INTELLECTUAL DEVELOPMENTAL DISORDERS AND MENTAL HEALTH: CLASSIFICATION AND DIAGNOSTIC ISSUES

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ID is a health condition

ID is a meta-syndrome characterised by an impairment in cognitive functioning prior to the acquisition of skills through learning

the intensity of the deficit is such to interfere in a significant way with individual normal functioning as expressed in limitations in activities and restriction in participation (disabilities)

• A group of developmental conditions characterized by a significant impairment of cognitive functions, which are associated with limitations of learning, adaptive behavior and skills.

• IDD is a life span condition requiring consideration of developmental stages and life transitions.

• Most individuals with IDD continue to acquire skills and competencies, especially with optimal care, training, education and opportunities for learning.

• However IDD is a vulnerable group associated with a higher rate of mental and physical disorders and related unmet care needs as well as an increased risk of abuse and neglect.
ID: DISABILITY OR DISORDER ?
ID: DISABILITY OR DISORDER ?
Is IQ reduction an useful criterion for ID?

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>ID level</th>
<th>Specific Cognitive Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down</td>
<td>Mild, moderate or severe</td>
<td></td>
</tr>
<tr>
<td>X Fragile</td>
<td>15% mild</td>
<td></td>
</tr>
<tr>
<td></td>
<td>49% moderate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>26% severe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10% profound</td>
<td></td>
</tr>
<tr>
<td>Williams 7q deletion</td>
<td>Mild or moderate</td>
<td></td>
</tr>
<tr>
<td>Smith-Magenis (17p deletion)</td>
<td>Mild or moderate</td>
<td></td>
</tr>
</tbody>
</table>
### Syndrome

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>ID level</th>
<th>Specific Cognitive Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warkany 2 (trisomy 8)</td>
<td>moderate or severe</td>
<td></td>
</tr>
<tr>
<td>Phenylketonuria</td>
<td>moderate or severe</td>
<td></td>
</tr>
<tr>
<td>Klinefelter (47 XXY)</td>
<td>absent or borderline</td>
<td></td>
</tr>
<tr>
<td>Galctosemia</td>
<td>absent or borderline</td>
<td></td>
</tr>
</tbody>
</table>

WAIS IV SUBTESTS AND SUBSCORES

- Full-Scale IQ (FSIQ)
  - Verbal IQ (VIQ)
    - Verbal Comprehension Index (VCI)
      - Vocabulary
      - Similarities
      - Information
      - Comprehension
    - Working Memory Index (WMI)
      - Arithmetic
      - Digit Span
      - Letter-Number Sequencing
  - Performance IQ (PIQ)
    - Perceptual Organization Index (POI)
      - Picture Completion
      - Block Design
      - Matrix Reasoning
    - Processing Speed Index (PSI)
      - Digit Symbol-Coding
      - Symbol Search
SCFs AND NOT IQ FOR BIOLOGICAL SUBSTRATES

Findings of recent studies of genetics, neuroimaging and neurophysiology identified more correlations with cognitive functions (such as perceptual organization deficit, poor working memory, lexical, visual-spatial and phonological processing) than with IQ scores1,2,3,4,5,6
BORDERLINE INTELLIGENCE

N = 8450 adults

- around 1/8 of the population has borderline intelligence (12.3% of the sample)

- this people present higher rate of:
  - neurotic disorders
  - substance abuse
  - personality disorders
  - social disability
  - psycho-pharmacological therapies, but not speech therapies
  - health service use, including emergency services

Is the age limit of 18 an useful criterion for ID?

Although the specific age limit of 18 is clearly arbitrary, WPA-SPID members expressed general agreement on the importance to keep a distinction between a persistent process that begins at birth and a change occurring after a normal development.
INCREASE OF AUTISM AND ASDs PREVALENCE RATE

1. Newschaffer et al., 2007.
2. Lazoff et al., 2010; Baron-Cohen et al., 2009
PDD in ID = 30-40%\(^1\)

ID in autism = 25-80%\(^2\)

in ID around 50% of ASDs has been previously diagnosed with schizophrenia\(^3\)

risk of underestimating ASD in ID in favour of schizophrenia\(^4\)

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1. Kraijer 1997 (N=718); Morgan et al. 2002 (N=571); La Malfa et al., 2004 (N=166 adults); Cooper et al., 2007
2. Hoekstra et al., 2009 BJP; Centers for Disease Control and prevention USA, 2006; Edelson, 2006; Matson e Shoemaker, 2009; Baird et al., 2006; Noterdaeme e Wriedt, 2010; Bryson and Smith, 1998
4. Palucka et al., 2009; Savage et al., 2007
PREVALENCE RATE (%)
ASD AND SCHIZOPHRENIA

- 21% of people with schizophrenia receive a lifetime diagnosis of PDD-NOS\(^1\)

- around 50 % of people with autismo also meets criteria for schizophrenia disorganised-type\(^2\)

- at least 1.5% of psychiatric outpatients don’t receive the right diagnosis of ASD; 26% of these is diagnosed with schizophrenia\(^3\)

