Brain, Behavior, and Immunity 39 (2014) 42–55

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Assessing for unique immunomodulatory and neuroplastic profiles of physical activity subtypes: A focus on psychiatric disorders

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ARTICLE INFO

Article history:
Available online 20 November 2013

Keywords:
Physical activity
Exercise
Subtypes
Depression
Cognitive dysfunction
Psychiatry
Immune
Neuroplasticity
Mild cognitive impairment
Alzheimer's disease

ABSTRACT

Physical activity (PA) is emerging as a safe and effective tool in the prevention and treatment of psychiatric disorders. PA subtypes include aerobic, resistance, flexibility, neuromotor (involving balance, agility and co-ordination), mind–body (e.g. tai chi, qi gong and yoga) and mixed type trainings. Evidence from clinical trials suggests that PA subtypes can have positive clinical effects, however the effects on the symptomatology may vary according to the PA subtype. It therefore stands to reason that various PA subtypes may modulate the immune system and neuroplastic processes differently. This systematic review aims to assess the immunomodulatory and neuroplastic profiles of various PA subtypes, particularly in unipolar depression and age-related cognitive decline (ARCD). The literature suggests several unique immunomodulatory and neuroplastic profiles for PA subtypes (i.e. resistance, aerobic and mind–body) in depression and ARCD. In depression, levels of various cytokines at baseline may predict treatment response to subtypes of PA and pharmacological agents. The pro-neuroplastic effects of resistance and aerobic PA in ARCD may differ due to variances in neurotrophin profiles. At this stage of literature in the field, it is difficult to draw firm conclusions on the specific immunomodulatory and neuroplastic pathways involved in these PA subtypes given of the small number of comparative studies and methodological heterogeneity between studies (e.g. study population age and illness severity, as well as duration and intensity of PA intervention). This important field requires well-designed, high-quality comparative studies to better describe unique immunomodulatory and neuroplastic profiles.

1. Introduction

Debate is ongoing regarding the differing clinical effects of subtypes of PA in the treatment of psychiatric disorders (Cooney et al., 2013; Hotting and Roder, 2013; Rethorst and Trivedi, 2013; Schuch and de Almeida Fleck, 2013; Voelcker-Rehage and Niemann, 2013). Understanding the neurobiological effects of various PA subtypes may assist in understanding target populations, differences and similarities in clinical efficacy, as well as providing biomarkers to enhance the clinical utility of PA in unipolar depression and ARCD (i.e. across the spectrum of cognitive aging, to Mild Cognitive Impairment (MCI) and Alzheimer's dementia (AD). A comprehensive assessment of the field pertaining to the neuroimmune and neuroplastic effects of PA subtypes has not been published to date.

A significant amount of literature is emerging allowing for a comparison of PA subtypes in unipolar depression and ARCD, however a thorough analyzis of this literature is outside of the scope of this review. A number of studies have examined the effect of various types of PA in ARCD (see Balsamo et al., 2013; Brown et al., 2012; Cassilhas et al., 2007; Davis et al., 2013; Hotting and Roder, 2013; Kramer et al., 1999; Liu-Ambrose et al., 2010; Nagamatsu et al., 2012, 2013; Pitkala et al., 2013; Roig et al., 2013). A number of primary research, meta-analyzes and systematic reviews provide a comparison between subtypes of PA in depression (see Bridle et al., 2012; Chi et al., 2013; Erickson et al., 2013; Krogh et al., 2009, 2011, 2012; Lavretsky et al., 2011; Oh et al., 2013; Penninx et al., 2002; Ravindran and da Silva, 2013; Rimer et al., 2012; Wang et al., 2013).

From a neuroplasticity perspective, data has emerged suggesting aerobic and resistance PA have a more potent neuroplastic effect than other PA subtypes (Voelcker-Rehage and Niemann, 2013). A recent review by Voelcker-Rehage and Niemann (Erickson et al., 2013; Voelcker-Rehage and Niemann, 2013) compares the clinical effect of 'metabolic exercise' (i.e. cardiovascular and resistance training) and co-ordinative PA (i.e. motor fitness, co-ordination and flexibility) on cognitive function and markers of neuroplasticity. The authors present evidence arguing pure metabolic PA has greater effects on brain volume and functional activity, particularly in the prefrontal and hippocampal (HC) areas, as compared to

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http://dx.doi.org/10.1016/j.bbi.2013.10.026

stretching, toning or relaxation interventions (for primary evidence see Erickson et al., 2011; Ruscheweyh et al., 2011; Voelcker-Rehage et al., 2011); they contribute this effect to differing metabolic demands (Voelcker-Rehage and Niemann, 2013). The recent RCT by Nagamatsu et al. (2012) noted differing neuroplastic effects of resistance PA vs. balance and toning (BAT) PA. Over 6 months, the study examined 86 community-dwelling women aged 70–80 years with probable MCI. Resistance training improved selective attention/conflict resolution, associated memory and regional patterns of functional brain plasticity (right lingual gyrus under functional MRI analysis) compared with BAT. A recent rodent study suggests aerobic and resistance PA have divergent pro-neuroplastic effects (Cassilhas et al., 2012). This study found both types of PA improved learning and spatial memory, resistance PA induced central and peripheral insulin-like growth factor-1 (IGF-1) and AKT in the hippocampus (HC), whereas aerobic PA showed an increase in IGF-1, brain-derived neurotrophic factor (BDNF), TrkB and β-CaMKII (calcium-dependent kinase II) in the HC.

