Chapter 14
Anhedonia in Heart Disease

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Abstract Several recent studies have reported that anhedonia could constitute a particular cardiotoxic symptom in subjects with acute coronary syndrome (ACS) or other cardio-vascular diseases. The aim of this overview was to briefly present the recent studies and propose several guidelines taking the limitations of these studies into account. Several hypotheses concerning the relationships between anhedonia and ACS are proposed as well as the relevance of using more restricted and validated definition of hedonic deficits taking into account the distinction between consummatory and anticipatory pleasures.

Keywords Anhedonia • Acute coronary syndrome • Anticipatory pleasure • Consummatory pleasure

Abbreviations

ACM	All-cause mortality
ACS	Acute coronary syndrome
ANP	Atrial natriuretic peptide
BDI-FS	The fast seven-item version of the Beck Depression Inventory
CIDI	The Composite International Interview
HADS-A	Hospital Anxiety and Depression Scale anxiety subscale
HADS-D	Hospital Anxiety and Depression Scale depression subscale
HF	Heart failure

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LPS	Lipopolysaccharide
MACE	Cardiovascular mortality, recurrent ACS, unplanned revascularization
MI	Myocardial Infarction
PAD	Peripheral arterial disease
PAS	Physical anhedonia scale
TEPS	Temporal Experiences of Pleasure Scale
SAS	Chapman Social Anhedonia Scale
SHAPS	Snaith and Hamilton Pleasure Scale

14.1 Introduction

In the general cardiovascular literature, there is a recent increased interest in the role of positive affect and notably anhedonia, the lowered ability to experience pleasure, on clinical outcomes. The role of anhedonia has been explored in acute coronary syndrome (ACS) and also in heart disease, peripheral arterial disease and hypotension. Firstly we present the three studies that have explored anhedonia in heart disease, peripheral arterial disease and hypotension. Secondly we present the eight studies that have examined the role of anhedonia in the prognosis of subjects who have ACS.

14.2 Anhedonia in Heart Failure, Hypotension and Peripheral Arterial Disease

Impaired health status of chronic heart failure has been associated with several psychological factors and notably type D personality and one study has tested the potential effect of low positive affect (anhedonia) associated or not with type D personality on health status in a 12-months follow-up study in 276 patients chronic heart failure [1]. After controlling for demographic and clinical confounders, anhedonic non-type D patients reported lower mental health status, more feeling of disability and lower physical health status when compared with patients with non-type D without anhedonia.

Concerning hypotension, researches associating hypotension with depression have produced inconsistent results suggesting to take into account the different symptoms of depression and notably the distinction between negative and positive affects. One study [2] examined the association between hypotension, with depressive symptoms, negative affect and positive affect in a sample of 340 elderly persons aged from 77 to 99 years. Positive and negative affects were rated using the Positive and Negative Affect Scales. Diastolic hypotension was associated with anhedonia and use of antihypertensive medication was independently associated with anhedonia.

Unlike in ACS, the relationship between psychological variables and the symptoms of peripheral arterial disease (PAD) has not been studied. Patients with PAD report intermittent claudication or atypical leg symptoms and one study [3]

has examined the association between these symptoms and anxiety, depressive symptoms and anhedonia in sample of 628 PAD patients. Anhedonia rated by positive affect subscale of the HAD was only significantly associated with pain at rest.

14.3 Anhedonia in ACS

In subjects with ACS, depression has been associated with poor prognosis and notably a high risk of severe cardiac events or mortality. As depression constitutes a heterogeneous psychiatric disorder, several authors have tried to identify more specifically cardiotoxic symptoms. Among potential cardiotoxic symptoms, anhedonia could constitute a major poor prognostic factor, as suggested by six recent studies. Moreover, two studies have reported that when anhedonia is not taken into account separately but included with other symptoms into a specific syndrome, it becomes a non-significant prognostic factor.

Independently of these eight studies, one study found that anhedonia was associated with poor health status and more somatic and cognitive symptoms in patients with coronary artery disease [4].

14.3.1 Presentation of the Eight Studies

In the first study [5], 291 ACS patients completed the Chapman Physical Anhedonia Scale (PAS) and the Hospital Anxiety and Depression Scale depression subscale (HADS-D). Over a 3-year follow-up period, clinical events were classified as severe cardiac events (mortality or Myocardial Infarction, MI) or clinical events (mortality, MI, recurrence of ACS, hospital readmission and onset or deterioration of heart failure (HF)). Anhedonia was the only predictor of severe cardiac events and clinical events after adjusting for demographic and clinical variables. In contrast with depression, categorical anhedonia (PAS > 23) was an independent and significant predictor of severe cardiac events after adjusting for clinical variables. The incidence of death/MI in hedonics versus anhedonics was 11.1 % vs 22.1 %.

