Tone-matching ability in patients with schizophrenia: A systematic review and meta-analysis

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ABSTRACT

Context: Patients with schizophrenia display abnormalities in pitch discrimination of non-verbal tones as revealed by the Tone-Matching Task (TMT). It may lead to deficits in higher-order cognitive functions and clinical symptoms.

Objectives: We conducted a systematic review and meta-analysis pooling data about TMT score differences between patients with schizophrenia and healthy controls, to evaluate the deficit's effect size, and to develop reliable knowledge about pitch processing impairment and its pejorative impact.

Method: Relevant publications were identified by a systematic search of PubMed and EMBASE databases. Then, we excluded non-relevant studies for the meta-analysis. Effect size for percent of correct responses to the TMT was expressed as standardized mean difference (SMD).

Results: Eighteen of 167 identified studies met eligibility criteria for review, of which 10 were included in the meta-analysis. Our meta-analysis showed that the effect size for the percent of correct response to the TMT between patients ($N = 371$) and controls ($N = 342$) was large: SMD = 1.17 [95% CI: 0.926–1.418] (z-value = 9.338 and *p*-value < 0.001). Meta-analysis showed moderate heterogeneity between studies ($Q(9) = 17.22$, $p = 0.04$, $I^2 = 47.74\%$). The relationship between tone-matching impairment and clinical symptoms of schizophrenia remains heterogeneous across studies. Some authors observed significant correlations between tone-matching performance and a number of higher-order cognitive abilities.

Conclusion: This review and meta-analysis highlights a large significant disturbance in tone-matching ability in patients as compared with controls. The study of basic auditory processing opens promising perspectives for pathophysiological modelling of the disorder and therapeutic issues.

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1. Introduction

Schizophrenia is a severe psychiatric disorder that affects approximately 1% of the population worldwide (McGrath et al., 2008). Although its pathophysiology remains unclear, it is commonly theorized thought that the disorder's origins stem from neurodevelopmental disruption, where genes and environment risk factors interact over the course of development to determine abnormalities in neural systems. Mechanistically schizophrenia has been linked to dopamine neurotransmission and NMDAR (*N*-methyl-D-aspartate receptor)/glutamatergic hypofunction (van Os et al., 2010; Brunelin et al., 2013; Javitt and Sweet, 2015; Owen et al., 2016). These neurobiological mechanisms underlie a wide range of cognitive dysfunctions whose relationships with other clinical manifestations remains poorly understood (Javitt, 2009). However, large gaps in linking genes, behavior brain to clinical disability in schizophrenia remain, and despite concerted interest in schizophrenia biomarkers diagnosing the illness still relies on clinical examination (Schmitt et al., 2016). A growing interest is emerging for low-level sensory function. This interest is predicated on the demonstration that lower order deficits in early sensory processing can lead to the higher-order cognitive disturbances found in schizophrenia (McKay et al., 2000; Javitt et al., 2000). In the field of auditory processing, patients with schizophrenia display impaired abilities to discriminate length (Davalos et al., 2003), intensity (Holcomb et al., 1995) and pitch of non-verbal sounds. Disabilities in segregating sequences of pitches into different perceptual categories (melodic streaming) were also identified (Nielzén and Olsson, 1997; McLachlan et al., 2013). Such basic perceptual impairments can contribute to higher-order social and cognitive impairments: For example, pitch

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discrimination impairments contribute to impairment in the perceiving social intent as conveyed through speech intonation patterns or prosody (Leitman et al., 2005, 2006, 2010). These findings raised our interest on basic auditory performance in patients with schizophrenia. To date, the most documented impairment in the literature concerns static pitch discrimination. Several studies we reviewed here explored this sensory ability with a "Tone-Matching Task" (TMT) that was first developed in Strous et al., 1995. This test is a simple, accurate and reliable way to assess pitch discrimination performance for non-verbal sounds. The experiment consists of presenting to subjects pairs of non-verbal and not-too-distant short tones series presented open-field–via speakers, or through headphones. Within each pair, tones are either identical or differ in frequency by several specified amounts. Participants have to respond by pressing "same" or "different" on a 2-button press. The way of scoring the tests is to obtain the percent correct responses across all items, as recommended in the study of Petkova et al., 2014.

