

European Child & Adolescent Psychopharmacology Network (ECAPN)

Established by members of the European Child & Adolescent Network of the
European College of Neuropsychopharmacology (ECNP; <https://www.ecnp.eu/>)

Mission

To foster, facilitate, and conduct **high-quality translational and clinical research** in the field of child and adolescent psychopharmacology .

Alessandro Zuddas, UNICA, Cagliari, [Italy](#), *Chair*

Carmen Moreno, SERMAS, Madrid, [Spain](#), *Co-Chair*

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Veit Roessner, **UNIDRE**, Dresden, [Germany](#)

Filip Rybakowski, Warsaw, [Poland](#)

Benedetto Vitiello, Turin, [Italy](#)

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Tamar Wohlfarth, Utrecht, [NL](#)

Ian Chi Kei Wong, London, [UK](#)

Gil Zalsman, Petah Tikva, [Israel](#)

David Coghill, [Melbourne](#), [AU](#)

The ECAPN Centres



European network of paediatric research
at the European Medicines Agency



Melbourne

Groningen
Nijmegen

Paris
Montpellier

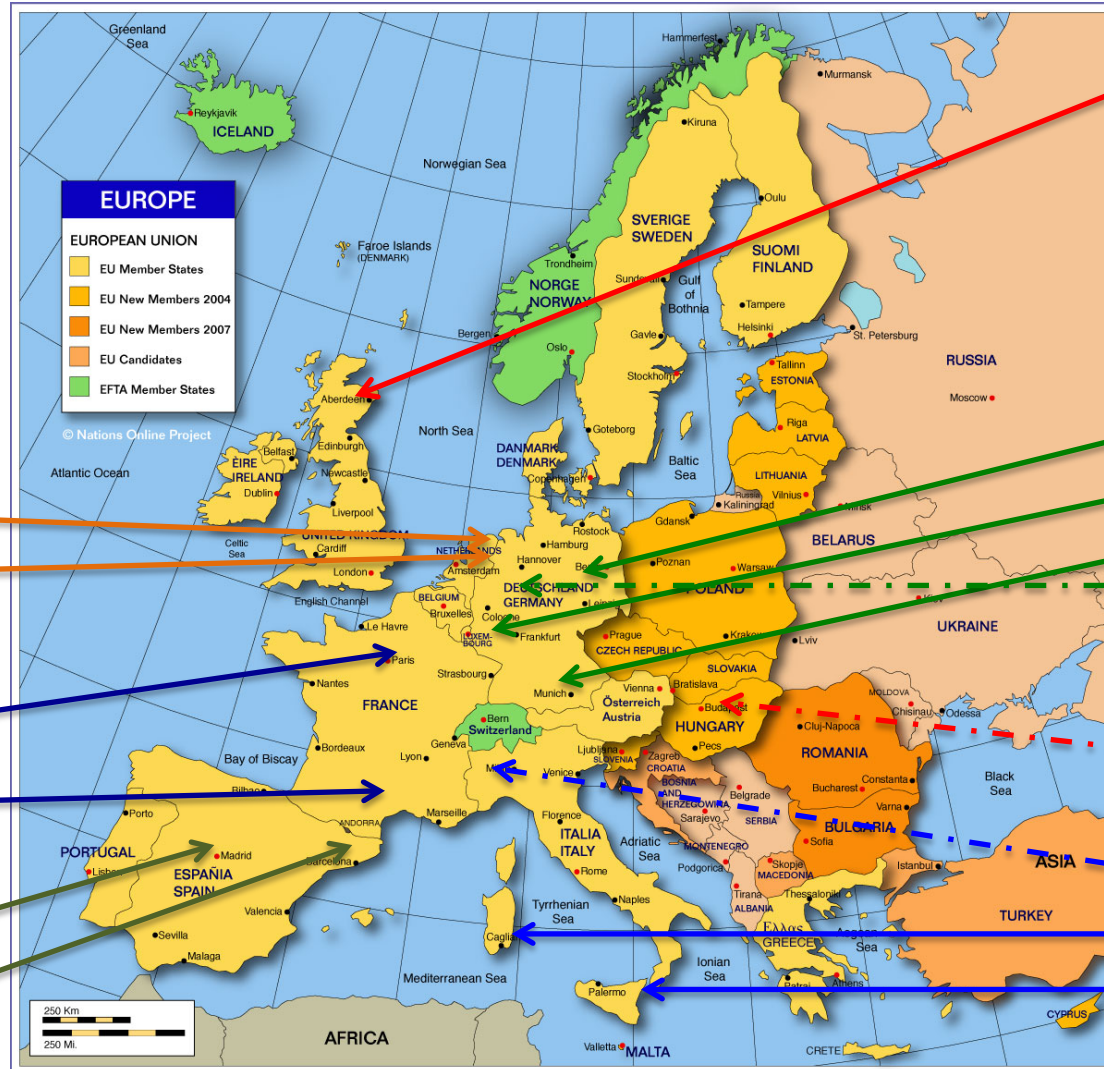
Madrid
Barcelona

Dresden
Mannheim
Ulm
Würzburg

Budapest

Torino

Cagliari
Messina



ECAPN members

Network Participant	Organisation type (short name)*	Country	Address	Principal Investigator(s)
University of Cagliari	University Hospital UNICA	Italy	"A,Cao" Paediatric Hospital, "G.Brotzu" Hospital Trust, Cagliari	Alessandro Zuddas
Consortio Ciber Para El Area Tematica de Salud Mental	University Hospital SERMAS	Spain	Hospital General Universitario Gregorio Marañón, Madrid,	Celso Arango Mara Parellada Carmen Moreno
Université Pierre & Marie Curie, Paris Assistance Publique – Hopitaux de Paris	University Hospital	France	Pitié Salpêtrière Hospital, Paris	David Cohen
Université de Montpellier	University Hospital UoM	France	Hôpital Saint Eloi , Montpellier I	Diane Purper Ouakil
Central Institute of Mental Health Mannheim / University of Heidelberg ,	University Hospital CIMH	Germany	Department C&A Psychiatry and Psychotherapy Mannheim	Tobias Banaschewski
University of Ulm	University Hospital UULM	Germany	Department of Child and Adolescent Psychiatry/Psychotherapy Ulm	Jörg M. Fegert