Understanding the immunomodulatory effects of PA subtypes may provide insight into the similarities and differences between neuroplastic and clinical effects (Baune and Eyre, 2012). This is relevant given the positive and negative effects of immune factors (e.g. cytokines and microglia) on neuroplasticity processes and markers (i.e. volumetric analysis, neurogenesis, synaptic plasticity, long-term potentiation/depression (LTP/D)) and symptomatology in unipolar depression and ARCD (for reviews see Eyre and Baune, 2012a; McAfoose and Baune, 2009; Wyss-Coray and Rogers, 2012). A number of examples of comparative studies assessing the immunomodulatory profiles of PA are offered in the literature, and will be reviewed in this paper.

This paper will initially outline the involvement of the immune system in unipolar depression and ARCD. Following this, the systematic review aims to assess the immunomodulatory and neuroplastic profiles of various PA subtypes, particularly in clinical populations with unipolar depression and ARCD.

2. Methods

The literature search for this review was carried out according to the PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines as they apply to systematic reviews (Moher et al., 2009). An electronic search of reputable databases including PubMed, PsychoInfo, OvidSP and ScienceDirect were utilized in the creation of this systematic review. An initial search was conducted using the following keywords: (Immune OR cytokine OR inflammatory OR microglia) OR (neuroplastic* OR neurogenesis OR synap* OR volume) AND (aging brain OR cognition OR Alzheimer's OR cognitive decline OR cognitive dysfunction) OR (depression OR depressive OR stress OR mood disorder). A second search was conducted as above, but with the addition of the following: AND (exercise OR physical activity OR strength OR aerobic OR flexibility OR mind–body). Articles were also obtained by reviewing reference lists of review and research articles. A total of 680 studies were found using these search terms. A total of 316 articles remained after assessment of abstracts for relevance to the aims of this review. Abstracts were also selected based on the year of publication (between 1969 and October 2013), publication in the English language and of peer-reviewed type. Of these, 201 studies were excluded after review of the full text if they did not either directly compare between subtypes of PA or provide data on the neuroplastic/neuroimmune effects of PA subtypes, if they included anecdotal evidence or did not include measurement of clinical information or relevant biomarkers. Where possible, risks of bias across studies has been reported. Finally, 115 articles were utilized in the making of this literature review (Fig. 1 depicts this strategy).

3. Results

3.1. The involvement of the immune system in psychiatric disorders

Prior to investigating clinical and immunological effects of PA subtypes, we will first frame the most up-to-date understanding

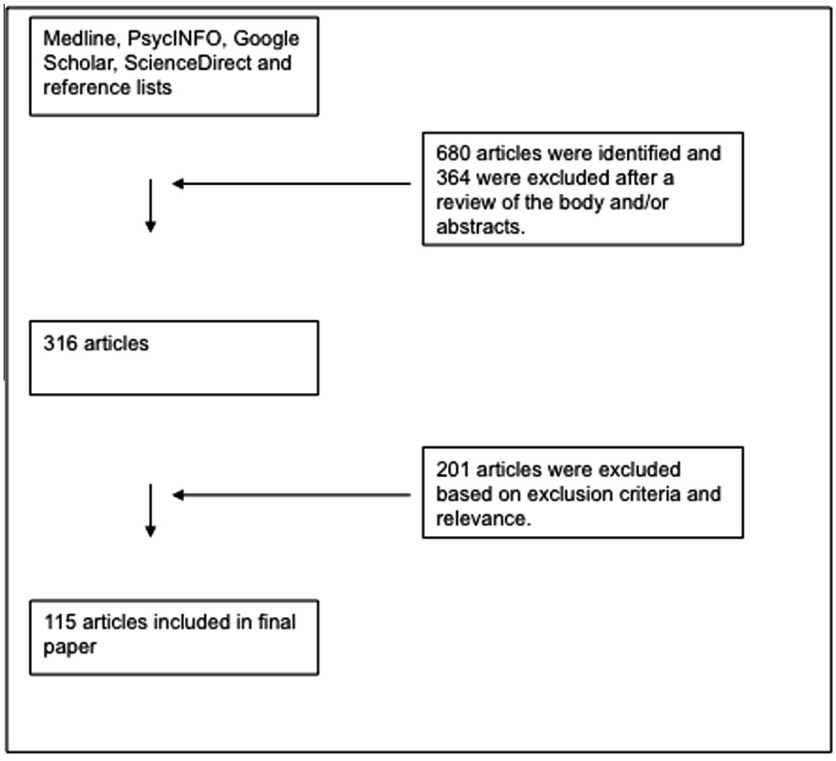

Fig. 1. Study inclusion flowchart.