Taking into consideration the growing interest for TMT in schizophrenia and the need to expand our knowledge in the field of biomarkers we aimed to assess reproducibility of TMT failures for patients with schizophrenia, we conducted a systematic review and a meta-analysis to 1) pool data about TMT score differences between schizophrenia patients and healthy controls, 2) better ascertain the value of pitch discrimination impairment as a biomarker for schizophrenia, 3) develop reliable knowledge about pitch discrimination abilities in patients with schizophrenia, 4) provide perspectives for future studies involving pitch discrimination assessment in these patients. This review presents the first meta-analysis of studies assessing pitch discrimination abilities that employ the TMT in schizophrenia.

2. Materials and methods

A literature search was conducted following the recommendations of the Cochrane collaboration (Chandler et al., 2011) and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Moher et al., 2009). See study flow chart (Fig. 1) for further details.

2.1. Eligibility

We required English language publications in peer-reviewed journals assessing static pitch of non-verbal sound discrimination performance in patients with schizophrenia versus healthy controls. For patients with schizophrenia, we required an established clinical diagnosis of schizophrenia or schizoaffective disorder according to standardized
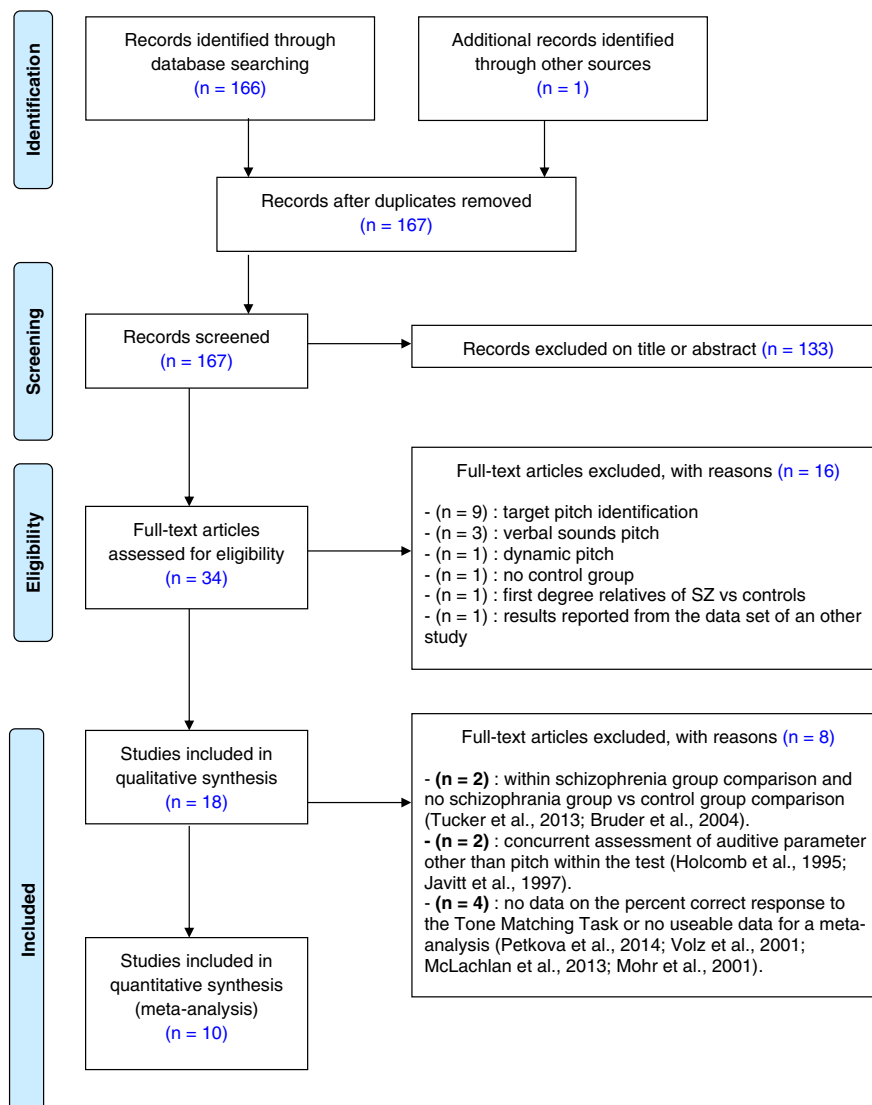

Fig. 1. Flow Diagram of Tone Matching Task studies' selection process. The literature search was performed from the PubMed and EMBASE electronic databases and using the Mesh heading: ("Schizo*"[Mesh] OR Schizo* [Text Word]) AND ("Pitch"[Mesh] OR "Pitch"[Text Word]).