Universitätsklinikum Carl Gustav Carus. Dresden	University Hospital UNIDRE	Germany	Department of Child and Adolescent Psychiatry/Psychotherapy	Veit Roessner
University "Campus Bio-Medico", Rome	University Hospital UCBM	Italy	Policlinico Campus Biomedico	Antonio Persico
Consorti Institut D'Investigacions Biomèdiques	University Hospital IDIBAPS	Spain	Institute. Hospital Clínic I Provincial de Barcelona-	Josephina Castro-Fornieles
Radboud University Nijmegen Medical Centre,	University Hospital RUNMC	The Netherlands	Department of Cognitive Neuroscience Nijmegen	Jan Buitelaar
University Medical Centre Groningen	University Hospital UMCG	The Netherlands	Department of Psychiatry & Accare C&A Psychiatry, Groningen	Pieter Hoekstra
University of Melbourne	University Hospital UNIMEL	Australia	RCH Mental Health Royal Children's Hospital Melbourne	Davis Coghill

Candidate ECAPN members

Network Participant	Organisation type (short name)*	Country	Address	Principal Investigator(s)
University of Würzburg	University Hospital UNIWUR	Germany	Klinik und Poliklinik für Kinder- u. Jugendpsychiatrie, Psychosomatik u. Psychotherapie, Würzburg	Marcel Romanos
University of Turin	University Hospital UNITO	Italy	“Regina Margherita” Paediatric Hospital, Turin ,	Benedetto Vitiello
Vadaskert Child and Adolescent Psychiatric Hospital , Budapest	Specility Hospital	Hungary	Vadaskert Child and Adolescent Psychiatric Hospital , Budapest	Pietr Nagy

The ECAPN Centres

ECAPN Centres have a solid track record in paediatric psychopharmacology, assuring:

- Clinical management in large-scale studies, including formal RCTs for the registration of innovative medications.
- Patient recruitment
- Scientific approach: innovative experimental designs, biomarker definition.....

Many ECAPN centres lead a national network of affiliated centres

European Child & Adolescent Psychopharmacology Network (ECAPN)

ECAPN aims

- To identify unmet needs in child & adolescent psychopharmacology
- To conduct collaborative scientific studies and clinical trials
- To develop strategies to improve state-of-the-art prescribing of medication to children and adolescents with psychiatric disorders in clinical practice.

