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Oropharyngeal microbiome composition as a possible diagnostic marker for true psychosis in a forensic psychiatric setting: A narrative literature review and an opinion

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ABSTRACT

The malingered psychosis has increasingly occurred over the past few years due to the tendency towards care in the community and the closures of long-stay psychiatric institutions. Thus, it is required to identify malingered psychosis to reach accurate forensic assessments and inhibit misuse of restricted healthcare resources and miscarriages of justice. Despite the fact that some practical psychometric tools and strategies have been proposed for diagnosing true psychosis over the past decades, the differentiation between true psychosis and malingered psychosis is still sometimes challenging. Accordingly, it seems crucial to identify innovative and reliable diagnostic alternatives. Hence, the present article summarizes a collection of evidence that can be used by researchers to improve future assessment of oropharyngeal microbiome composition as a feasible diagnostic marker for true psychosis in a forensic psychiatric setting.

Keywords: diagnostic marker, forensic psychiatric setting, oropharyngeal microbiome, psychosis, review

INTRODUCTION

Malingered psychosis encompasses intentionally falsifying psychiatric symptoms aiming to externally benefit the presenting patient in a tangible manner [1]. As the term “psychosis” includes a broad variety of clinical presentations [2], it is very likely for malingering patients to decide to falsify psychosis for another kind of disorder to derive external benefits and provoke clinicians to cast doubt on their diagnoses, who usually categorize malingering with factitious disorders and analogous clinical phenomena by giving benefit of the doubt [2, 3].

Persons usually malinger psychosis to reach one of the following objectives:

(a) Criminals are likely to be in the pursuit of avoiding punishment by pretending insanity when committing the crime, incompetent to stand trial, worthy of alleviation at sentencing, or not guilty enough to be executed.

(b) The odds are that malingerers keep trying to inhibit being drafted into the military, be exempt from unwelcome military assignments, or prevent combat.

(c) Malingerers are likely to fake psychosis to financially benefit from social security disability, receive workers’ compensation, gain veterans’ benefits, or reach recompense for damages of alleged psychological injury.

(d) Prisoners may malinger to receive medication or to be moved to a psychiatric hospital to escape facilitation or do “easier time”.

(e) Malingerers probably intend to be transferred to a psychiatric hospital to prevent arrest or offered a free room and board (known as “three hots and a cot”) [3].

Although it has been complicated to estimate the true number of cases of malingered psychosis [4], the study [5] has shown that it may exist in 8% of criminal defendants. Nevertheless, the incidence of malingered psychosis has grown over recent years due to the tendency toward care in the community and the closures of long-stay psychiatric institutions [4]. Thus, forensic psychiatrists are crucially required to develop the skill to detect malingered psychosis [6].

In this respect, recent scientific evidence has shown major differences in the oropharyngeal microbial composition between psychotic patients and healthy subjects [7]. Such a hypothesis seems almost likely according to the available evidence despite that no study has been conducted directly on

how oropharyngeal microbiota plays a feasible diagnostic role among forensic psychiatric patients with psychosis. Accordingly, the present paper provides a summary of collected evidence for improving the future evaluation of oropharyngeal microbiome composition as a possible marker to diagnose true psychosis in a forensic psychiatric setting.

METHODOLOGY

According to the search terms (including diagnostic marker, forensic psychiatric setting, oropharyngeal microbiome, and psychosis), we searched relevant English publications from 1980 to 2022 in the Web of Science, Scopus, PubMed, Cochrane Library, EMBASE, and Google Scholar databases. Fundamental research on oropharyngeal microbiome composition in psychosis and forensic psychiatric patients was studied to include the entire related literature. Quality appraisal was evaluated provided that the material showed an almost sensible and correct argument for the given themes. Finally, the narrative technique was employed in order for the material synthesis to comprise the creation of a cohesive and compelling story. This is dependent on the description proposed in [8] of how a researcher engages with the material, i.e., reading, writing, thinking, interpreting, arguing, and justifying. These data were used in the present article for discussing critical topics in this area, including

(a) the challenges of identifying malingered psychosis,

(b) the link between oropharyngeal microbiome composition and true psychosis, and

(c) the possible diagnostic role of oropharyngeal microbiome composition among forensic psychiatric patients with true psychosis.

IDENTIFYING MALINGERED PSYCHOSIS–THE CHALLENGES

The diagnosis of malingered psychosis was a chief concern in the time of forensic psychiatry development in the nineteenth century. Several clinical facilitating methods were adopted in this regard. However, interest in the topic faded into insignificance during the twentieth century, seemingly due to the incorrect assumption about malingerers faking symptoms to avoid impending psychosis [4]. The United Kingdom has largely ignored the subject. However, as instruments systematizing clinical observations were developed in the 1980s (first made during the preceding century), malingering re-attracted a great deal of attention from forensic psychiatrists in the United States [4].

