Journal of Affective Disorders 172 (2015) 219–230

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Review

The influence of inflammatory cytokines in physiopathology of suicidal behavior

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ARTICLE INFO

Article history:
Received 20 September 2014
Accepted 30 September 2014
Available online 12 October 2014

Keywords:
Cytokines
Inflammation markers
Suicide

ABSTRACT

Background: Based on the urgent need for reliable biomarkers in relation to suicide risk both for more accurate prediction as well as for new therapeutic opportunities, several researchers have been studied evidences of the potential participation of inflammatory processes in the brain, in particular cytokines, in suicide. The purpose of this review was to analyze the associations between inflammation markers and suicide.

Methods: To achieve this goal, a systematic review of literature was conducted via electronic database Scopus using the Medical Subject Headings (MeSH) terms: "cytokines", "suicide" and "inflammation". Through this search it was found 54 articles. After analyzing them 15 met the eligibility criteria and were included in the final sample.

Results: One of the most mentioned inflammatory markers was Interferon-α (IFN-α), a pro-inflammatory cytokine which has been shown to increase serum concentrations of pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, tumor necrosis factor-a (TNF- α) and IFN-Ɣ, which are factors increased suicide victims and attempters. In this line, IL-6 is not only found to be elevated in the cerebrospinal fluid of suicide attempters, even its levels in the peripheral blood have been proposed as a biological suicide marker. Another study stated that increased levels of IL-4 and IL-13 transcription in the orbitofrontal cortex of suicides suggest that these cytokines may affect neurobehavioral processes relevant to suicide.

Limitations: A lack of studies and great amount of cross-sectional studies.

Conclusion: Inflammation may play an important role in the pathophysiology of suicide, especially, levels of some specific inflammatory cytokines.

Contents

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http://dx.doi.org/10.1016/j.jad.2014.09.057
0165-0327/

1. Introduction

The present review aims to elucidate associations between inflammation markers and suicide by correlating several studies findings. Based on them, altered inflammatory parameters seem to be a state marker of suicidality irrespective of ongoing treatment.

Several mechanisms have been proposed to explain how cytokines may affect brain function and behavior (Tonelli et al., 2008). First of all, is it important to clarify that cytokines are regulatory peptides that participate in host defense and repair processes of tissues. Among many roles, they modulate neuroendocrine functions, sleep, and sickness behavior and participate in neuroinflammatory and neurodegenerative processes (Serafini et al., 2013). They have also been implicated in the neurobiology of mood disorders (Anisman et al., 2005; Pollak and Yirmiya, 2002; Raison et al., 2006; Schiepers et al., 2005; Tonelli et al., 2005; Tonelli and Postolache, 2005; Serafini et al., 2013).

In this line, recent evidence indicates that inflammation might be involved in the pathophysiology of psychiatric disorders. The expression of cytokines, chemokines, and other inflammatory markers is often altered in the blood of patients with depression, schizophrenia and bipolar disorder (Goldstein et al., 2009; Maes et al., 1995; Potvin et al., 2008; Janelidze et al., 2011; Raison et al., 2006). Additionally, neuroimmune factors have been proposed as contributors to the pathogenesis of major depression (Sublette et al., 2011; Dantzer et al., 2011; Maes et al., 2009).

It is also important to explain the correlation between suicide and major depressive disorders (MDD). MDD is associated with an increased risk for suicidal behaviors (Pompili et al., 2011; Pompili et al., 2012a; Pompili et al., 2012; Serafini et al., 2013; Serafini et al., 2012; Serafini and Pompili 2011; Innamorati et al., 2011).

However, the current knowledge regarding the neurobiology of suicide is still insufficient. Considering this scenario, our findings are relevant in light of inflammatory mechanisms that link depressive disorders with immunity processes. Besides, our review aims to elucidate reliable biomarkers in relation to suicide risk fulfilling the need of more accurate prediction as well as of new therapeutic opportunities.

2. Methods

The present study is a systematic review of literature. At first, a search of the literature was conducted via international electronic database Scopus in 24 August 2014. The search terms browsed in databases were “cytokines”, “suicide” and “inflammation” using Medical Subject Headings (MeSH) terms with no time limit. For assessing risk of bias of individual studies, where a title or abstract seemed to describe a study eligible for inclusion, the full article was examined to assess its relevance based on the inclusion criteria. Three independent researchers (VM, LC and CM) conducted a three-step literature search. Any discrepancies between the three reviewers who, blind to each other, examined the studies for the possible inclusion were resolved by consultations with six senior authors (SP, RP, SS, AR, BB, MR).

The article analysis followed previously determined eligibility criteria. The studies must have met all the following criteria for inclusion: (1) manuscripts written in English; (2) original articles with online accessible full text available in Coordination of Improvement of Higher Education Personnel (CAPES) Journal Portal, a virtual library linked to Brazil's Ministry of Education and subjected to content subscription; (3) articles about the

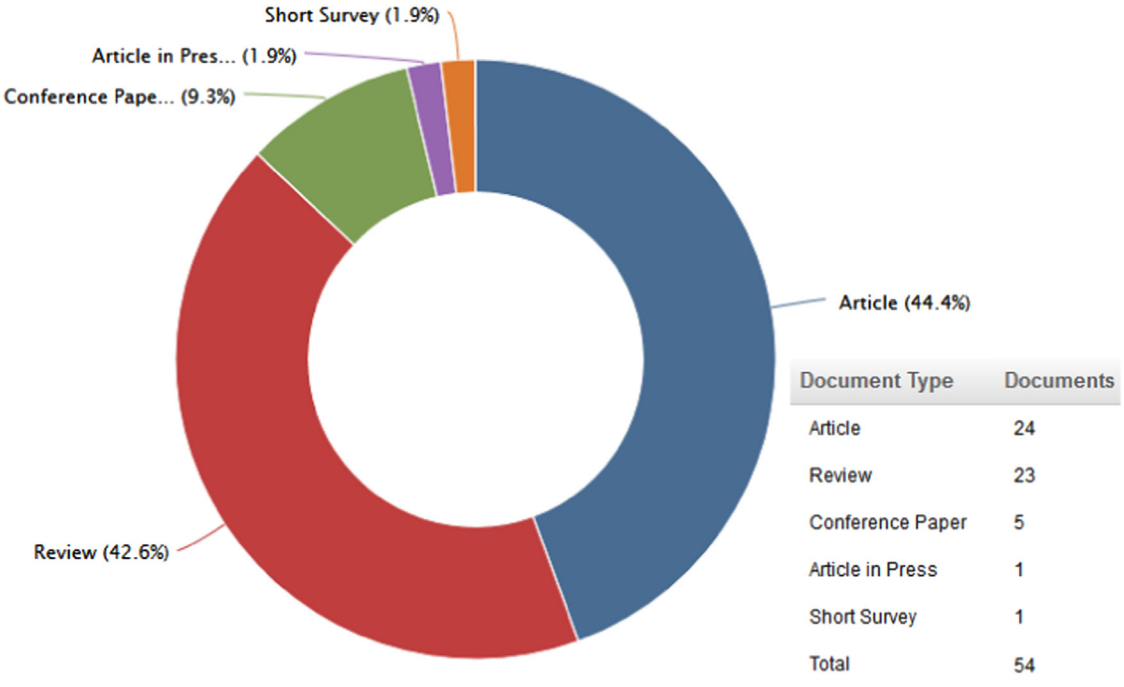

Fig. 1. This chart provided by Scopus database shows the total of documents for this query by Document Type.