Unmet needs in paediatric psychopharmacology: Present scenario and future perspectives



Antonio M. Persico^{a,b,*}, Celso Arango^c, Jan K. Buitelaar^d,
Christoph U. Correll^e, Jeffrey C. Glennon^d, Pieter J. Hoekstra^f,
Carmen Moreno^c, Benedetto Vitiello^g, Jacob Vorstman^h,
Alessandro Zuddasⁱ, the European Child and Adolescent Clinical
Psychopharmacology Network^j

European Neuropsychopharmacology (2015) 25, 1513–1531

Unmet Needs in Paediatric Psychopharmacology

- Off-label prescription to children and adolescents of medications with regulatory approval only in adults
- Lack of effective drugs for many childhood disorders
- Paediatric clinical trials: methodological issues, problems and potential solutions
- The potential limit set by categorical psychiatric nosology on paediatric drug development
- Search for evidence-based approaches to prevent mental disorders with adolescent-onset
- Need for better preclinical data to foster novel drug therapies
- The regulatory context of paediatric psychopharmacology in Europe: strengths and limitations
- Limited public acceptance of treating children with medications
- European collaborative efforts and future directions

Unmet needs in paediatric psychopharmacology: Present scenario and future perspectives



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Table 2 Psychotropic medications approved in Europe for use in children and adolescents.

Medication	Indication	Age for prescription
Aripiprazole	Schizophrenia	≥ 15 years
	Bipolar disorder, manic or mixed episodes	≥ 13 years
Amphetamines (incl. Lisdexamphetamine)	Attention-Deficit Hyperactivity Disorder ^a	≥ 6 years
Atomoxetine	Attention-Deficit Hyperactivity Disorder	≥ 6 years
Fluoxetine	Major depressive episode	≥ 8 years
Fluvoxamine	Obsessive-compulsive disorder	≥ 8 years
Methylphenidate	Attention-Deficit Hyperactivity Disorder	≥ 6 years
Risperidone	Aggression ^b	≥ 5 years
Sertraline	Obsessive-compulsive disorder	≥ 6 years
Ziprasidone	Bipolar disorder, manic or mixed episode ^c	≥ 10 years

^aApproved only in some European countries for children and adolescents with ADHD.

^bApproved only in some European countries for children and adolescents with conduct disorder, in the presence of sub-average intellectual functioning or intellectual disability and when all non-pharmacological strategies have been found insufficient.

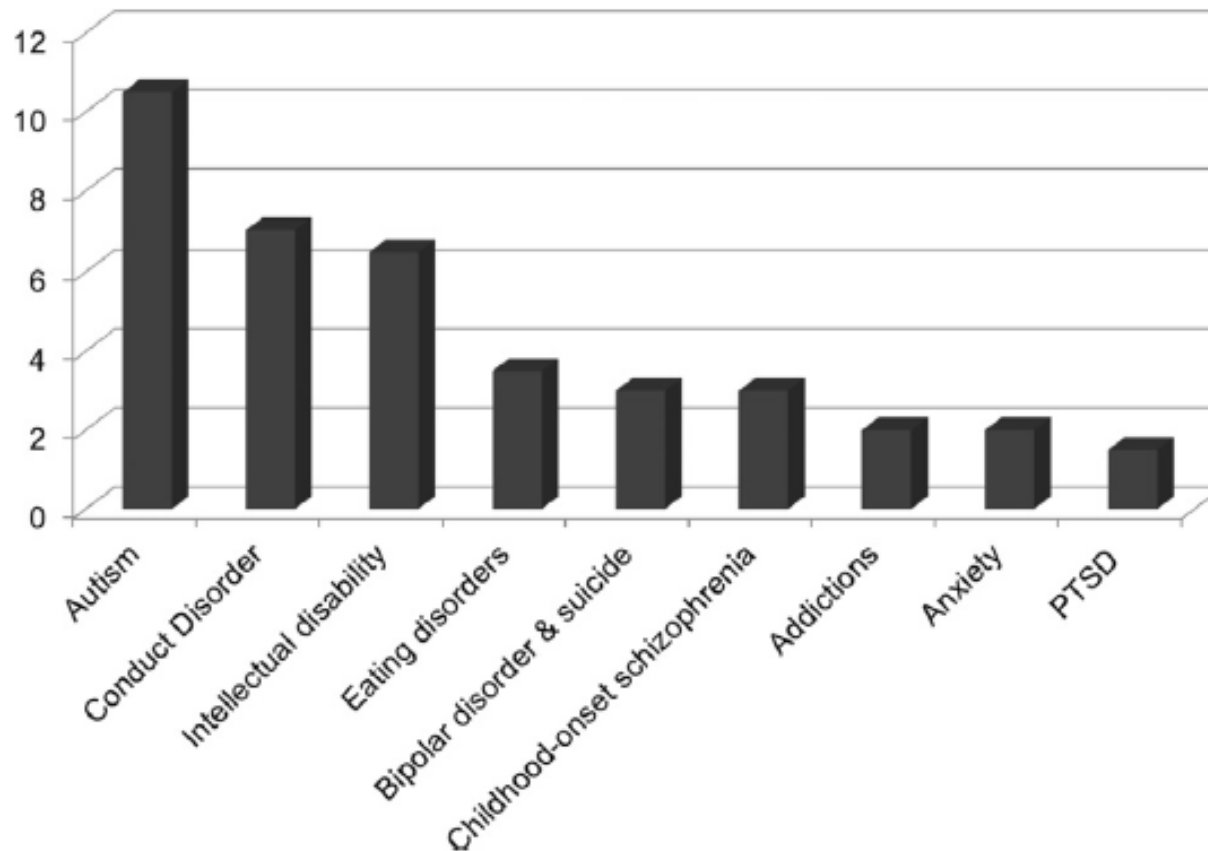
^cApproved only in some European countries based on one randomized controlled trial (Findling et al., 2013), found by the US Food and Drug Administration to have quality assurance issues, requiring the sponsor to repeat the trial.