During a forensic psychiatric evaluation, it is critical to identify malingered psychosis for preventing misuse of restricted healthcare resources and miscarriages of justice. Malingered psychosis detection can be challenging and needs a systematic approach. To ensure that an individual has malingering psychotic symptoms, the clinician must possess a deep understanding of genuine psychotic symptoms and review data from multiple sources. The clinician needs to collect clues from a thorough assessment, collateral data, clinical records, and particularly psychological testing. Despite the tremendous effort required, the clinician takes significant responsibility for aiding society in telling apart malingering from true psychosis [1, 3]. If a malingerer is misdiagnosed as genuinely ill, they manage to obtain unjustified recompense or avoid any responsibility for criminal offenses. The fallacious classification of malingering, on the other hand, may cause injustice and make psychiatric care refuse an individual's true psychosis in need of treatment [3]. The study [9] introduced three factors hampering malingering detection, including an incorrect clinical viewpoint on one's capability to ascertain the probability of malingering when a clinical rapport has been developed, the hazard of an expert's attribution error or confirmatory bias resulting in either under- or over-detection, and merely employing psychometric performance data. Based on the study [10], even immensely experienced clinicians faced many challenges in identifying actors simulating illness. Also, there is some evidence for the probable reluctance of clinicians to label a person a malingerer for diverse reasons, namely fears of medico-legal consequences and concerns about therapeutic relationships. Such concerns could bias clinicians into embracing a more conservative and 'safer' position [11]. Although some psychometric tools and practical strategies have been developed to transcend these limitations, distinguishing patient claims is sometimes very difficult [12, 13]. However, innovative and yet reliable diagnostic alternatives are required more than ever to overcome the current restrictions of the question-and-answer method. In this respect, the present review puts focuses on the feasible role of oropharyngeal microbiome composition as a diagnostic marker to make a differentiation between true psychosis and malingered psychosis.

LINK BETWEEN TRUE PSYCHOSIS & OROPHARYNGEAL MICROBIOME COMPOSITION

Human oral microbiota has turned into a highly focused research interest since bacterial products, oral bacteria, and inflammatory molecules are capable of invading the human body through the digestive tract or bloodstream [7]. Huge differences were observed in the present review between the oropharyngeal microbiota of psychotic patients and controls (**Table 1**). In detail, compared to controls, it was shown a lactobacillus increase in samples from psychotic patients [14]. *Lactobacillus gasseri* (*L. gasseri*) is the chief host bacteria for *Lactobacillus phage phiadh*, which is a common constituent of the gastrointestinal and oral mucosae; capable of binding to the intestinal epithelium. Different health benefits can be provided by *L. gasseri* through its bacteriocin production, immunomodulation of the innate and adaptive systems, and antimicrobial activity [15]; thus, this bacterium is positively being employed as a probiotic [16].

According to the results obtained by [14], *L. gasseri* has a moderate correlation with different *Lactobacillus phage phiadh* levels, suggesting a lysogenic state for phage infection in many cases. Varied environmental conditions can induce the virus reactivation, causing the host bacteria to be killed. Further, other effects may be posed by *Lactobacillus phage* on the bacteria ecology by controlling additional species of *Lactobacilli*. Although some phages are capable of modulating the immune system irrespective of their capacity for modulating the bacteria level, the presence of these properties in *Lactobacillus phage phiadh* is not proven. As the host of this phage, *L. gasseri* was found to be more prevalent in psychotic

Table 1. A summary of differences observed in the oropharyngeal microbiota between psychotic patients and healthy controls

Year/article	Country	Study design	Objectives	Positive findings
2011/[21]	Egypt	Case-control study 35 schizophrenia patients 35 healthy controls	Estimating quantity & prevalence of *Porphyromonas gingivalis* in schizophrenic patients' saliva in comparison with healthy controls	A significantly lower prevalence of *Porphyromonas gingivalis* was detected in healthy subjects' saliva compared to schizophrenia patients. Levels of *Porphyromonas gingivalis* were highly attributed to schizophrenia psychopathology severity as presented by PANSS scores, where negative symptoms stand for the most robust correlation.
2014/[15]	India	Cross-sectional study 250 schizophrenia patients (males=140; females=110)	Exploring feasible bidirectional link between schizophrenia & periodontal disease	It reveals that patients with long schizophrenic histories have highlighted poor periodontal conditions, being illustrated by gingival, & plaque indexes. Results suggest possible role of periodontal disease in schizophrenia pathogenesis.
2015/[14]	USA	Case-control study 41 schizophrenia patients 33 healthy controls	Characterizing bacteriophage genomes in oropharynx of schizophrenia patients & healthy subjects	*Lactobacillus phage phiadh* in schizophrenic patients was considerably higher than number of matches in controls. *Lactobacillus phage phiadh* level had a correlation with an elevated rate of comorbid immunological disorders among schizophrenic patients.
2015/[17]	USA	Case-control study 16 schizophrenia patients 16 healthy controls	Characterizing schizophrenia microbiome by interrogating oropharyngeal microbiome structure regarding its taxonomic & functional diversity	*Lactobacillus gasseri* was 400 times more prevalent in psychotic patients than in controls; however, whereas levels of *Neisseria*, *Prevotella Weeksellaceae*, & *subflava* were significantly lower.
2021/[19]	USA	Case-control study 316 individuals, including 121 schizophrenia patients, 62 with mania, 48 with major depressive disorder 85 healthy controls	Confirming relationship between altered oropharyngeal microbiome & schizophrenia	It revealed a difference in oropharyngeal microflora between schizophrenic patients & individuals with mania. *Weeksellaceae*, *Neisseria subflava*, & *Prevotella* were reduced in patients with mania or schizophrenia compared with controls, whereas *Streptococci* were augmented in these groups. *Neisseria subflava* had also a positive association with cognitive functioning. Beta diversity was altered in patients with mania & schizophrenia, compared to healthy controls.
2021/[20]	China	Case-control study 85 patients with first-episode schizophrenia 43 with clinical high risk 80 healthy controls	Investigating salivary microbiome among schizophrenia patients, characterizing microbial profiles at different clinical stages of schizophrenia, & understanding role of salivary microbes in initiation of schizophrenia	A high ratio of *Firmicutes/proteobacteria* was observed in schizophrenic patients in salivary microbiome. Metabolic functions of salivary microbiome were found to be disturbed in schizophrenia.

