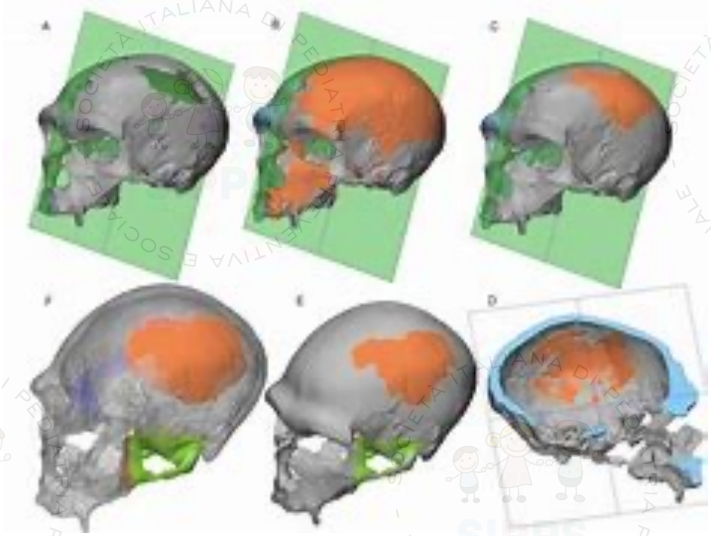
Your Child's Early Development is a Journey

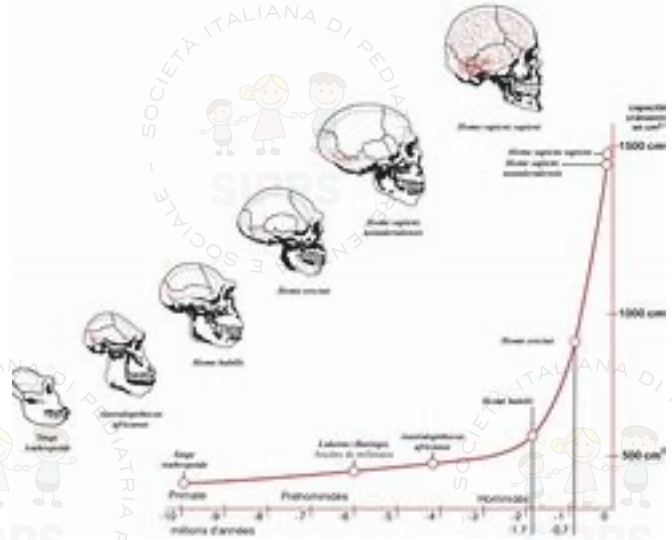
Check off the milestones your child has reached and share your child's progress with the doctor at every visit.

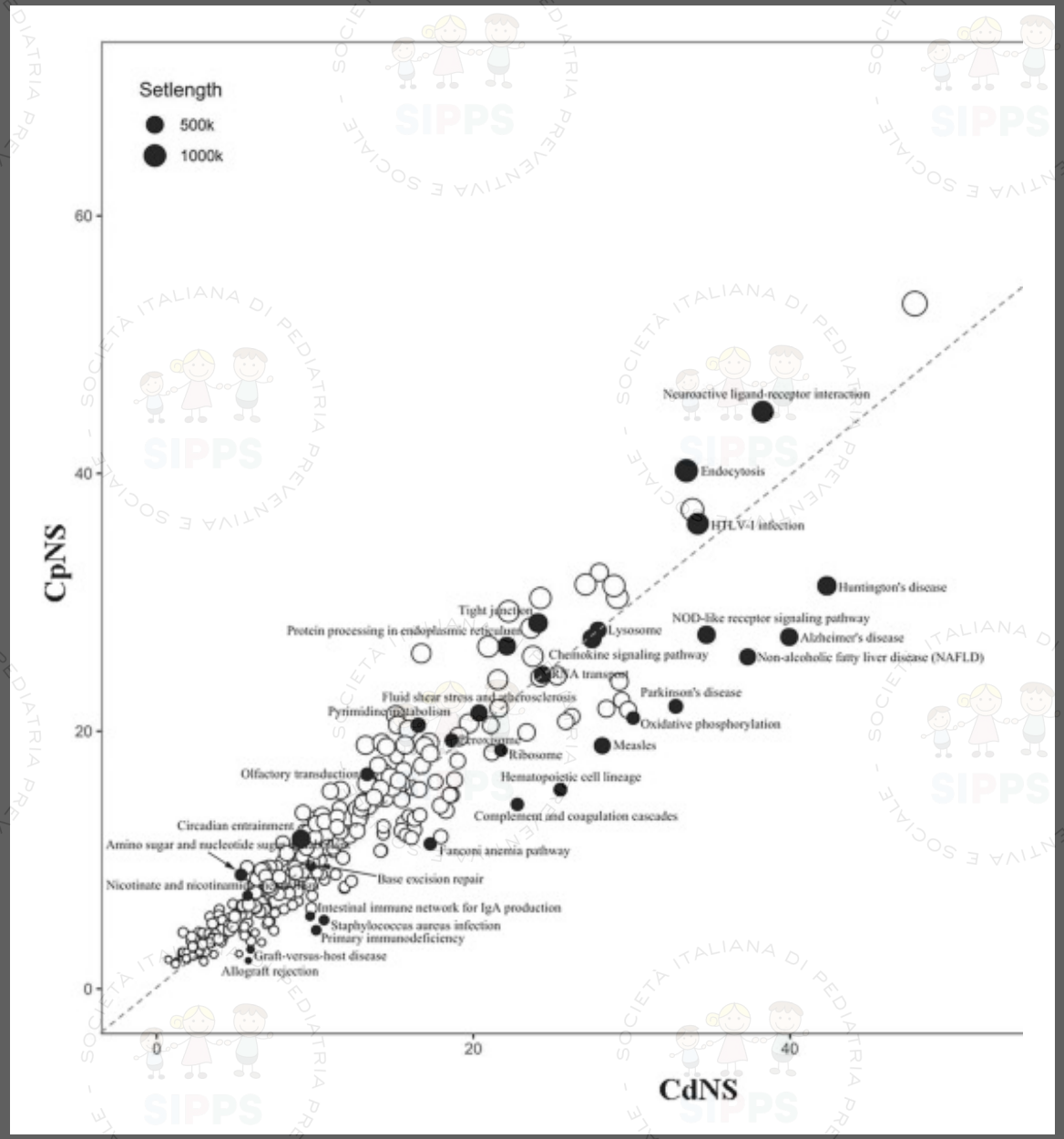
These are just a few of many important milestones to look for. For more complete checklists by age visit **www.cdc.gov/ActEarly** or call **1-800-CDC-INFO**.

