Journal of Psychiatric Research 102 (2018) 159–167

Contents lists available at ScienceDirect

Journal of Psychiatric Research

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

Smaller hippocampal volume in current but not in past depression in comparison to healthy controls: Minor evidence from an older adults sample☆

Ismaïl Bensassi[a,b,1], Jorge Lopez-Castroman[a,b,1], Jerome J. Maller[c,d], Chantal Meslin[e], Marilyn Wyart[b], Karen Ritchie[a,f], Philippe Courtet[a,g,h], Sylvaine Artero[a,2], Raffaella Calati[a,h,*,2]

[a] INSERM, University of Montpellier, Neuropsychiatry: Epidemiological and Clinical Research, Montpellier, France
[b] Department of Adult Psychiatry, CHRU Nimes, Nimes, France
[c] Monash Alfred Psychiatry Research Centre, The Alfred & Monash University Central Clinical School, Melbourne, Victoria, Australia
[d] General Electric Healthcare, Victoria, Australia
[e] Centre for Mental Health Research, Australian National University, Canberra, Australia
[f] Centre for Clinical Brain Sciences, Faculty of Medicine, University of Edinburgh, United Kingdom
[g] Department of Psychiatric Emergency & Acute Care, Lapeyronie Hospital, CHU Montpellier, Montpellier, France
[h] FondaMental Foundation, Créteil, France

ARTICLE INFO

Keywords:
Depression
Neuroimaging
Brain imaging/neuroimaging
Biological markers
Mood disorders

ABSTRACT

Background: Structural neuroimaging studies revealed a consistent pattern of volumetric reductions in both hippocampus (HC) and anterior cingulate cortex (ACC) of individuals with major depressive episode(s) (MDE). This study investigated HC and ACC volume differences in currently depressed individuals (n = 150), individuals with a past lifetime MDE history (n = 79) and healthy controls (n = 287).

Methods: Non-demented individuals were recruited from a cohort of community-dwelling older adults (ESPRIT study). T1-weighted magnetic resonance images and FreeSurfer Software (automated method) were used. Concerning HC, a manual method of measurement dividing HC into head, body, and tail was also used. General Linear Model was applied adjusting for covariates.

Results: Current depression was associated with lower left posterior HC volume, using manual measurement, in comparison to healthy status. However, when we slightly changed sub-group inclusion criteria, results did not survive to correction for multiple comparisons.

Conclusions: The finding of lower left posterior HC volume in currently depressed individuals but not in those with a past MDE compared to healthy controls could be related to brain neuroplasticity. Additionally, our results may suggest manual measures to be more sensitive than automated methods.

1. Introduction

According to the World Health Organization, the overall prevalence rate of depressive disorders among older adults ranges from 8 to 20% in the community and up to 37% in primary care (World Health Organization, 2001). Recurrent and chronic major depression is associated with high levels of morbidity and functional impairment (McMahon et al., 2012). Duration of depression appears to be associated with the extent of global cerebral gray matter change (Lampe et al., 2003). Structural magnetic resonance imaging (MRI) has been widely used to examine the neuro-structural correlates of depression, in young and elderly populations (Schweitzer et al., 2001). Meta-analyses of volumetric MRI studies in patients with unipolar depression in comparison with healthy controls have shown volume reductions in the hippocampus (HC) (Campbell and MacQueen, 2004; McKinnon et al., 2009; Videbech and Ravnkilde, 2004), the subgenual cortex (Bora et al., 2012), the amygdala (Hamilton et al., 2008), the putamen and the caudate nucleus (Koolschijn et al., 2009), and the right cingulate cortex (Arnone et al., 2012). The most frequently observed regions of atrophy are the HC, the anterior cingulate cortex (ACC), the prefrontal cortices,

☆ The work was performed at INSERM, University of Montpellier, Neuropsychiatry: Epidemiological and Clinical Research, Montpellier, France.

* Corresponding author. INSERM, University of Montpellier, Neuropsychiatry: Epidemiological and Clinical Research, 39, avenue Charles Flahault, 34093 Montpellier cedex 5, France.
E-mail address: raffaella.calati@gmail.com (R. Calati).

[1] Co-first Authors.
[2] Co-last Authors.

https://doi.org/10.1016/j.jpsychires.2018.04.008
Received 30 December 2017; Received in revised form 5 April 2018; Accepted 6 April 2018