In the second study [6], 408 hospitalized ACS patients were followed for 67 weeks. The patients filled out the HADS-D, the fast seven-item version of the Beck Depression Inventory (BDI-FS) and the brief 10-item version of the Maastricht Questionnaire (MQ-10) rating anergia. Three derived depressive symptom scales evaluating fatigue-sadness, anhedonia and depressive cognitions were constructed from these three rating scales. Major adverse cardiac events (MACE: cardiovascular mortality, recurrent ACS, unplanned revascularization) were assessed and the MACE rate at the endpoint was 14.5 %. Using categorical definitions, only the HADS-D and Fatigue-sadness scales were significant predictors of MACE in univariate and multivariate analyses and the anhedonia scale was a significant predictor only in multivariate analysis. Moreover, when both fatigue-sadness and

anhedonia were included in the multivariate models, fatigue-sadness predicted MACE but anhedonia did not.

In the third study by the same team [7] reported in 598 patients with ACS followed during 8 years that all-cause mortality status was significantly associated with the HADS-D score and not with the HADS-A or BDI fast screen scores. The significant effect of the HADS-D score remained significant after adjustment for major clinical/demographic factors.

In the fourth study [8], 453 consecutive ACS patients were followed for 1 year. A structured psychiatric interview assessing depressed mood, anhedonia and major depressive episode was filled out and depressed mood and anhedonia were also assessed using two subscales extracted from the BDI. The mood subscale contains the sadness (item 1) and crying (item 10) items of the BDI, whereas the anhedonia subscale contains the loss of enjoyment (item 4) and loss of interest in others (item 12) items of the BDI. The main outcome measures were all-cause mortality (ACM) and major adverse cardiac events (MACEs: myocardial infarction, hospitalization for unstable angina, or urgent/emergency coronary revascularization). Controlling for demographic and medical covariates, anhedonia was a significant predictor of combined MACE and ACM, but depressed mood was not. Anhedonia remained a significant predictor after controlling for major depression or depressive level. Combined MACE and ACM were present in 29.9 % and 11.7 % of patients with and without anhedonia, respectively.

The fifth study [9] included 568 Myocardial Infarction (MI) patients. During follow-up (2.5 years), 115 MI patients experienced a cardiac event including death. Using the Composite International Interview (CIDI) to assess depressive symptoms, the authors computed sum scores for the presence of cognitive symptoms including lack of interest and somatic symptoms. Univariate as well as multivariate Cox regression analyses found that lack of interest was a significant predictor of cardiac events demonstrating that, after adjusting for potential confounders, interview ratings of anhedonia were associated with a significantly higher risk of cardiac events.

The sixth study [10] found that anhedonia, rated by the positive affect scale of the HAD, was independently associated with increased risk for all-cause mortality during 7 years of follow-up in 1206 patients who survived the first 6 months after percutaneous coronary intervention.

The seventh study [11] included 913 subjects with unstable angina pectoris or MI who were followed for 12 months. Fifty-one patients died (5.6 %) during follow-up and, according to the BDI, only somatic/affective symptoms (including loss of enjoyment (item 4) and loss of libido items (item 21)) and not the cognitive/affective symptoms (including the loss of enjoyment (item 4) and social withdrawal (item 12) items) were significantly related to mortality after adjusting for sociodemographic and clinical variables (Odds ratio = 1.92, 95 % CI = 1.36–2.71, $p < 0.001$).

The eighth study [12] included 226 coronary artery bypass graft patients who filled out the BDI-II and who were followed for a median of 4.9 years. Using confirmatory factorial analyses, the authors found a three-factor solution of the BDI-II. The affective factor contains the loss of pleasure (item 4) and loss of interest (item 12) items, whereas the somatic factor contains the loss of interest in sex item (item 21).

Sixty-five cardiac events (29 %) including deaths (4.4 % deaths or MI) were observed and only the cognitive factor was significantly associated with cardiac events with or without adjustment for covariates (left ventricular function, age, respiratory disease, heart failure, renal disease and diabetes). The affective factor of the BDI-II that contains three items (loss of pleasure (item 4), crying, loss of interest (item 12)) was not associated with cardiac outcome, but a trend towards significance was observed in non-adjusted or adjusted analyses ($p = 0.09$ and 0.08, respectively).

