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Early motor developmental milestones and schizophrenia: A systematic review and meta-analysis

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ABSTRACT

The neurodevelopmental hypothesis of schizophrenia proposes that impaired brain development is a cause of the illness. Early motor developmental milestones, such as learning to walk, are predictors of later schizophrenia but studies have not been systematically reviewed. The aim of the present systematic review and meta-analysis was to explore the association between early motor developmental milestones and the risk of adult schizophrenia. In addition, we updated a systematic review on motor function and risk of schizophrenia.

The PubMed, PsycINFO and Scopus databases were searched for original research articles published up to July 2015. Motor milestones were measured between ages 0 and 13 years. Random effect meta-analysis calculated effect estimates (Hedges' g) for the association between individual motor milestones and schizophrenia risk. An electronic database and selected articles reference list search identified 5990 articles after removing duplicates. Sixty-nine full text articles were assessed for eligibility of which six were included in the review. Five studies provided sufficient data for meta-analyses.

The following motor milestones were significantly associated with adult schizophrenia risk: walking unsupported ($g = 0.46$; 95% CI 0.27–0.64; $p < 0.001$), standing unsupported ($g = 0.28$; 0.16–0.40; $p < 0.001$) and sitting unsupported ($g = 0.18$; 0.05–0.31; $p = 0.007$). Results for the milestones 'holding head up' and 'grabbing object' were not statistically significant. Delayed walking, sitting and standing unsupported were associated with adult onset schizophrenia. The findings emphasise the importance of timely achievement of these motor milestones in childhood and can contribute to the identification of individuals at risk of psychosis.

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1. Introduction

The neurodevelopmental hypothesis of schizophrenia proposes that abnormalities in the developing nervous system betray vulnerability to the illness (Murray and Lewis 1987; Weinberger 1987; Maynard et al.

2001). Evidence from both genetic high risk and population-based cohort studies that observed an association between motor abnormalities or delayed motor development and adult schizophrenia contributed to shaping the theory. In these studies various concepts are used to define the observed phenomenon such as pandysmaturation (Fish 1957), motor coordination (Rosso et al. 2000; Schiffman et al. 2004), fine and gross motor skills (Burton et al. 2016), motor function (Dickson et al. 2012), motor development milestones (Jones et al. 1994; Isohanni et al. 2001; Sorensen et al. 2010), neurological soft and hard signs (Schiffman et al. 2009).

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Few attempts were made to systematically review the evidence in this area and to estimate the effect size for later development of schizophrenia by meta-analysis. The meta-analysis by Dickson et al. (2012) showed a moderate effect size for motor function in youth, but studies on early motor developmental milestones were not included. Recently, in the meta-analysis by Burton et al. (2016), several developmental motor phenomena were explored, namely gross and fine motor development, movements, neurological soft signs, coordination, motor skills and walking. Moderate effect sizes were found for delayed gross and fine motor development, impaired coordination and delayed walking in children with first-degree relatives affected by schizophrenia. More involuntary movements had a small effect size. This review included only one measure for early motor developmental milestone (i.e. walking). Thus, other motor milestones in relation to risk of subsequently developing schizophrenia at individual level were not assessed.

Early motor milestones play a significant role in assessment of child development and delay in these milestones contributes to impaired overall motor function. However, it seems that an important prerequisite of achieving a motor developmental milestone is learning, which is based on a series of attempts (Corbetta and Bojczyk 2002) and recalibration of the sensimotor system (Chen et al. 2007). Since early motor developmental milestones can be seen as a complex interrelation between both motor and cognitive aspects (Diamond 2000; Murray et al. 2006; Piek et al. 2008), it is probably necessary to study them separately from motor function.

Delayed attainment of early motor development milestones, such as walking or standing unsupported and deficits in motor function in future cases of adult schizophrenia have been a key piece of evidence underpinning the neurodevelopment hypothesis of this severe illness, despite the heterogeneity in the method and age of assessment of these motor phenomena in longitudinal studies. To our knowledge, the findings from these studies have not been summarised, and a robust estimate of the association between adult schizophrenia and various early motor developmental milestones has not been provided. The aim of the present study was to systematically review and meta-analyse the scientific evidence regarding early motor developmental milestones and adult schizophrenia risk. In addition, we updated the systematic review of motor function.