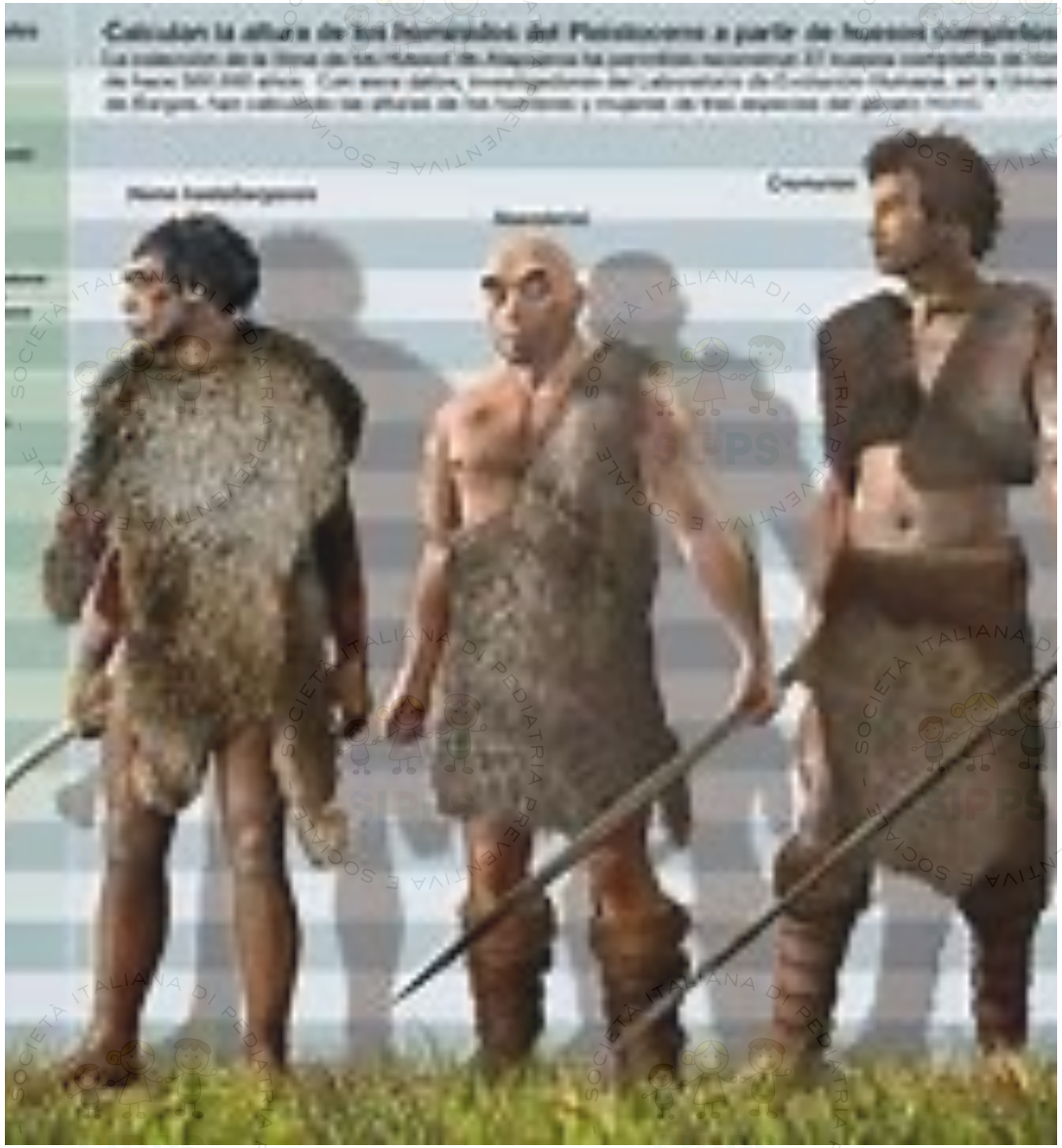

(a)
MH vs. NT
EH vs. NT
MH vs. EH
LH
RH
P value
0
0.05
(b)
LH
RH
Displacement
10mm
-10mm