Unmet needs in paediatric psychopharmacology: Present scenario and future perspectives



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Priority order for drug development in Child & Adolescent Psychiatry by disorder/ condition

Paediatric clinical trials:

methodological issues, problems and potential solutions

- **Limited generability** due to sample selection criteria
- Enrolment of **pathogenetically heterogeneous patients**
- Enhanced risk of false negatives due to **high placebo effects**
- Enhanced risk of false positives due to **primary efficacy endpoints** defined only as significant decrease in symptoms to reach a pre-established threshold.
- Overestimation of clinical benefits observed in an “**artificial**” **clinical setting**
- **Inefficiency** (expensive , time- and labour- consuming, high drop-out rates)

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Child and Adolescent Neuropsychopharmacology Network

Member participation to registrative clinical trials

Atomoxetine for ADHD (Lilly)

Lisdexamphetamine for ADHD (Shire)

RO5186582 for Down Syndrome (Roche)

Vortioxetine for Major Depression (Lundbeck)

Esketamine for Suicidal Behaviour (Janssen)

Bumetanide (Servier)

Member formal consultation (PIP) for **designing** registrative clinical trials

Lurasidone for child Bipolar depression / schizophrenia (Takeda→Angelini))

Trazodone for sleep problems in neurodevelopmental disorder (Angelini)

Member formal consultation for **conducting** registrative clinical trials

RO5285119 (Vasopressin) for Autism Spectrum disorder (Roche)



Child and Adolescent Neuropsychopharmacology Network

The Network has been instrumental in building an infrastructure prompting several EU-funded projects



PERS Pediatric European Risperidone Studies, www.pers-project.com),



STOP (Suicidality: Treatment Occurring in Paediatrics, www.stop-study.com),



ADDUCE (Attention-Deficit Hyperactivity Disorder Drugs Use Chronic Effects, www.adhd-adduce.org)



TACTICS (The “Translational Adolescent and Childhood Therapeutic Interventions in Compulsive Syndromes”, <http://www.tactics-project.eu/>)



AGGRESSOTYPE (“Aggression Subtyping for Improved Insight and Treatment Innovation in Psychiatric Disorders”, <http://www.aggressotype.eu/>)



MATRICS (“Multidisciplinary Approaches to Translational Research In Conduct Syndromes”, <http://matrics-project.eu/>)



EU-AIMS (“European Autism Interventions - A Multicentre Study for Developing New Medications”, <https://www.eu-aims.eu/>)



c4c (*conect* for children: “Collaborative Network for European Clinical Trials for Children”,

ECAPN future plans

- Systematic review of all the **pediatric psychopharmacology studies conducted under the US and UE regulatory initiatives**
- Defining **new targets for medication**:
 - Antipsychotics (D2 blockers) for Conduct disorder
 - Emotional lability (irritability) as transdiagnostic target
- **Conect 4 children** active participation