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INPLASY

Can Drug-Induced Yawning Serve as a Biomarker for Drug Safety and Effectiveness

INPLASY202540048

doi: 10.37766/inplasy2025.4.0048

Received: 15 April 2025

Published: 15 April 2025

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202540048

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 April 2025 and was last updated on 15 April 2025.

INTRODUCTION

Review question / Objective This review synthesizes current evidence on Drug-Induced Yawning (DIY), with a particular focus on its neurobiological mechanisms, clinical implications, and potential as a biomarker.

Rationale We hypothesized that synthesizing existing evidence would clarify yawning's neurobiological mechanisms and establish its potential as a biomarker. We proposed that addressing current research gaps may advance personalized medicine and enhance understanding of yawning's clinical significance.

Condition being studied Drug-induced Yawning (DIY).

METHODS

Search strategy The DIY search focused on studies evaluating yawning as a pharmacological effect (wanted or unwanted) of opioids, dopamine agonists, serotonin agonists, and related drugs. Preliminary searches helped refine keywords and MeSH terms, ensuring both sensitivity and specificity. The search iteratively adjusted Boolean operators, filters, and exclusion terms to optimize results. The search was conducted using PubMed, Scopus, and Web of Science, chosen for their comprehensive biomedical and pharmacological literature coverage. Reference lists of included studies were also manually reviewed to identify additional relevant publications.

Participant or population Studies focusing on human participants.

Intervention Research addressing yawning's neurobiological mechanisms or pharmacological triggers.

Comparator Human studies investigating the neurobiological mechanisms of physiological yawning.

Study designs to be included Clinical and observational studies (case-control, cohort, and randomized controlled trials).

Eligibility criteria
Inclusion Criteria
• Peer-reviewed studies published within the last 10 years.
• Clinical and observational studies (case-control, cohort, and randomized controlled trials).
• Studies focusing on human participants.
• Research addressing yawning's neurobiological mechanisms or pharma-cological triggers.
Exclusion Criteria
• Studies without direct relevance to yawning or DIY.
• Animal studies, excluded to focus on clinical human applications. Since preclinical findings may not directly translate to human pharmaco-dynamics, animal models were omitted but may be referenced in the discussion for comparative insights.
• Non-peer-reviewed sources, including gray literature (conference abstracts, dissertations).
• Review articles, editorials, and opinion pieces.

Information sources The search was conducted using PubMed, Scopus, and Web of Science, chosen for their comprehensive biomedical and pharmacological literature coverage. Reference lists of included studies were also manually reviewed to identify additional relevant publications.

Main outcome(s) Thematic analysis was performed to synthesize key findings and elucidate mechanisms. Key themes were considered to be extracted and summarized descriptively: differentiation of physiological vs. drug-induced yawning; neurobiological pathways involving dopamine, serotonin, and oxytocin; correlation between yawning and drug responses; clinical implications of yawning as a biomarker for therapeutic efficacy and safety; and quantitative data, such as yawning frequency and timing. Although yawning frequency and timing were considered, they were analyzed within other themes rather than as a standalone category. While meta-analysis was not feasible due to heterogeneity, patterns and trends were highlighted to support qualitative findings.

Quality assessment / Risk of bias analysis Since this is not mandatory for scoping review, we followed PRISMA for scoping review, and provided the PRISMA 2020 checklist, with no further appraisal for the included studies.

Strategy of data synthesis Thematic analysis was performed to synthesize key findings and elucidate mechanisms.

Subgroup analysis None.

Sensitivity analysis None.

Language restriction English.

Country(ies) involved Norway.

Keywords Yawning; Drug-induced yawning; Neurotransmitters; Serotonin (5-HT); Dopamine; Oxytocin; Opioids; Selective Serotonin Reuptake Inhibitors (SSRIs); Opioid withdrawal; Non-invasive biomarkers.

Dissemination plans Publication as scoping review in Future Pharmacology Journal.

Contributions of each author
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