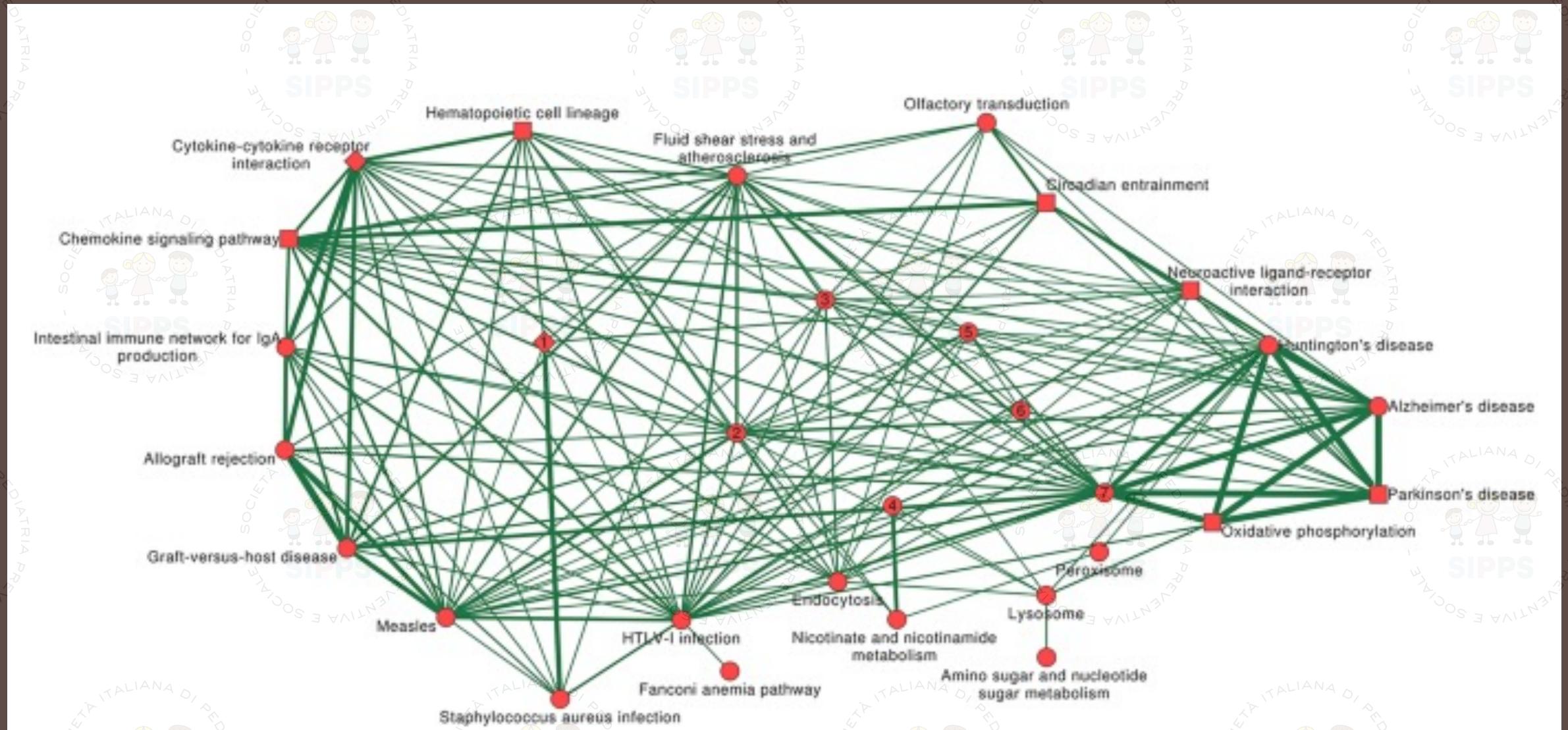


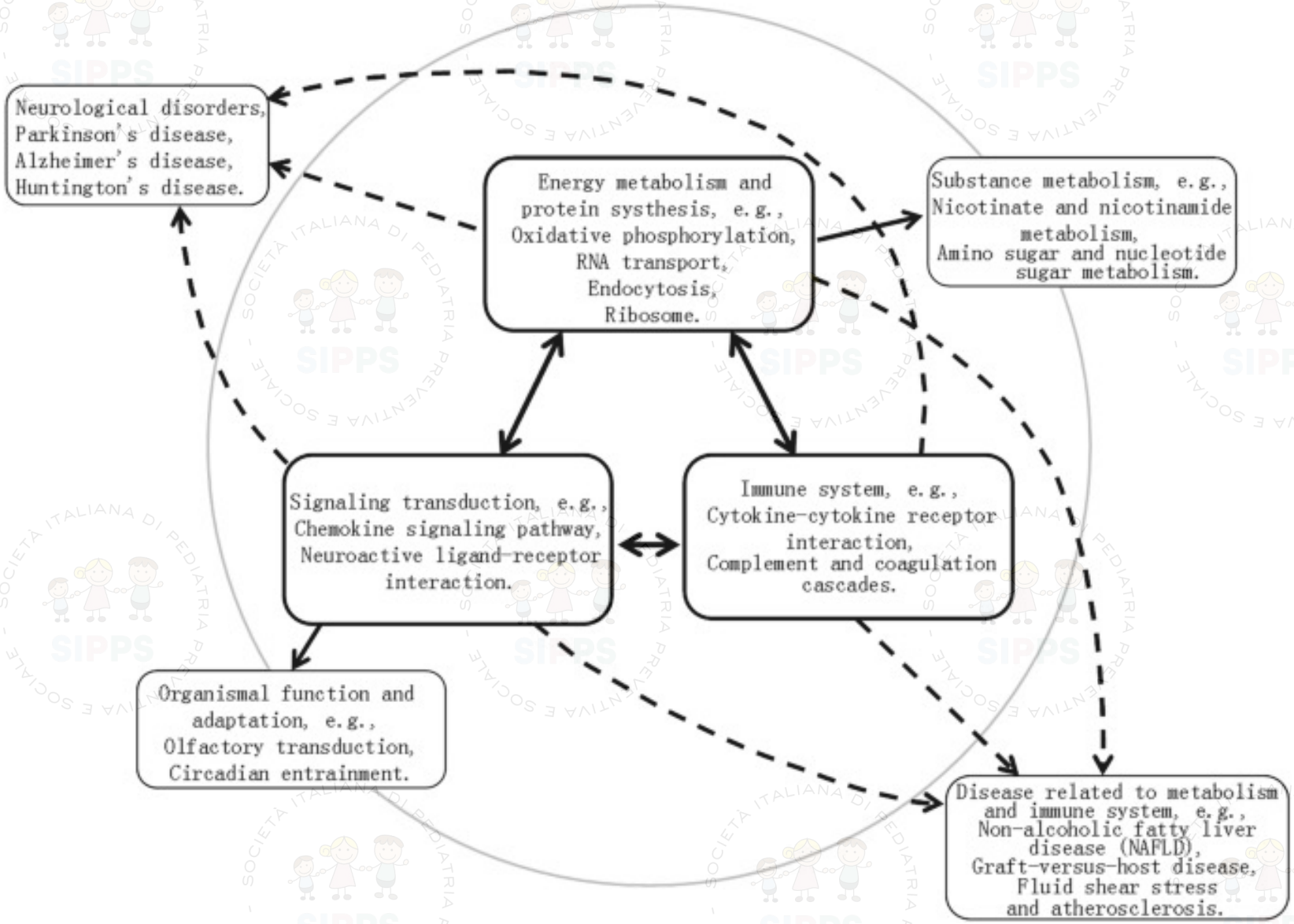


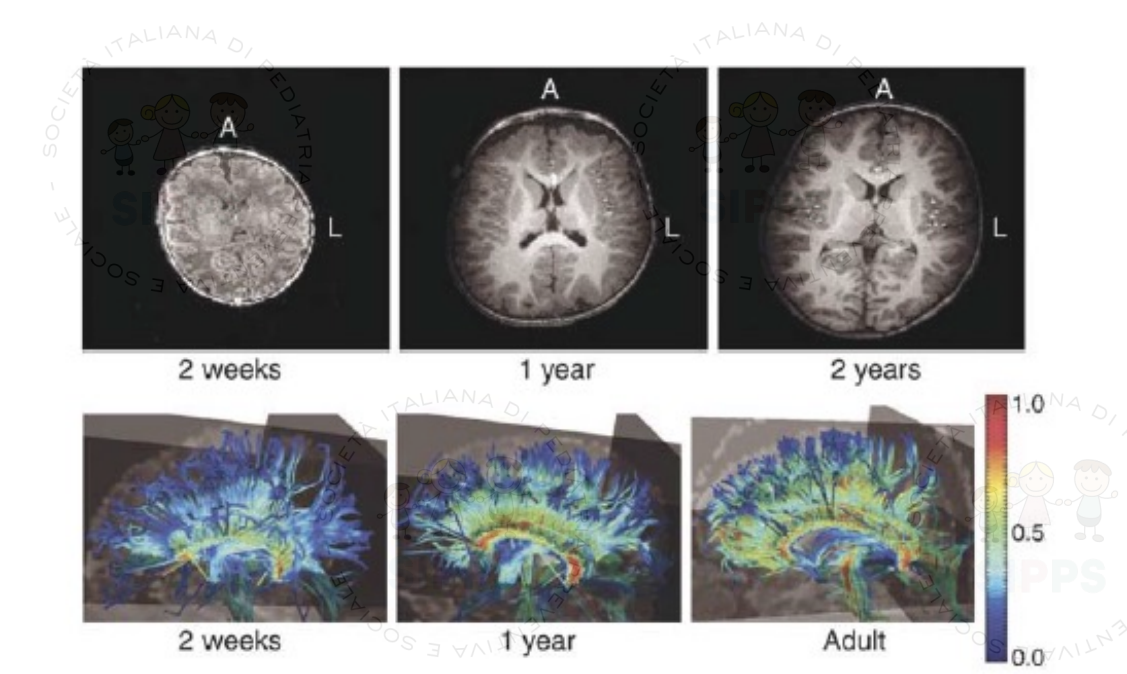


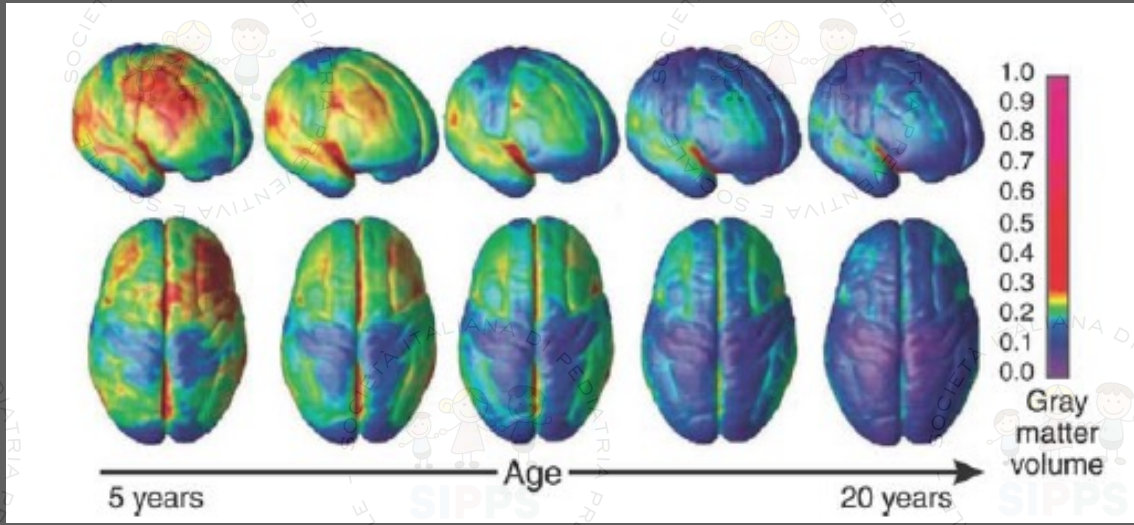

Setlength
500k
1000k
CpNS
CdNS
0
20
40
60
Neuroactive ligand-receptor interaction
Endocytosis
HTLV-I infection
Huntington's disease
Tight junction
Protein processing in endoplasmic reticulum
Lysosome
NOD-like receptor signaling pathway
Alzheimer's disease
Chemokine signaling pathway
Non-alcoholic fatty liver disease (NAFLD)
RNA transport
Fluid shear stress and atherosclerosis
Parkinson's disease
Pyrimidine metabolism
Oxidative phosphorylation
Measles
Ribosome
Olfactory transduction
Hematopoietic cell lineage
Complement and coagulation cascades
Circadian entrainment
Fanconi anemia pathway
Base excision repair
Intestinal immune network for IgA production
Staphylococcus aureus infection
Primary immunodeficiency
Graft-versus-host disease
Allograft rejection


Calculan la altura de los homínidos del Pleistoceno a partir de huesos completos


Hematopoietic cell lineage
Olfactory transduction
Cytokine-cytokine receptor interaction
Fluid shear stress and atherosclerosis
Circadian entrainment
Chemokine signaling pathway
