

Dextromethorphan Beyond the Cough: Exploring Its Psychedelic Potential – a Systematic Review

Running Title: Dextromethorphan as a Psychedelic: Systematic Review

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Supplemental Table 2. GRADE scoring.

	Outcome	Anticipated absolute effects (DXM vs placebo)	Studies	Participants (n)	Certainty of evidence (GRADE)
Primary Outcomes	Hallucinations / perceptual alterations	DXM increases hallucinogen-type perceptual effects (visual distortions, imagery, hallucinations) compared with placebo	Reissig 2012 [21]; Carbonaro 2020 [35]	32	⊕⊕○○ Low
	Cognitive changes (objective performance) (attention, working memory, episodic memory, executive function)	DXM produces domain-specific cognitive impairments ; no consistent global delirium, but some participants unable to complete tasks at peak intoxication	Barrett 2018 [22] (primary); Carter 2013 [37] (supportive)	20	⊕⊕○○ Low
	Mystical-type experience (SOCQ / Mysticism Scale)	Inconsistent effects : one study reports high rates at very high doses; another reports 0% meeting full criteria at 400 mg/70 kg	Reissig 2012 [21]; Carbonaro 2018 [23]	32	⊕○○○ Very low
Secondary Outcomes	Subjective experiences (meaningfulness, spiritual significance, insightfulness, “distance from ordinary reality”)	DXM produces moderate increases in meaningful/spiritual subjective ratings vs placebo (generally lower than classic serotonergic psychedelics)	Carbonaro 2018 [23]; Carbonaro 2020 [35]	20	⊕⊕○○ Low
	Nausea / vomiting	Common and dose-related : vomiting in ~50–60% of participants at ≥400 mg/70 kg; rare at placebo	Reissig 2012 [21]; Carbonaro 2018 [23]	32	⊕⊕⊕○ Moderate
	Other adverse effects (dizziness, headache, light-headedness, physical distress)	DXM increases somatic adverse effects , including dizziness and headache, compared with placebo	Reissig 2012 [21]; Mathai 2023 [39]	32	⊕⊕○○ Low

Summary**Population:** Healthy adult volunteers (often hallucinogen-experienced)**Intervention:** Acute oral DXM (typically **400 mg/70 kg**; some escalation up to 800 mg/70 kg)**Comparator:** Placebo (± active comparators in some studies)**Setting:** Controlled laboratory studies**Outcome timeframe:** Acute session (peak effects) ± short follow-up (≤1 week)