patients than in controls by a factor of 400 [17, 18], whereas the levels of *Weeksellaceae*, *Prevotella*, and *Neisseria subflava* were substantially lower [19]. On the contrary, there were higher levels of *Streptococcal* in psychotic cases [19]. It was also found a high ratio of firmicutes/proteobacteria in patients with schizophrenia in the salivary microbiome [20]. A considerably greater abundance of *Porphyromonas gingivalis* was also observed in the schizophrenia patients' saliva compared to healthy controls [21], leading to a state of neuroinflammation [22, 23]. However, it seems hard to comment on the presence of a bidirectional link between the oropharyngeal microbiome and the brain at this stage of knowledge [7]. Certainly, more research is needed to give a clear answer to the remaining questions in this area.

POSSIBLE DIAGNOSTIC ROLE OF OROPHARYNGEAL MICROBIOME COMPOSITION AMONG FORENSIC PSYCHIATRIC PATIENTS WITH TRUE PSYCHOSIS

Although no study has yet directly examined the possible diagnostic role of oropharyngeal microbiome composition among forensic psychiatric patients with psychosis, but such a hypothesis does not seem very unlikely based on the available evidence [7, 14-23]. A possible explanation for our hypothesis is a state of neuroinflammation existing in psychotic patients [7]. In detail, increased levels of inflammatory cytokines in the central nervous system can activate glial and immune cells (i.e., neuroinflammation) through the inflammatory process provoked by periodontal disease [22]. Neuroinflammation may also have a role in true psychosis pathogenesis [24]. The pathways such as proinflammatory cytokines, microglial activation, antineuronal autoantibodies, molecular mimicry, disturbance of the blood–brain barrier, and self-reactive T cells are likely to be involved in developing true psychosis [24-27]. This innate inflammation can have a mechanistic association with glutamatergic abnormalities, amplified oxidative injury, and traditional monoaminergic reported in true psychosis [24-27]. These findings highlight the role of the periodontal disease-related inflammatory process and the bacterial load in developing a neuroinflammation state that favors the brink of true psychosis [28]. Since there is limited knowledge about the possible diagnostic role of oropharyngeal microbiome composition in true psychosis [24], future research can be interestingly established in a forensic psychiatric setting.

LIMITATIONS

The present review has faced some limitations, as presented in what follows. None of the addressed studies proposed a formal causal link between the true psychosis and oropharyngeal microbiota due to numerous confounding biases, namely specific environmental exposures impacting

the microbiota, sexually transmitted diseases that can have adverse impacts on the mouth, use of drugs (e.g., cannabis), consuming alcohol, anticholinergic treatments, respiratory viruses, drugs with antioxidant properties (e.g., clozapine, olanzapine, valproate, risperidone, or lithium), and poor oral hygiene common among psychotic patients [15, 30-35]. In [21], it was indicated a correlation between detecting *Porphyromonas gingivalis* and lower levels of education. Further, a momentous correlation exists between smoking and detecting *Porphyromonas gingivalis* [21]. All controls were nonsmokers in the research [17], which makes it possible to mistake the effects of smoking for those of psychosis. Although the reduced abundance of *Capnocytophaga* and *Neisseria* was associated with smoking [36], a link with mental illness is difficult to be proved.

CONCLUSIONS

The present article is aimed to review research on the relationship between oropharyngeal microbiome composition and the pathophysiology of psychosis. Also, it was intended to highlight the possible diagnostic role of oropharyngeal microbiome composition in identifying true psychosis in a forensic psychiatric setting. The results showed the saliva microbiome and periodontal disease to be potentially related to true psychosis. Therefore, due to the significantly different oropharyngeal microbial compositions among patients with true psychosis and healthy controls, saliva can be an interesting substrate for future research on the differentiation between true psychosis and fake psychosis during early forensic psychiatric evaluation. Saliva could also be a substrate of interest to characterize the various stages of psychosis in a forensic psychiatric setting.

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