Neuroactive ligand-receptor interaction
Intestinal immune network for IgA production
Huntington's disease
Alzheimer's disease
Allograft rejection
Parkinson's disease
Oxidative phosphorylation
Graft-versus-host disease
Peroxisome
Endocytosis
Lysosome
Measles
HTLV-I infection
Nicotinate and nicotinamide metabolism
Amino sugar and nucleotide sugar metabolism
Fanconi anemia pathway
Staphylococcus aureus infection


Neurological disorders,
Parkinson's disease,
Alzheimer's disease,
Huntington's disease.
Energy metabolism and protein systhesis, e.g.,
Oxidative phosphorylation,
RNA transport,
Endocytosis,
Ribosome.
Substance metabolism, e.g.,
Nicotinate and nicotinamide metabolism,
Amino sugar and nucleotide sugar metabolism.
Signaling transduction, e.g.,
Chemokine signaling pathway,
Neuroactive ligand-receptor interaction.
Immune system, e.g.,
Cytokine-cytokine receptor interaction,
Complement and coagulation cascades.
Organismal function and adaptation, e.g.,
Olfactory transduction,
Circadian entrainment.
Disease related to metabolism and immune system, e.g.,
Non-alcoholic fatty liver disease (NAFLD),
Graft-versus-host disease,
Fluid shear stress and atherosclerosis.


