Depression and cardiovascular disease: the end of simple models

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Summary
In this editorial, we propose that the association between depression and cardiovascular disease may be conceptualised as a continuous, bidirectional process that originates in youth. The paper by Åberg and colleagues in this issue adds to this literature showing that low cardiovascular fitness at adolescence increases the risk of future depression.

Declaration of interest
None.

How does this translate to clinical practice?
Based on the study by Åberg et al, researchers with clinical ambitions may start to develop interventions aimed at cardiovascular parameters in an attempt to prevent or ameliorate depression, now that the reverse strategy has turned out largely unsuccessful. However, we believe such an approach is likely to fail as well. Instead, we favour an approach in which the complex nature of the association between depression and cardiovascular disease is taken well into account, based on the following reasoning.

First, information on mechanisms underlying the relationship between cardiovascular disease and depression, and therefore information on specific targets for intervention, is incomplete. This is problematic as ideally this type of research would provide the targets for effective interventions. In the literature, numerous potentially mediating mechanisms have been proposed and these include psychophysiological factors such as reduced heart rate variability, inflammatory processes, disturbed platelet function and hypothalamus–pituitary–adrenal (HPA) axis dysfunction, and behavioural factors such as physical inactivity, unhealthy diet, smoking and poor medication adherence. As depression and cardiovascular disease are both multifactorial and heterogeneous disorders, it is unlikely that any specific factor will explain a substantial part of the association between depression and cardiovascular disease. The literature in this field is still limited, as the abovementioned potential mediators are mostly studied in isolation while in reality they are all interrelated. Furthermore, the directions of potential mediational pathways are far from clear. In principle, these mechanisms are largely non-specific to the direction of the association, and may explain both cardiotoxic effects of depression and depressogenic effects of cardiovascular fitness. For example, depressive symptoms may lead to inflammation, but might also be the result of inflammatory processes. The same holds for behavioural factors such as physical activity and obesity. Directions of effects may even differ between individuals. Finally, genetic factors may underlie the development of both cardiovascular disease and depression.
representing yet another kind of mediation, namely by a factor that was already present before depression and cardiovascular disease were. In sum, we still know little of the nature of the association between the two intertwined disorders, and there is little to support that a one-size-fits-all approach will be the solution to improve the prognosis of the two.

A second factor that adds to the complexity of translating these findings into effective interventions is the heterogeneity of the depression construct. Since its operationalisation in the DSM-III, numerous attempts have been made to detect relevant depression subtypes in terms of severity, symptom patterns and aetiologies. In cardiac patients, a differentiation in somatic and cognitive symptom dimensions of depression is often reported in which the somatic dimension is more strongly predictive of cardiac prognosis. Notably, symptom dimensions of distress also differ in clinical care.

The solution: no more simple models

We believe that simple models with respect to aetiology and thus treatment of depression or cardiovascular fitness will turn out to be inadequate and even hamper progress in this field. New models are needed in which the bidirectionality of the association, heterogeneity of depression, interdependency of mediators and inter-individual heterogeneity in the association is accounted for. Depression and cardiovascular disease are highly intertwined diseases which continuously influence each other. The inter-individual heterogeneity of the association implies that, for instance, an underlying process such as atherosclerosis-based inflammation might lead to cardiovascular disease followed by a higher risk of depression in one individual, and depression followed by a higher risk of heart disease in another. In a third individual, atherosclerosis may even result from depression and subsequent poor lifestyle. To deal with this in clinical care, and as opposed to previously proposed simple models, we argue for an alternative research approach based on the following foundations.

(a) Research to date supports bidirectional associations between depression and cardiovascular parameters throughout the life span. Scientific progress on concepts that are so much intertwined will not be achieved by clinging to simple hypotheses stressing only one side of the story. Instead of treating one disorder in order to improve prognosis of the other, we need to treat both simultaneously.

(b) The massive interdependencies between physiological and behavioural mediators explaining the association between depression and cardiovascular disease suggest that networks of effects may even give a more complete representation of reality. In addition, research should take into account potential bidirectional effects of mechanisms. This argues for interventions that are relatively unselective, i.e. affecting several mechanisms simultaneously.

(c) The heterogeneity of the depression construct suggests that any attempt to improve cardiovascular parameters in order to influence depression, or to reduce depression in order to improve cardiovascular parameters, should be adjustable to the level of individuals.

Collaborative care and personalised medicine, in which depression and cardiovascular disease are not conceptualised as separate entities and in which interventions can be adjusted to the stages of the disease, in principle might offer the opportunity to address these issues. Lifestyle interventions including exercise therapy will likely play an important role in such programmes as they have the potential to improve depression and cardiovascular fitness simultaneously and may affect several of the proposed mediators simultaneously. Research to date has shown that collaborative care may be an effective tool in addressing depression in the general population, but also depression as a comorbid disorder in patients with somatic diseases. Still, collaborative care is not a golden solution in itself, and its active ingredients are far from being fully understood. The true effectiveness of collaborative care in specific patients will depend on how well clinicians are able to adjust the interventions to the needs of individuals, based on a thorough understanding of the association between depression and cardiovascular fitness within individuals. Needless to say perhaps, this may hold for the depression–cardiovascular disease link as well as for the link between depression and other medical conditions.

References

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