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1. Sporn et al., 2004; Towbin et al., 2005
2. Konstantareas and Hewitt, 2001
3. Nylander and Gilberg, 2001
# Prevalence Rate (%) of Psychiatric Disorders in ID with and without Autism

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Tool</th>
<th>with A</th>
<th>without A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradley &amp; Bolton, 2006</td>
<td>SAPPA</td>
<td>50</td>
<td>16.7</td>
</tr>
<tr>
<td>Bradley et al., 2004</td>
<td>DASH</td>
<td>&gt;50</td>
<td>25</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disorder</th>
<th>with A</th>
<th>without A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>50</td>
<td>8</td>
</tr>
<tr>
<td>Mania</td>
<td>67</td>
<td>8</td>
</tr>
<tr>
<td>Eating Disorders</td>
<td>58</td>
<td>25</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

GENETIC OVERLAPPING BETWEEN AUTISM AND IDD

Gene:
- FMR1 Xq27.3²
- GRIK2 6q16.3²
- HOXA1 7p15.3²
- PTCHD1¹
- NLGN4 and IL1RAPL1²
- RPL10²
deletion
- 1q21.1²
- 15q13.3²
- 16p11.2²

Protein:
- neuroligina³
- neurexina³
- SHANK-3³
- CNTNAP2⁴
- PUM2⁵ implications in mRNA
- CGG trinucleotide⁶
- LTD on mGluR⁷

¹Noor A, Scherer SW. Disruption at the PTCHD1 locus on Xp22.11 in autism spectrum disorder and intellectual disability. Sci Transl Med. 2010 September 15; 2(49)
²Pinto D, Scherer SW. Functional Impact of Global Rare Copy Number Variation in Autism Spectrum Disorder Nature. 2010 July 15; 466(7304): 368–372. doi:10.1038/nature09146
GENETIC OVERLAPPING BETWEEN AUTISM AND SCHIZOPHRENIA

- Chromosome 1q21.1 deletion
- Chromosome 15q13.3 deletion
- Chromosome 3q29 and 22q11.21 deletion
- Chromosome 16p11.2 duplication
- Exonic NRXN1 deletion
- Exonic VIPR2 and C16orf72 duplication
- Chromosome 16p11.2
- NRXN1 2p16.3 gene disrupted in ASD, MR, schizophrenia
- 16p13.11 deletion
- Deficits in RNA transcription without changes in DNA sequence

6. Singh SM, O'Reilly R. (Epi)genomics and neurodevelopment in schizophrenia: monozygotic twins discordant for schizophrenia augment the search for disease-related (epi)genomic alterations. Genome, 2009 Jan;52(1):8-19
Neurexine 1 (NRXN1)

N= 3540 under genomic comparative hybridization
NRXN1 mutation resulted to be associated with ASDs, IDD, and SLD

Pum 2 and eIF4E and Scn1a
Neuroligina
SHANK-3
CNTNAP2
'cadherin' (Calcium dependent adhesion molecules) 10 and 9

Fragile X Mental Retardation Protein is highly enriched in neurons and binds to approximately 4% of mRNAs in mammalian brain.

FMRP loss is a hallmark of fragile X syndrome (FXS), the most common inherited form of mental retardation.

reductions of FMRP in psychiatric disorders
- autism
- schizophrenia
- bipolar disorder
- major depressive disorder
<table>
<thead>
<tr>
<th>Gene</th>
<th>Function</th>
<th>Chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>RELN</td>
<td>Reelin, neuronal migration and synaptic function</td>
<td>1q21.1</td>
</tr>
<tr>
<td>Npas4G</td>
<td>Npas4, social and cognitive functions</td>
<td>1q21.1</td>
</tr>
<tr>
<td>CHD1, PBKAB2</td>
<td>Chromatin and AMP kinase regulation</td>
<td>1q21.1</td>
</tr>
<tr>
<td>SEZ6L2</td>
<td>Expressive language and socialisation</td>
<td>16p11.2</td>
</tr>
<tr>
<td>NDE1, NTAN1</td>
<td>Synaptic plasticity, memory</td>
<td>16p13.1</td>
</tr>
<tr>
<td>NMDA rec</td>
<td>Working memory and perceptual binding</td>
<td>16p13.1</td>
</tr>
<tr>
<td>TCF4</td>
<td>TCF4, memory and attention (N150)</td>
<td>16p13.1</td>
</tr>
<tr>
<td>Neurexine</td>
<td>Synaptic functions</td>
<td>16p13.1</td>
</tr>
<tr>
<td>Contactin-L2</td>
<td>Cell adhesion and receptors</td>
<td>16p13.1</td>
</tr>
<tr>
<td>ProSAP2</td>
<td>Synapse and dendritic spine formation</td>
<td>16p13.1</td>
</tr>
</tbody>
</table>

WPA-SPID proposed to include in a cluster of disorders sharing salient cognitive symptoms and similarities on risk factors, clinical factors, genetic phenotype, early onset, course, and co-morbidity.
05 Mental and behavioural disorders