A
L
2 weeks
1 year
2 years
2 weeks
1 year
Adult
1.0
0.5
0.0

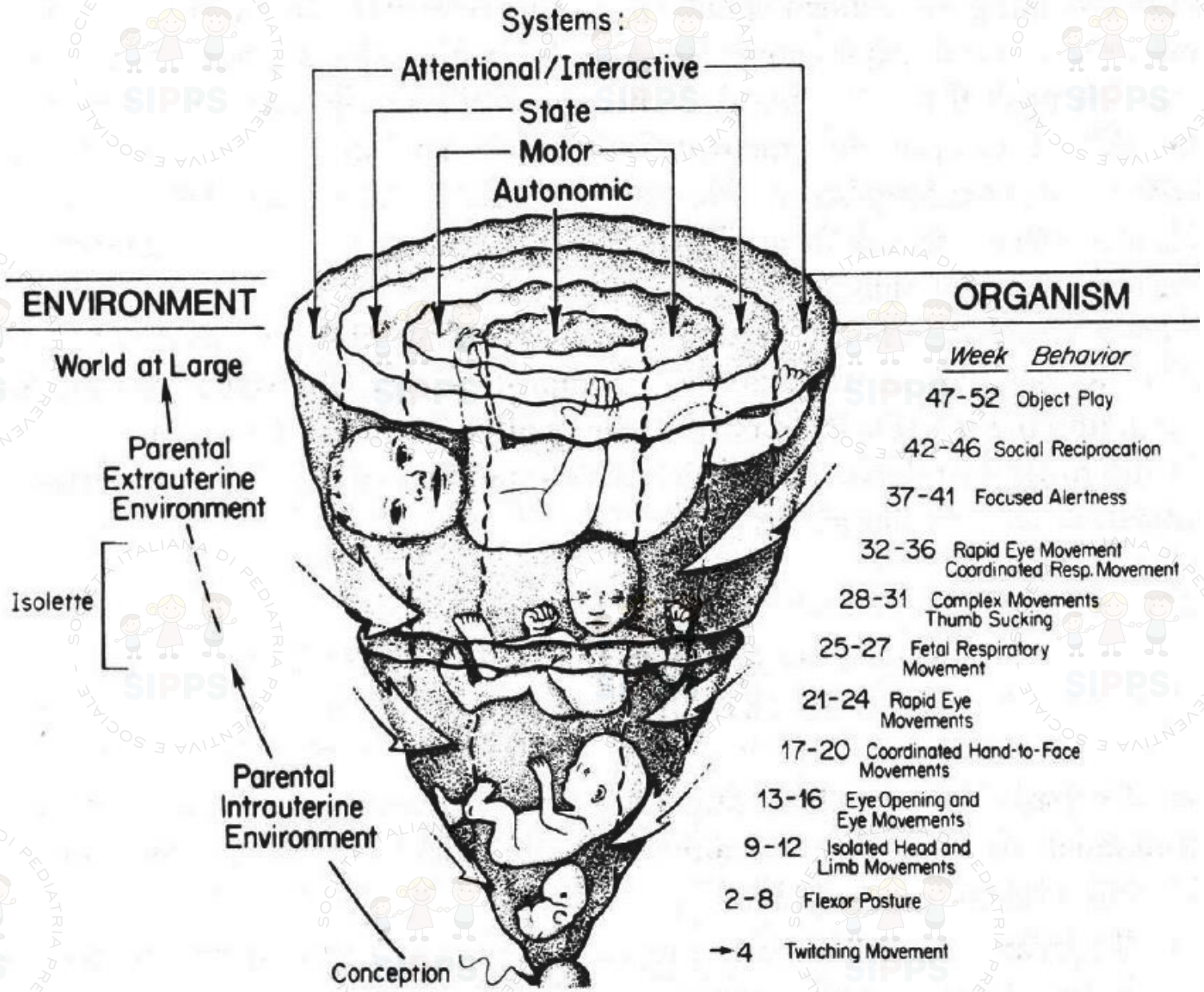

1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Gray matter volume
Age
5 years
20 years

Cambiamenti del ritmo sonno/veglia in età pediatrica

Age	
1-2 wks	Perdita del ciclo fetale
1-2 mesi	Strutturazione ritmo sonno/veglia Coliche: I ritmo circadiano
3-4 mesi	Inizio ciclo 24 ore. MLT stabile
6-9 mths	cc Aumento periodi di veglia diurna; NAPS
12 mths	70-80% sonno notturno.
>3 anni	Sonno notturno stabile. No NAPS
10 yrs	Ritmo circadiano stabile
>12 anni	Ritardo di fase. Sonnolenza diurna.

24.39 ore...

La teoria sinattiva



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BMC Psychiatry

STUDY PROTOCOL Open Access

Role of cortical excitatory/inhibitory imbalance in autism spectrum disorders from a symptom severity trajectories framework: a study protocol

Abstract

Background There is considerable evidence reporting an excitatory/inhibitory (E/I) cortical imbalance in autism spectrum disorders (ASD). However, previous findings on the direction of this imbalance and its relationship to ASD symptomatology are heterogeneous. Some factors contributing to these mixed results might be the methodological differences between studies assessing the E/I ratio and the intrinsic variability within the autistic spectrum. Studying the evolution of ASD symptoms and the factors that modulate it might help to explain and reduce this variability. Here we present a study protocol to explore the longitudinal role of E/I imbalance in ASD symptoms, combining different approaches to measure the E/I ratio and using the trajectories of symptom severity as a framework.

Methods This observational two time-point prospective study assesses the E/I ratio and the evolution of the behavioural symptoms in a sample of at least 98 participants with ASD. Participants are enrolled at 12 to 72 months of age and followed from 18 to 48 months after. A comprehensive battery of tests is applied to evaluate ASD clinical symptoms. The E/I ratio is approached from electrophysiology, magnetic resonance, and genetics. We will calculate the individual change for the main ASD symptoms and, based on that, we will define the trajectories of symptom severity. Then, we will investigate the correlation between measures of excitation/inhibition balance and autistic symptomatology cross-sectionally, as well as the ability of these measurements to predict changes in symptoms over time.

Discussion This study presents a robust multisystemic approach to the E/I imbalance theory in autism and its relation to divergent symptom trajectories. That setting will allow us to relate and compare the neurobiological information coming from different sources and its impact on behavioural symptoms while accounting for the high variability in ASD. The findings derived from this study could contribute to the ASD biomarkers research and might provide valuable evidence for the development of more personalized treatments in ASD.

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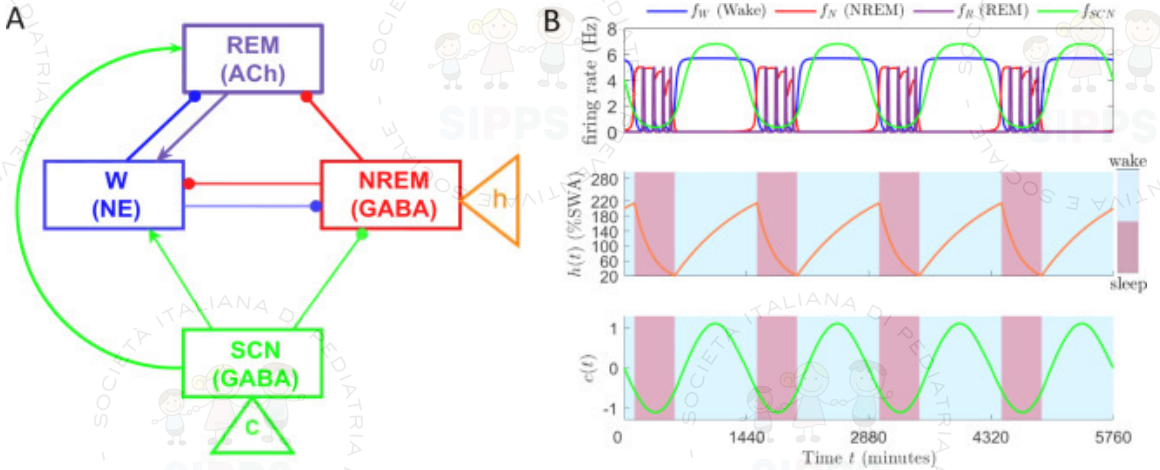
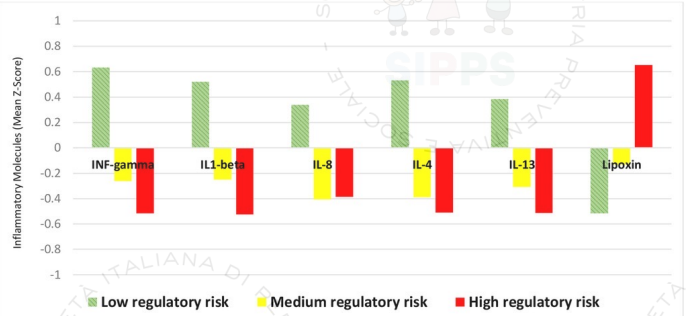
Original Research Article

NREM–REM alternation complicates transitions from napping to non-napping behavior in a three-state model of sleep–wake regulation☆

