





Mental health

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Psychopharmacology in children and adolescents: unmet needs and opportunities

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ECNP: European College of Neuropsychopharmacology

Concerned with setting the ground for development, implementation and education on neuropsychopharmacology in children and adolescents





For the first time, a major group of international experts and patients have cooperated defining new parameters for the development of medicines to treat children and young people.

They make a series of recommendations on how the processes should be improved.

Position Paper

Psychopharmacology in children and adolescents: unmet needs and opportunities

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Psychopharmacological treatment is an important component of the multimodal intervention approach to treating mental health conditions in children and adolescents. Currently, there are many unmet needs but also opportunities, alongside possible risks to consider, regarding the pharmacological treatment of mental health conditions in children and adolescents. In this Position Paper, we highlight and address these unmet needs and opportunities, including the perspectives of clinicians and researchers from the European College of Neuropsychopharmacology–Child and Adolescent Network, alongside those of experts by lived experience from national and international associations, via a survey involving 644 participants from 13 countries, and of regulators, through representation from the European Medicines Agency. We present and discuss the evidence base for medications currently used for mental disorders in children and adolescents, medications in the pipeline, opportunities in the development of novel medications, crucial priorities for the conduct of future clinical studies, challenges and opportunities in terms of the regulatory and legislative framework, and innovations in the way research is conducted, reported, and promoted.



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Medicine, University of Southampton, Southampton,

Psychopharmacological treatment in CAP

Highlight and address the unmet needs and opportunities, including the perspectives of:

1. clinicians and researchers from the European College of Neuropsychopharmacology–Child and Adolescent Network

2. experts by lived experience from national and international associations, via a survey involving 644 participants from 13 countries

3. regulators, through representation from the European Medicines Agency (EMA)

Current status...

Compound	Approved by EMA (note: national approvals are not included)	Age (years)	Approved by the FDA	Age (years)
		ADHD		
Amphetamines/dextroamphetamine			\checkmark	3-17
mixed salts				
Amphetamines/dextroamphetamines			\checkmark	6-17
mixed salts				
Atomoxetine			\checkmark	6-17
Clonidine, extended release			\checkmark	6-17
Dexmethylphenidate			\checkmark	6-17
Dextroamphetamine			\checkmark	<mark>3-17</mark>
Dextroamphetamine SR			\checkmark	6-16
Guanfacine, extended release	\checkmark	6-17	\checkmark	6-17
Lisdexamfetamine			\checkmark	6-17
Methamphetamine				6-17
Methylphenidate	(√)	> 6 years	 ✓ (Immediate release tablet, Immediate solution, Extended- release (tablet, chewable), Controlled delivery, Multilayer extended-release, extended-release orally disintegrating tablets, transdermal system) 	6-17
Viloxazine			\checkmark	6-17

		Anxiety disorders				
Duloxetine			√ (generalised anxiety disorder) 7-17			
Escitalopram			\checkmark (generalised anxiety disorder)	≥7		
	Autism spectrum disorder (irritability)					
Aripiprazole			√ 6-17			
Risperidone			\checkmark	5-17		
	Bipolar disorder (depressive episodes)					
Lurasidone			\checkmark	10-17		
Olanzapine/fluoxetine combination			\checkmark	10-17		
Bipolar disorder (manic or mixed episodes)						
Aripiprazole	✓ (manic episodes)	≥ 13 years	\checkmark	10-17		
Asenapine			\checkmark	10-17		
Olanzapine			\checkmark	13-17		
Quetiapine XR			\checkmark	10-17		
Risperidone			\checkmark	10-17		
Lithium			\checkmark	12-17		
Conduct disorder						
Risperidone	\checkmark	5-18				
	Depressive disorder					
Fluoxetine	 ✓ (major depressive episode unresponsive to psychotherapy)* 		✓	8-18		

Enuresis						
Imipramine			\checkmark	6-17		
Insomnia (in ASD or Smith Magenis syndrome)						
Melatonin extended release	\checkmark	2-18				
		Narcolepsy				
Amphetamines/dextroamphetamine mixed salts			\checkmark	6-17		
Dextroamphetamine			\checkmark	6-17		
Dextroamphetamine SR			✓	6-17		
Sodium oxybate	\checkmark	≥7				
Obsessive Compulsive Disorder						
Clomipramine			\checkmark	10-17		
Fluoxetine			\checkmark	7-17		
Fluvoxamine			\checkmark	8-17		
Sertraline	√*	6-17	\checkmark	6-17		
Schizophrenia						
Aripiprazole	\checkmark	≥ 15 years	\checkmark	13-17		
Brexpiprazole			\checkmark	13-17		
Lurasidone	\checkmark	≥ 13 years	\checkmark	13-17		
Olanzapine			\checkmark	13-17		
Paliperidone	\checkmark	≥ 15 years	\checkmark	12-17		
Quetiapine			\checkmark	13-17		
Risperidone			\checkmark	13-17		
		Tourette's disorder				
Aripiprazole			\checkmark	6-17		