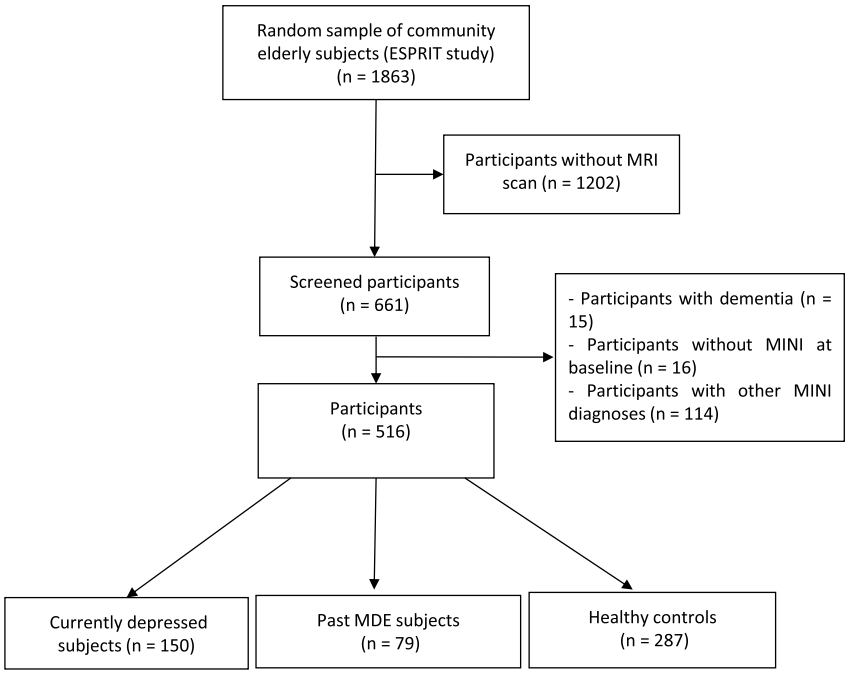

Fig. 1. Flow chart of the inclusion/exclusion process of participants (MRI: magnetic resonance imaging; MINI: Mini International Neuropsychiatric Interview; MDE: major depressive episode). They have been included: currently depressed subjects (n = 150), subjects with a past lifetime history of major depressive episode (n = 79), and healthy controls (n = 287).

the striatum, the amygdala (Du et al., 2014) and the thalamus (Andreescu et al., 2008). Among them two limbic structures, the HC and the ACC, seem particularly consistent (Ballmaier et al., 2004; Steffens et al., 2000). In particular, HC volume reduction has been repeatedly reported in neuroimaging studies of depressed patients (Campbell et al., 2014; Malykhin and Coupland, 2015; Schmaal et al., 2015; Sheline, 1996), including older adults (Ballmaier et al., 2008; Hickie et al., 2005; Lloyd et al., 2004; O'Brien et al., 2004; Sheline, 1996; Steffens et al., 2000). This reduction could be due to stress, through increased glucocorticoid release which in turn suppresses adult neurogenesis in the dentate gyrus (a HC sub-region) eventually promoting onset of a depressive episode (Eker and Gonul, 2010; Jacobs et al., 2000; Sapolsky et al., 1986). However, HC volume reduction in late life depression (LLD) may also be linked to neurodegenerative disorders, like Alzheimer's disease, in an early or pre-clinical stage (de Flores et al., 2015). ACC volumes as well seem to decrease in major depressive disorder (MDD) in adulthood (Arnone et al., 2012; Bora et al., 2012) but also in LLD (Ballmaier et al., 2004; Gunning et al., 2009). This region may play a key role in functions disrupted in depression in older adults as it is connected to brain structures that regulate mood, emotional valence of thought and autonomic and visceral responses (Alexopoulos et al., 2008).

Brain volume changes due to depression in older adults may be modified by a number of confounding factors. First, female gender (Mulsant and Ganguli, 1999) and past history of depression seem to increase the risk of LLD (Cole and Dendukuri, 2014). Second, magnitude of brain volume reduction has been associated with the severity of the depressive episode (Lorenzetti et al., 2009; Vakili et al., 2000). Third, longitudinal studies have shown that cardiovascular risk factors pertaining to the metabolic syndrome increase the risk of LLD (Alexopoulos, 2005; Krishnan, 2002; Laks and Engelhardt, 2010; Reaven, 1988). Finally, antidepressant use reduces time to recovery (Alexopoulos et al., 1996) and induces brain plasticity especially in prefrontal cortex, ACC, and medial temporal areas (Bellani et al., 2011).

In order to further understand the differences between currently depressed individuals and persons with past major depressive episode (MDE), who may have recovered in terms of brain atrophy, we investigated the volume differences in the HC and ACC in a general population sample of French older adults. The aim of the present study was to compare HC and ACC volumes in older adults with current or past depression versus healthy controls. To this end we focused on regional reconstruction and segmentation of both regions obtained through FreeSurfer image analysis suite (automated method). Manual HC volume estimation was also undertaken. We hypothesized that HC and ACC volumes would be reduced in depressed older adults controlling for potential confounders, such as gender, metabolic syndrome and antidepressant use.

2. Materials and methods

2.1. Sample

We used data from a prospective study of psychiatric disorders in older adults' community dwellers (the "Enquête de Santé Psychologique – Risques, Incidence et Traitement", or ESPRIT study). In this project, 1863 subjects aged 65 and over were randomly recruited from the 15 electoral rolls of Montpellier district (South of France) between March 1999 and February 2001 (Ritchie et al., 2004). Participants underwent clinical, biological and neuroimaging assessment administered by trained staff at the Gui de Chauliac Neurology Hospital of Montpellier. Ethical approval was obtained by the ethics committee and written informed consent was collected from all the participants. For the current study, we selected individuals aged $\leq$80 with available MRI imaging data, specifically of estimated HC, ACC and total intracranial volumes (n = 661). We then excluded participants with a diagnosis of dementia (n = 15), with missing baseline Mini International Neuropsychiatric Interview (MINI) data (n = 16), and with MINI diagnosis other than depression (n = 114). A total of 516 individuals were finally retained (see Fig. 1 for the flow chart).

2.2. Assessment

Participants completed a standardized interview covering sociodemographic characteristics along with a general health questionnaire about medical history, medications, current alcohol consumption, and tobacco use. Psychiatric diagnoses, including current and lifetime MDE, were assessed using the Mini International Neuropsychiatric Interview (MINI; French version 5.00), validated in the general population and providing DSM-IV diagnoses (Sheehan et al., 1998). The MINI was administered by trained interviewers (nurses and psychologists) and