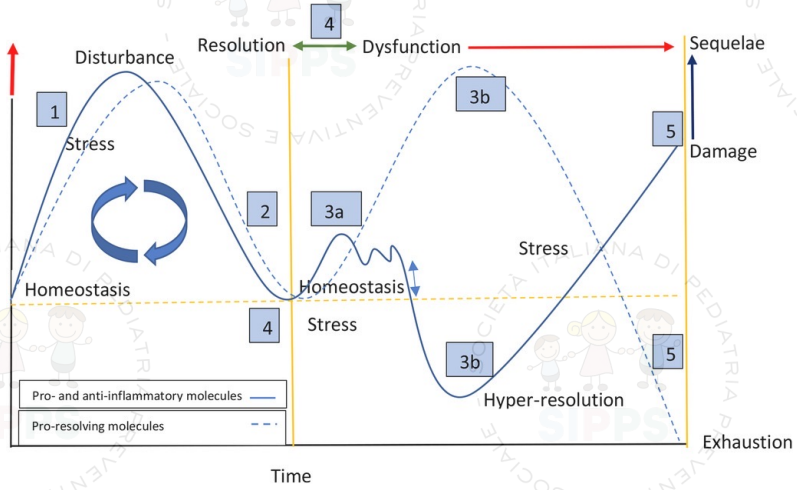


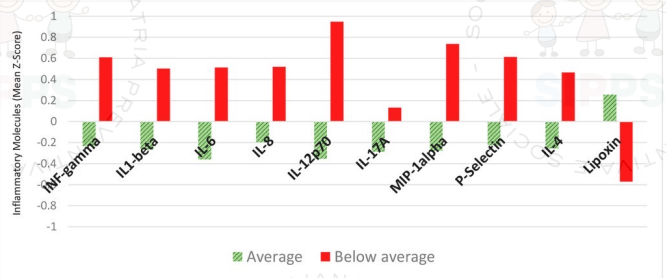
ABSTRACT

The temporal structure of human sleep changes across development as it consolidates from the polyphasic sleep of infants to the single nighttime sleep episode typical in adults. Experimental studies have shown that changes in the dynamics of sleep need may mediate this developmental transition in sleep patterning, however, it is unknown how sleep architecture interacts with these changes. We employ a physiologically-based mathematical model that generates wake, rapid eye movement (REM) and non-REM (NREM) sleep states to investigate how NREM–REM alternation affects the transition in sleep patterns as the dynamics of the homeostatic sleep drive are varied. To study the mechanisms producing these transitions, we analyze the bifurcations of numerically-computed circle maps that represent key dynamics of the full sleep–wake network model by tracking the evolution of sleep onsets across different circadian (~ 24 h) phases. The maps are non-monotonic and discontinuous, being composed of branches that correspond to sleep–wake cycles containing distinct numbers of REM bouts. As the rates of accumulation and decay of the homeostatic sleep drive are varied, we identify the bifurcations that disrupt a period-adding-like behavior of sleep patterns in the transition between biphasic and monophasic sleep. These bifurcations include border collision and saddle–node bifurcations that initiate new sleep patterns, period-doubling bifurcations leading to higher-order patterns of NREM–REM alternation, and intervals of bistability of sleep patterns with different NREM–REM alternations. Furthermore, patterns of NREM–REM alternation exhibit variable behaviors in different regimes of constant sleep–wake patterns. Overall, the sequence of sleep–wake behaviors, and underlying bifurcations, in the transition from biphasic to monophasic sleep in this three-state model is more complex than behavior observed in models of sleep–wake regulation that do not consider the dynamics of NREM–REM alternation. These results suggest that interactions between the dynamics of the homeostatic sleep drive and the dynamics of NREM–REM alternation may contribute to the wide interindividual variation observed when young children transition from napping to non-napping behavior.



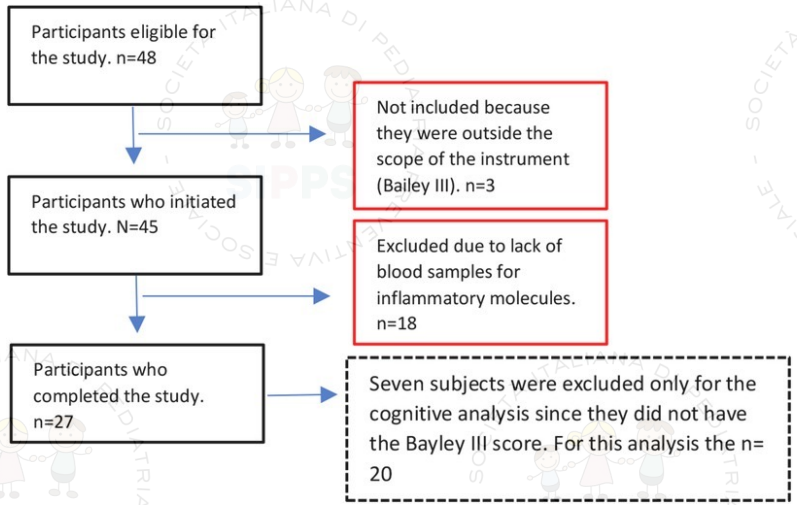
Inflammatory Molecules (Z-scores)	Low regulatory risk (n=10)	Medium regulatory risk (n=7)	High regulatory risk (n=10)	Significance
INF-gamma	0.63179	-0.26268	-0.51683	0.0233
IL1-beta	0.5189	-0.25149	-0.52557	0.0341
IL-8	0.33933	-0.40533	-0.38626	0.0536
IL-4	0.53152	-0.38754	-0.50868	0.0132
IL-13	0.38308	-0.30828	-0.51371	0.0145
Lipoxin	-0.5151	-0.13184	0.65333	0.0258

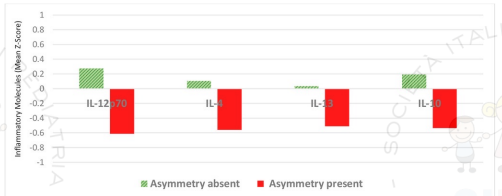




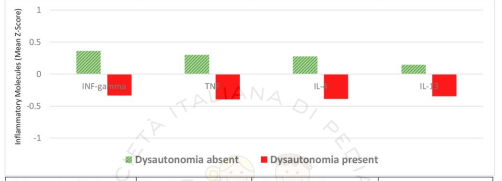
Inflammatory Molecules (Z-scores)	Average (n=12)	Below average (n=8)	Significance (right tail)
INF-gamma	-0.23223	0.61146	0.0466
IL1-beta	-0.26496	0.50426	0.0478
IL-6	-0.35969	0.51278	0.0071
IL-8	-0.19663	0.52049	0.0162
IL-12p70	-0.35188	0.94722	0.0058
IL-17A	-0.28497	0.13208	0.0073
MIP-1alpha	-0.27805	0.73795	0.0124
P-Selectin	-0.227	0.61285	0.0491
IL-4	-0.25626	0.46776	0.05
Lipoxin	0.25698	-0.57131	(left tail) 0.0330

The molecular profile of the inflammatory process differs among various neurodevelopmental disorders with or without cognitive component: A hypothesis of persistent systemic dysfunction and hyper-resolution