14.3.2 Discussion of the Eight Studies

These studies reported that anhedonia, rated by questionnaires or structured interviews, was an independent predictor of cardiac events in ACS or MI patients. Moreover, this effect remained significant after controlling for demographic and clinical variables. However, in multivariate analyses, when depression [5, 8] or depressed mood [8] was included as predictors, anhedonia remained a significant and independent predictor. When both fatigue-sadness and anhedonia were included in multivariate analysis, only fatigue-sadness was a significant predictor [6]. When anhedonia was rated by one or several anhedonia items (items 4, 12, 21) of the BDI or BDI-II, the results differed according to whether anhedonia was rated alone or together with other BDI items. Firstly, when anhedonia was rated alone it constitutes a poor prognostic factor [8]. Secondly, when anhedonia was rated with other BDI items, variable results were obtained. In the study by Roest et al. [11], using principal component analysis of the BDI, the authors distinguished cognitive/affective and somatic/affective components. Items 4 and 12 loaded on the cognitive/affective component, whereas items 4 and 21 loaded on the somatic/affective component. Only the somatic/affective component was predictive of all-cause mortality in non-adjusted or adjusted analyses. The results concerning anhedonia were uninterpretable, as two-thirds of the anhedonia items of the BDI loaded in each factor. In the study by Tully et al. [12], only the cognitive component of the BDI-II that did not contain any anhedonia item was a significant predictor of cardiac events although the affective component that contains two BDI-II anhedonia items did not reach significance. It is interesting to note that the affective factor of the BDI-II contained three items, two anhedonia items and the crying item. Moreover, several studies have reported that crying is moderately associated with depression severity and that there is no consensus to include this symptom in the diagnostic criteria of depression.

Three main conclusions can therefore be drawn from these studies. Firstly, anhedonia constitutes an independent predictor of cardiac events in ACS or MI patients, with an effect not related to depression. Secondly, the effect of anhedonia is no longer significant when fatigue-sadness is simultaneously taken into account in the analyses. Thirdly, the results concerning the factors extracted from the BDI suggest that the anhedonia items must be taken into account separately instead of in combination with other symptoms.

14.3.3 Guidelines for Better Evaluation of the Role of Anhedonia in ACS: Five Important Points

Firstly, the authors used nonspecific anhedonia scales to explore the relative effects of anhedonia. Nonspecific anhedonia rating scales were built by using either items of structured interviews (CIDI, DSM-IV) or items of questionnaires (BDI, HAD-D). Three of the 21 items of the BDI rate anhedonia [13]: Dissatisfaction (item 4), Social withdrawal (item 12), Loss of libido (item 21). In the study by Davidson et al. [8], only items 4 and 12 of the BDI were used to build an anhedonia scale. In the study by Doyle et al. [6], anhedonia was rated using a 4-item subscale (3 items of the HAD-D with two items rating pleasure and one rating humor, one item of the BDI-FS rating loss of pleasure). The use of these rating scales could lead to poor reproducibility of the results. Moreover, subjects were divided into anhedonic or hedonic groups using ad hoc cutoff scores that have not been rigorously determined. There is a consensus in the psychiatric literature, notably based on meta-analyses of the existing anhedonia scales, in favor of the use of anhedonia scales presenting satisfactory psychometric properties [14, 15]. The most widely used rating scales are the Chapman revised social (SAS) and physical anhedonia (PAS) scales and the Snaith and Hamilton Pleasure Scale (SHAPS). Moreover, well-defined cutoff scores have been proposed for the SAS and the PAS. We therefore suggest that the above limitation should be taken into account to allow replication of studies. It would be useful to conduct meta-analyses to establish a consensus for each relevant psychological variable of the recommended rating scales studied in ACS patients.

Secondly, the dependent variables are relevant severe or non-severe cardiac events at the endpoint, but various definitions for relevant events were used. In the study by Hoen et al. [9], cardiac events including mortality were evaluated but the authors did not distinguish between the various cardiac events. In one study [5], Major Adverse Cardiac Events (MACEs) included cardiovascular mortality, recurrent ACS, and unplanned revascularization but did not include myocardial infarction and, in another study [8], MACE comprised myocardial infarction, hospitalization for unstable angina, or urgent/emergency coronary revascularization but did not include cardiovascular mortality although all-cause mortality was rated independently. The fist study [5] defined severe cardiac events by all-cause mortality and myocardial infarction. The seventh study [11] assessed all-cause mortality and the eighth study [12] evaluated nonfatal cardiac events (MI, unstable angina pectoris, repeat revascularization, heart failure, sustained arrhythmia, stroke or cerebrovascular accident, left ventricular failure) and fatal cardiac events (mortality due to cardiac causes). A consensus should be reached, notably concerning a precise definition of severe cardiac events.