	Partic (N=6	tipants 44)
	N	%
What doy ou think are the most important questions children or teenagers with mental problems that rese try to answer in the future?		
Rationale for using medications		
When a non-pharmacological Intervention is better	24	372%
Why a pharmacological treatment is needed	5	0.77%
What are the effects of taking versus not taking medications	1	0.16%
What are the goals of the pharmacological treatment	1	0.16%
Efficacy-effectiveness		
Finding curative rather than symptomatic treatments	15	2-33%
Efficacy versus tolerability	9	1-39%
Efficacy	6	0.93%
Improve adherence	4	0.62%
Tolerance	4	0.62%
Find medications with effectiveness	3	0-47%
Costs-benefits	3	0-47%
Effects on quality of life	3	0-47%
Understand factors that might increase the effects of medications (eg, diet or exercise)	3	0-47%
How to measure If a medication is working	1	0.16%
Improve duration of action	1	0.16%
Timely treatment	1	0.16%
Tackling prodromal symptoms	1	0.16%
Aiming at normalisation	1	0.16%
Risk of not taking medications	1	0.16%
Disorders or conditions for which (additional) medicatio	-	
Cognitive issues or executive dysfunctions	2	0.31%
Disorders of early childhood	2	0.31%
Academic underperformance	1	0.16%
Agitation	1	0.16%
Conduct disorders	1	0.16%
	1	0.16%
Emotional dysregulation Inattention	1	0.16%
	1	0.16%
Sleep disturbance	1	0-10%
Tolerability and safety	261	56 05W
Understanding side effects (in general or in the long- term more specifically)	361	56-05%
Potential of medication of being addictive	83	12-88%
Effects on brain	9	1-39%
Contraindications	8	1.24%
Negative effects on personality	6	0.93%
Rebound effects	4	0.62%
Negative effects on weight	3	0-47%
Interactions among medications	2	0.31%
Negative effects on cognitive functions	2	0.31%
Finding medications with fewer side effects	i	0.16%
Link with neurodegenerative disorders	1	0.16%
Practical issues related to prescribing	1	0.10.8
Individualise treatment	10	1.55%
IT HAVE INCOMEDICE AT CONTINUES.	40	
Finding alternative formulations	10	1.55%

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macologically treat epilepsywhy not mental ditions?) it stigma : senting medication as second-line choice after pharmacological options cation promoted by adults who used medication in dhood	12	1-86%
it stigma senting medication as second-line choice after pharmacological options cation promoted by adults who used medication in dhood	11	1.70%
enting medication as second-line choice after pharmacological options cation promoted by adults who used medication in dhood	10	1-55%
cation promoted by adults who used medication in dhood	7	1.08%
	4	0.62%
	4	0.62%
p accepting the disorder	3	0-47%
wing medication does not change the personality	3	0.47%

		Participants (N=644)	
	N	%	
(Continued from previous column)			
Saying that medication is only a temporary help	3	0.47	
Trial of medication with strict monitoring	21	0-33	
Education promoted by famous peoplewith the disorder	21	0-33	
Publish more studies	21	0-33	
Education to children in school	21	0-33	
Improve ethical procedures of drug companies	1	0.16	
Urge caution vis-a-vis what is reported by lay press	1	0.16	
Promote empathy for people who need medication	1	0-16%	
Studies not funded by drug companies	1	0-16%	
Education especially for newer medications	1	0-16%	
Doing studies on natural products	1	0-16%	
Use simple examples (eg. like wearing glasses)	1	0-16%	
Normalise the concept of mental condition	1	0-16%	
Make service access easier	1	0-16%	
Seeing medication as the last resort	1	0-16%	
Trusting professionals rather than internet	1	0-16%	
Listening to parents' concerns and discuss with them	1	0-16%	
Patience and persistence	1	0-16%	
Consider faith or religion of parents	1	0-16%	
Education Independent from drug companies	1	0-16%	



Survey among n=644 experts by lived experiences – most common responses:

1. What do you think are the most important questions on medicines for children or teenagers with mental problems that researchers should try to answer in the future?

-Understanding side effects (in general or in the long-term more specifically): 361 (56.05%) -Potential of medication of being addictive: 83 (12.88%)

2. In your opinion, do people think that taking medicines for mental problems is bad? -Yes: 518 (80.43%)

3. What do you think we could do to help people understand that medicines may help children and teenagers with mental problems?

-Education on mental health issues and their treatment 216 (33.54%) -Education lead by people with personal lived

experience 91 (14.13%)

Issues which need to be addressed

• A greater focus on disorders for which no evidence-based or no wellstudied pharmacological interventions are available

Top-3: autism spectrum disorder, emotional dysregulation/irritability, anorexia nervosa

• Taking an overview of other important outcomes, not just the core symptoms tested in trials

• Adapting the approval process so that that effective medicines for children can be approved more efficiently

• A better understanding of long term-effect on the developing brain (both beneficial and harmful)

Recommendations

Key opportunities include

- learning from failed trials (e.g., insufficient recruitment) involve people with lived experiences
- reducing the placebo effect in trials –e.g., improve understanding how to minimize placebo effects
- assessing outcomes beyond core symptoms e.g., more PROMs (Patient-Reported Outcome Measures), functional level and QoL (quality of life) measures
- considering developmental stage e.g., adapt the timing of interventions to the underlying developmental windows and consider pubertal maturation stages
- comparing pharmacological and non-pharmacological treatments
- using innovative designs beyond standard randomised controlled trials e.g., pharmaco-epidemiological studies, self-control methods, emulated targeted trials

Recommendations (cont'd)

- moving towards precision medicine and stratification approaches well defined groups sharing similar clinical characteristics or profiles of biomarkers
- investigation and implementation of digital technologies ranges from incorporating artificial intelligence in diagnostic devices to using real world data
- focusing on conditions that are non-responsive to initial treatment
- improving the regulatory and legislative framework e.g., the EMA action plan
- innovation in the way research is conducted, reported, and promoted