2. Methods

2.1. Search strategy

The PubMed, PsycINFO and Scopus databases were searched for original research articles in July 2015. No language restrictions were applied. The following indexing terms (MeSH or Key words) were included: [(infant OR child* OR early) AND (schizophr*OR psychosis OR schizoaff* OR psychotic) AND (impairment OR delay OR skill OR ability OR function OR deficit OR coordination OR performance OR problem OR milestone* OR complication* OR risk* OR functioning OR precursor* OR predictor*) AND (motor OR movement OR neuromuscular OR psychomotor OR neuromotor OR development*)].

2.2. Inclusion and exclusion criteria

A standardised and reliable assessment of schizophrenia (e.g. registers, clinical diagnoses, interview diagnoses, validated diagnoses by physician, but not self-report) was required. Studies with only childhood onset cases of psychosis (<12 years) were excluded. Included studies assessed early motor developmental milestones between ages 0 and 13 years old. Studies exploring other aspects of motor function rather than milestones were excluded from the meta-analysis. We contacted the authors of articles for additional data so that studies could be included in the meta-analyses if data were not published in a suitable format.

2.3. Study selection

An electronic database and selected articles reference list search identified 5990 articles after removing duplicates (Fig. 1). Abstracts were screened by three reviewers working independently of each other (SF, AF, IL), which identified 69 potentially eligible articles. The first author obtained full text and assessed all of these 69 articles, of which 6 studies were included in the systematic review and 5 in the meta-analyses of early motor developmental milestones. In addition, 10 eligible studies on motor function were identified. A list of excluded full-text assessed studies is presented in Supplementary material 2.

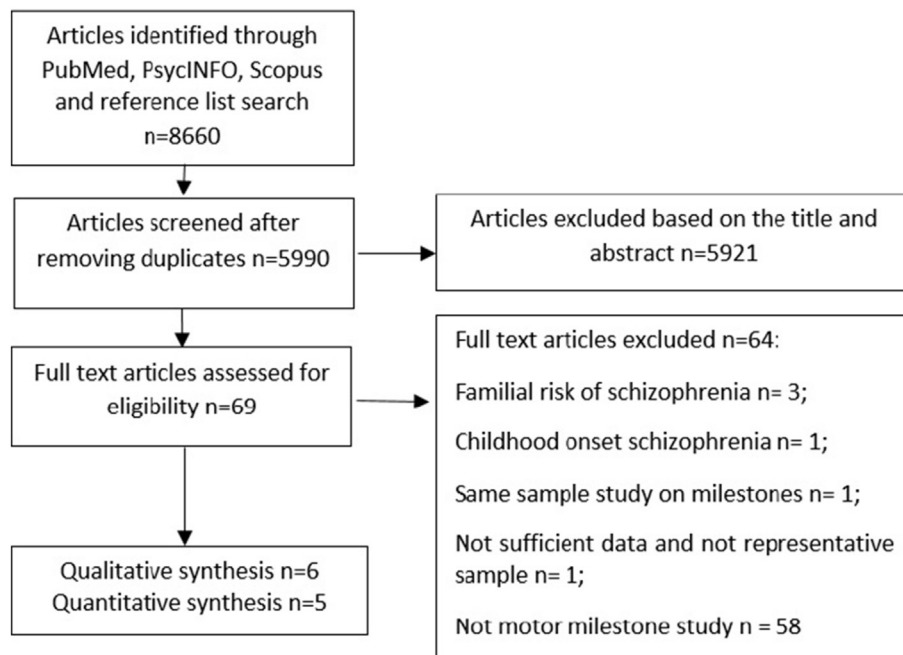


Fig. 1. Selection of the studies for the review of early motor developmental milestones and schizophrenia.

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