Thirdly, follow-up varied from one study to another (range: 1–4.9 years) but the prevalence of severe clinical events ranged from 4.4 to 15 % in the six studies. These results could suggest that severe clinical events tended to occur during the first year of follow-up.

Fourthly, the nature and number of sociodemographic and clinical covariables entered in the multivariate analyses varied between the studies. Selection criteria were based on either a priori selection (forced choice) or on the significance found in univariate analyses. The number of covariables ranged from 4 to 11. Guidelines must be defined concerning the modalities of covariable selection.

Fifthly, only two studies [5, 8] controlled for depressive level, using depression rating scale scores, when anhedonia was tested as an independent predictor of severe cardiac events. Moreover, the use of separate scales rating depressive level and anhedonia should be recommended to avoid the risk of multicolinearity in multiple regressions.

14.3.4 Concluding Remarks

14.3.4.1 What Is the Status of Anhedonia in ACS?

In the psychiatric literature, anhedonia [16] is conceptualized either as a symptom found notably in depression and schizophrenia or a trait found in specific personalities (e.g. schizoid or pre-depressive personalities). The design of the studies cannot determine whether anhedonia rated after ACS or MI constitutes a premorbid trait. One study [5] used the PAS that evaluates long-term deficit of hedonic capacity, but self-evaluation could be influenced by the subject's present mood state. One hypothesis could be that some subjects present chronic anhedonia that increases the risk of depression following ACS or MI. Only prospective studies in subjects at risk of ACS or MI could test this hypothesis that anhedonia constitutes a premorbid trait.

14.3.4.2 How Can the Relationship Between Anhedonia and Acute Coronary Syndrome Be Explained?

Another hypothesis is that inflammation could be a causal process partly responsible for both the development of depressive symptoms and adverse cardiac outcome. Acute inflammatory response is associated with ACS and the intensity of this acute inflammatory response during ACS is predictive of poor cardiac outcome (see review in 17). Moreover, sickness behavior is characterized notably by anhedonia and is triggered by the release of proinflammatory cytokines. Several studies in animals and humans have demonstrated that introduction of several of these cytokines induced hedonic deficit [17]. However, a recent study [18] in humans reported that inflammation alters reward-related neural responses in humans and that these reward-related neural responses mediate the effects of inflammation on depressed mood. However, a study in mice has assessed whether a chronic stressor of mild intensity that induced anhedonia, when coupled with a bacterial endotoxin (lipopolysaccharide, LPS) increased left ventricular atrial natriuretic peptide (ANP),

a marker for prognosis in cardiac disease [19]. LPS treatment increased atrial and ventricular proinflammatory cytokines (IL-1 beta, TNF-alpha mRNA expression), whereas the stressor had limited effects on these cytokines. In the absence of chronic stressor, circulating ANP was unaffected by LPS intake and the combination of the stressor and LPS administration augmented changes of plasma ANP and ANP mRNA expression in the left atrium. Thus, chronic stressor that induced anhedonia, and LPS treatment synergistically influenced the rise of plasma ANP. Chronic stress combined with inflammatory immune activation could explain the co-occurrence or comorbidity between anhedonia and cardiac disease.

14.3.4.3 An Interesting Perspective: The Use of a More Scientifically Validated Definition of Anhedonia

The usual definition of anhedonia takes into account the distinction between the physical and social components of anhedonia. This distinction is trivial and leads to the construction of well validated rating scales, the Physical and Social anhedonia scales or the Snaith Hamilton Pleasure Scale, but there is no scientific proof to validate this distinction. Taking this limitation of the anhedonia measure into account, several authors have proposed a more circumscribed definition of anhedonia that has been scientifically validated [20]. Recent studies have identified additional important distinctions between various aspects of pleasure, such as consummatory and anticipatory pleasures. Consummatory pleasure refers to satiation and resolution of desire, whereas anticipatory pleasure refers to motivation and goal-directed behavior. A new scale, the Temporal Experiences of Pleasure Scale (TEPS) [20], has recently been developed to evaluate these two trait experiences of pleasure and several studies have reported satisfactory psychometric properties of this scale. By taking this distinction into account, it would be interesting to explore what type of anhedonia may constitute a risk factor for severe cardiac events in ACS patients. For example, one hypothesis could be that consummatory anhedonia that characterizes severe depression could constitute a more severe cardiotoxic symptom than anticipatory anhedonia. It would be useful to separately test the potential predictive power of these two types of anhedonia.

