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de Jonge, P.

Published in:
Biological Psychiatry

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2009

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

de Jonge, P. (2009). The importance of incident depression in myocardial infarction patients. *Biological Psychiatry*, 65(4), e7-e8.

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The Importance of Incident Depression in Myocardial Infarction Patients

To the Editor:

Depression that is present in the aftermath of a myocardial infarction (MI), post-MI depression, may encompass different subtypes based on whether it is the first or a recurrent episode and based on its onset (i.e., started before or after the MI). Incident post-MI depression is defined as a first-ever episode with an onset after the MI. In a recent issue of *Biological Psychiatry*, Parker *et al.* (1) confirm that the association between post-MI depression and prospective cardiovascular events is due to those episodes that develop just after the cardiac event.

Although some still believe the results in this area of research are inconclusive (2), summarizing the evidence reveals there is only one relatively small study ($n = 222$) from 1996 by Lesperance *et al.* (3) suggesting that recurrent depression is associated with an increased risk of cardiac events. In contrast, there are four larger and more recent studies, namely by Grace *et al.* (4) ($n = 750$), de Jonge *et al.* (5) ($n = 468$), Dickens *et al.* (6) ($n = 588$), and recently the study by Parker *et al.* (1) ($n = 489$), suggesting that it is incident depression that is most strongly associated with prospective cardiovascular events. Apart from the larger sample sizes of these more recent studies, it is important to note that the estimated increased risk of post-MI depression on survival has dramatically decreased from the early studies by Frasure-Smith *et al.* (7) (hazard ratio [HR] = 5.8, unadjusted effect) to more recent, meta-analytic based estimations of around 2 (van Melle *et al.* [8]: HR = 2.4; Nicholson *et al.* [9]: HR = 1.8; Barth *et al.* [10]: HR = 2.2). As a result, the earlier studies may no longer accurately reflect the actual risk.

Some recent studies have also shown that incident depression is associated with aspects of MI severity (11) and coronary artery disease (CAD) severity (12), suggesting a different etiology than recurrent depression. This is not to say that post-MI depression is necessarily an artifact, although in part it may be, but at least that it may be a specific kind of reaction that is different from normal depression. Among the possible mechanisms of how post-MI depression may lead to impaired cardiovascular prognosis, the role of inflammation and low heart rate variability have been proposed (13). Both are associated with the severity of the underlying heart disease, depression, and cardiovascular prognosis. Of interest, both increased inflammation (14) and decreased heart rate variability (15) are specifically associated with somatic, rather than cognitive, symptoms of depression, which may be more prevalent in incident depression. In other words, incident post-MI depression may be a condition in which depression and heart disease are truly intertwined.

The finding that incident post-MI depression, relative to recurrent depression, is distinctively associated with subsequent negative cardiac outcomes is of utmost interest with respect to treatment options. The presence of incident post-MI depression may help to explain the disappointing results from intervention trials aimed to treat post-MI depression and thereby attempting to improve cardiovascular prognosis (16–18). Thus far, the distinction between incident depression and recurrent depression has been found helpful in distinguishing response to treatment in non-CAD depressed patients (19–21), in which only subjects who had repeated past episodes responded to therapy. With the results presented by Parker *et al.* (1), it is possible that in MI patients, we are currently able to effectively treat depression that is not associated with an increased risk of cardiovascular events but not depression that is associated with increased risk, as

observed in the Sertraline AntiDepressant Heart Attack Trial (SADHART) (16). The result is a failure to improve cardiovascular prognosis by treating post-MI depression as observed in the Enhancing Recovery in Coronary Heart Disease Patients, or ENRICHED, trial (17), and the Myocardial Infarction and Depression Intervention Trial, or MIND-IT (18). The presence of incident post-MI depression therefore urges us to keep our eyes open to new developments in this rapidly expanding area of research and to develop new interventions that might be quite different than what has been tried before.

Peter de Jonge

Interdisciplinary Center of Psychiatric Epidemiology
Department of Psychiatry
University Medical Centre Groningen
University of Groningen
Hanzeplein 1 Gebouw 32
PO Box 30 001
9700 RB Groningen
The Netherlands

Dr. de Jonge reports no biomedical financial interests or potential conflicts of interest.

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doi:10.1016/j.biopsych.2008.08.024