NEURODEVELOPMENTAL DISORDERS

Disorders of Intellectual Development (DID)

5A00. Mild DID: IQ 50-69; in adults mental age (MA) 9 - <12 y

5A01. Moderate DID: IQ 35-49; in adults, MA 6 - <9 y

5A02. Severe DID: IQ 20 – 34; in adults, MA 3 - <6 y

5A13. Profound DID: IQ <20; in adults, MA <3 y

5A0Y. Other disorders of intellectual development

5A0Z. Disorders of intellectual development, unspecified

ICD-10 impairment of behaviour F7x. 1 “RETIRED”
DSM-5 ID/IDD Position

- disturbo con insorgenza nell’età evolutiva che include deficit intellettivi e adattivi negli ambiti della concettualizzazione, della socializzazione e delle capacità pratiche

- i livelli di gravità vengono definiti sulla base del funzionamento adattivo e non sui punteggi di quoziente intellettivo (QI), poiché è stato giudicato che sia il funzionamento adattivo, nelle aree della concettualizzazione, della socializzazione e delle abilità pratiche, a determinare il livello di supporto necessario a mantenere una condizione di vita accettabile. In più, quando basse (inferiori a 60), le misure di QI perdono di validità

- si continuano a distinguere 4 livelli di gravità (lieve, moderato, grave e gravissimo), ma con criteri diversi dal DSM-IV e IV-TR.
Il disturbo è stato collocato in un raggruppamento meta-sindromico, o meta-strutturale, denominato ‘disturbi del neurosviluppo’.

Il gruppo include condizioni con insorgenza in età evolutiva, tipicamente precoci, spesso precedenti l’ingresso a scuola e caratterizzate da deficit di sviluppo che producono compromissioni del funzionamento personale, sociale, scolastico o occupazionale.

Il range di deficit spazia da limitazioni molto specifiche dell’apprendimento e del controllo delle funzioni esecutive ad una compromissione globale delle abilità sociali o dell’intelligenza.

I disturbi del neurosviluppo si presentano spesso insieme, per esempio individui con autismo hanno spesso anche disabilità intellettiva (disturbo dello sviluppo intellettivo) e molti bambini con disturbo da deficit d’attenzione e iperattività hanno spesso anche un disturbo specifico dell’apprendimento.
A. Deficit delle funzioni intellettive, come il ragionamento, la soluzione di problemi, la pianificazione, il pensiero astratto, il giudizio, l’apprendimento scolastico o l’apprendimento dall’esperienza, confermato sia da valutazione clinica che da prove d’intelligenza individualizzate e standardizzate.

B. Deficit del funzionamento adattivo che si manifesti col mancato raggiungimento degli standard di sviluppo e socio-culturali per l’indipendenza personale e la responsabilità sociale. Senza supporto continuativo i deficit adattivi limitano il funzionamento in una o più attività della vita quotidiana, quali la comunicazione, la partecipazione sociale e la vita indipendente, in più ambiti diversi, come la casa, la scuola, il lavoro e la comunità.

C. Insorgenza dei deficit intellettivi e adattivi nell’età evolutiva.
PROPOSAL OF LINEAR STRUCTURE FOR ICD-11

F: MENTAL AND BEHAVIOURAL DISORDERS (meta-structure)

F1: NEURO-DEVELOPMENTAL DISORDERS (meta-category)

F1.Y PROBLEM BEHAVIOURS/BEHAVIOUR DISORDER (category)

F1.Y.1 Mild and infrequent
F1.Y.2 Mild and frequent
F1.Y.3 Severe and infrequent
F1.Y.4 Severe and frequent
F1.Y.5 External boundary prevents expression of behaviour
F1.Y.8 Unspecified

F1.Y.1-8.1 Physical aggression to others
F1.Y.1-8.2 Verbal aggression (e.g. screaming)
F1.Y.1-8.3 Destructive to property (e.g. throwing/pulling objects)
F1.Y.1-8.4 Self-injury
F1.Y.1-8.5 Oppositional
F1.Y.1-8.6 Overly-demanding
F1.Y.1-8.7 Sexually inappropriate (e.g. repeatedstripping)
F1.Y.1-8.8 Other

Can multiple sub-sub categories be specified or not? – alternative descriptors if not
Association between recent life events and traumatic experiences across the life span and psychiatric disorders in PwID more than in general population.

Transition phases and PDs

Though they have been less studied by the literature regarding predictors of mental illness, traumatic experiences seem to play a more important role in psychopathology than life events. 

Martorell A., et al., 2009
A NEW CULTURAL MODEL FOR NEURODEVELOPMENTAL DISORDERS / CONDITIONS

PSYCHO-CHARACTERISATION
SPECIFIC COGNITIVE FUNCTIONS
INDIVIDUAL SKILLS
INDIVIDUAL ATTRIBUTION OF IMPORTANCE

OFFER OF A WIDE RANGE OF OPPORTUNITIES

IMPROVEMENT OF THE INDIVIDUAL IMPORTANCE/SATISFACTION
INDIVIDUAL QoL
MD, Psychiatrist, Psychotherapist

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