References

1. Pelle AJ, Pedersen SS, Szabó BM, Denollet J. Beyond Type D personality: reduced positive affect (anhedonia) predicts impaired health status in chronic heart failure. Qual Life Res. 2009;18(6):689–98.
2. Jorm AF. Association of hypotension with positive and negative affect and depressive symptoms in the elderly. Br J Psychiatry. 2001;178:553–5.
3. Smolderen KG, Hoeks SE, Pedersen SS, van Domburg RT, de Liefde II, Poldermans D. Lower-leg symptoms in peripheral arterial disease are associated with anxiety, depression, and anhedonia. Vasc Med. 2009;14(4):297–304.

4. Pelle AJ, Pedersen SS, Erdman RAM, Kazemier M, Spiering M, Van Domburg RT, Denollet J. Anhedonia is associated with poor health status and more somatic and cognitive symptoms in patients with coronary artery disease. Qual Life Res. 2011;20(5):643–51.
5. Leroy M, Loas G, Perez-Diaz F. Anhedonia as predictor of clinical events after acute coronary syndromes: a 3-year prospective study. Compr Psychiatry. 2010;51:8–14.
6. Doyle F, Conroy R, McGee H, Delaney M. Depressive symptoms in persons with acute coronary syndrome: specific symptom scales and prognosis. J Psychosom Res. 2010;68:121–30.
7. Doyle F, Conroy R, McGee H. Differential predictive value of depressive versus anxiety symptoms in the prediction of 8-year mortality after acute coronary syndrome. Psychosom Med. 2012;74(7):711–6.
8. Davidson KW, Burg MM, Kronish IM, Shimbo D, Dettenborn L, Mehran R, Vorcheimer D, Clemow L, Schwartz JE, Lespérance F, Rieckmann N. Association of anhedonia with recurrent major adverse cardiac events and mortality 1 year after acute coronary syndrome. Arch Gen Psychiatry. 2010;67:480–8.
9. Hoen PW, Conradi HJ, Denollet J, Martens E, de Jonge P. Interview-based ratings of somatic and cognitive symptoms of depression and their impact on cardiovascular prognosis. Psychother Psychosom. 2010;79:319–20.
10. Damen NL, Pelle AJ, Boersma E, Serruys PW, van Domburg RT, Pedersen SS. Reduced positive affect (anhedonia) is independently associated with 7-year mortality in patients treated with percutaneous coronary intervention: results from the RESEARCH registry. Eur J Prev Cardiol. 2013;20(1):127–34.
11. Roest AM, Thombs BD, Grace SL, Stewart DE, Abbey SE, de Jonge P. Somatic/affective symptoms, but not cognitive/affective symptoms, of depression after acute coronary syndrome are associated with 12-month all-cause mortality. J Affect Disord. 2011;131(1–3):158–63.
12. Tully PJ, Winefield HR, Baker RA, Turnbull DA, de Jonge P. Confirmatory factor analysis of the Beck Depression Inventory-II and the association with cardiac morbidity and mortality after coronary revascularization. J Health Psychol. 2011;16(4):584–95.
13. Joiner TE, Brown JS, Metalsky GI. A test of the tripartite model's prediction of anhedonia's specificity to depression: patients with major depression versus patients with schizophrenia. Psychiatry Res. 2003;119:243–50.
14. D'haenen H. Measurement of anhedonia. Eur Psychiatry. 1996;11:335–43.
15. Loas G. Measurement of anhedonia: additional remarks. Eur Psychiatry. 1997;12:266.
16. Loas G, Pierson A. L'anhédonie en psychiatrie: revue. Ann Med Psychol (Paris). 1989;147(7):705–17.
17. Poole L, Dickens C, Steptoe A. The puzzle of depression and acute coronary syndrome: reviewing the role of acute inflammation. J Psychosom Res. 2011;71(2):61–8.
18. Eisenberger NI, Berkman ET, Inagaki TK, Rameson LT, Mashal NM, Irwin MR. Inflammation-induced anhedonia: endotoxin reduces ventral striatum responses to reward. Biol Psychiatry. 2010;68(8):748–54.
19. Wann BP, Audet MC, Gibb J, Anisman H. Anhedonia and altered cardiac atrial natriuretic peptide following chronic stressor and endotoxin treatment in mice. Psychoneuroendocrinology. 2010;35(2):233–40.
20. Gard DE, Gard MG, Kring AM, John OP. Anticipatory and consummatory components of the experience of pleasure: a scale development study. J Res Pers. 2006;40:1086–102.