Inflammatory Molecules (Z-scores)	Asymmetry absent (n=19)	Asymmetry present (n=8)	Significance (left tail)
IL-12p70	0.27481	-0.61349	0.0188
IL-4	0.10551	-0.56115	0.0374
IL-13	0.03286	-0.51108	0.0422
IL-10	0.19209	-0.53439	0.0442



Inflammatory Molecules (Z-scores)	Dysautonomia absent (n=12)	Dysautonomia present (n=15)	Significance (left tail)
INF-gamma	0.36054	-0.33437	0.0374
TNF	0.29809	-0.3939	0.0232
IL-4	0.27525	-0.38583	0.0266
IL-13	0.14415	-0.34626	0.0454

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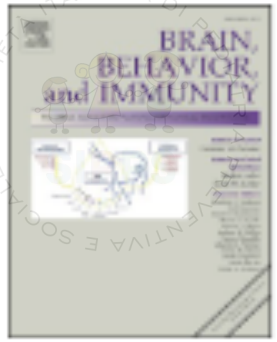

Review Article

Neutrophil-lymphocyte ratios as inflammatory biomarkers in psychiatric patients

- In a study of 82 children with ADHD, patients had greater NLR and lower lymphocytes
-
- No significant associations were found with severity measures

- Elevated NLR reflects a trait marker of ADHD rather than a state marker

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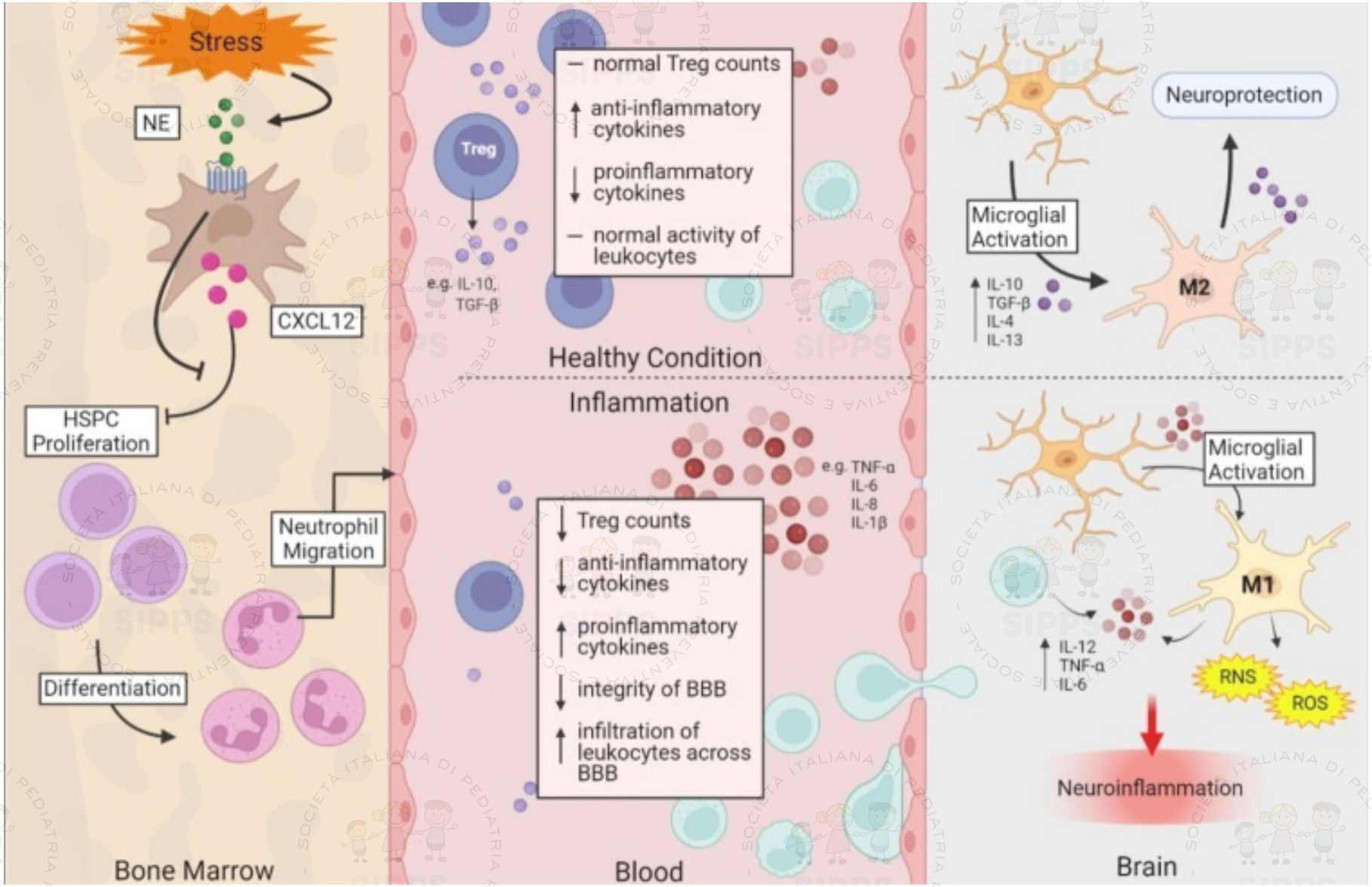
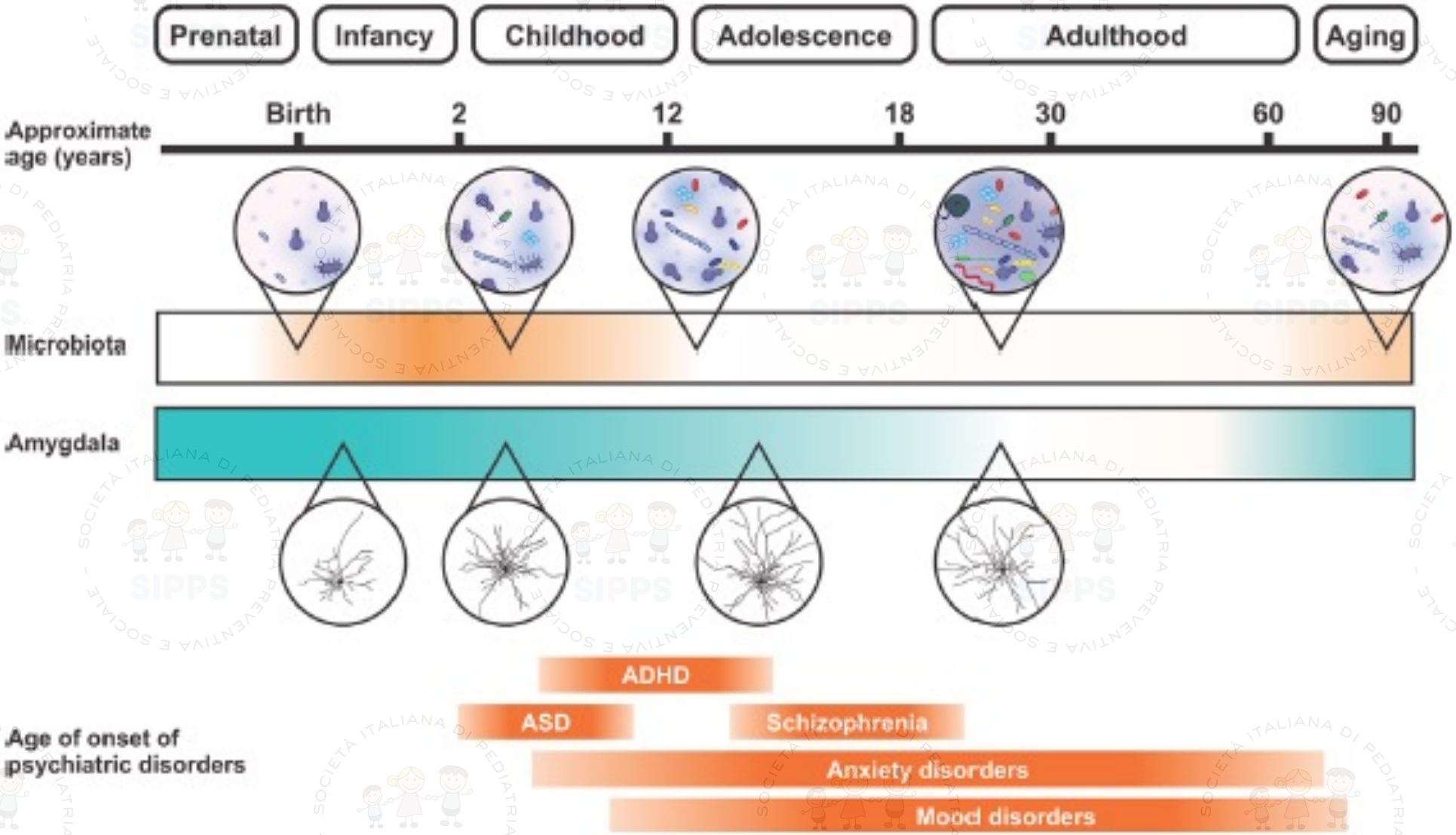
Review Article

Neutrophil-lymphocyte ratios as inflammatory biomarkers in psychiatric patients

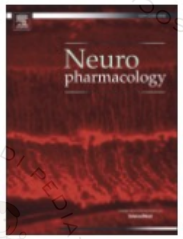
- In a study of ASD, 64 drug-naïve children between the ages of 2–5 with ASD were found to have elevated average NLR and reduced lymphocytes.

- However, ASD severity as measured by the Childhood Autism Rating Scale was negatively and positively associated with lymphocyte counts and NLR respectively, and NLR also predicted belonging to the patient group.


Stress
NE
CXCL12
HSPC Proliferation
Neutrophil Migration
Differentiation
Bone Marrow
Treg
e.g. IL-10, TGF-β
– normal Treg counts
↑ anti-inflammatory cytokines
↓ proinflammatory cytokines
– normal activity of leukocytes
Healthy Condition
Inflammation
e.g. TNF-α IL-6 IL-8 IL-1β
↓ Treg counts
↓ anti-inflammatory cytokines
↑ proinflammatory cytokines
↓ integrity of BBB
↑ infiltration of leukocytes across BBB
Blood
Neuroprotection
Microglial Activation
IL-10 TGF-β IL-4 IL-13
M2
Microglial Activation
M1
IL-12 TNF-α IL-6
RNS
ROS
Neuroinflammation
Brain


Prenatal
Infancy
Childhood
Adolescence
Adulthood
Aging
Approximate age (years)
Birth
2
12
18
30
60
90
Microbiota
Amygdala
Age of onset of psychiatric disorders
ADHD
ASD
Schizophrenia
Anxiety disorders
Mood disorders

Journal Pre-proof



Characterizing the metabolomic signature of attention-deficit hyperactivity disorder in twins

J.R. Swann, R. Diaz Heijtz, J. Mayneris-Perxachs, A. Arora, J. Isaksson, S. Bölte, K. Tammimies

Highlights

- The gut microbiota is implicated as a potential susceptibility factor in ADHD.
- Males, but not females, with ADHD excreted greater amounts of hippurate.
- This microbial-host co-metabolite was negatively correlated with IQ in males.
- Hippurate can cross the blood-brain-barrier and has bioactivity relevant to ADHD.

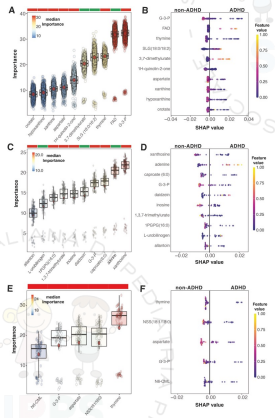
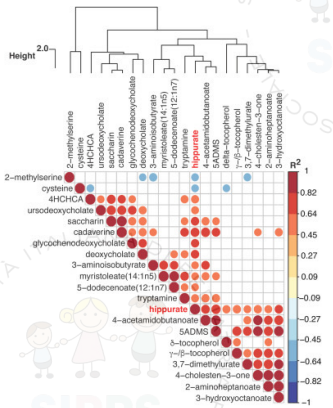


Table 1. Sample characteristics.

Characteristics	ADHD (n = 33)	non-ADHD (n = 79)
Age, mean years (SD) [range]	13.55 (3.01) [8-19]	15.17 (2.99) [8-22]
Sex, n females (%)	14 (42.4%)	37 (46.8%)
MZ:DZ concordant pairs (n)[a]	4:3	25:6
ADHD discordant pairs (n)[a]	8	
MZ	4	
DZ	4	
BMI, mean (SD) [range]	19.061 (2.957) [13–24]	20.835 (2.817) [14–27]
Parental-rated ADHD traits	0.84 (0.38) [0.20–1.700]	0.131 (0.174) [0.000–0.800]
Self-rated ADHD traits, mean (SD) [range]	1.03 (0.40) [0.000–1.889]	0.46 (0.34) [0.000–1.222]
IQ-General Ability Index, mean (SD) [range]	98.82 (12.39) [71–130]	103.5 (12.42) [81–138]
Fecal samples n (%)	26 (72.72%)	66 (83.54%)



CURE PRIMARIE (PRIMARY CARE)

- accesso diretto
- continuità dell'assistenza
- globalità dell'assistenza
- coordinamento dell'assistenza
- orientamento delle famiglie

Obiettivi della pediatria di famiglia

Consegnare alla collettività

un adolescente cresciuto nel rispetto di valori importanti riguardanti la sua persona

una famiglia che abbia acquisito la genitorialità adeguata alle varie fasi di crescità del bambino

un cittadino consapevole dei suoi diritti e dei suoi doveri nel campo della salute

OMS 1974: Pediatria = Medicina dello sviluppo e dell'educazione


STOP
WAR


Grazie per l’attenzione