

Put on a Happy Face—It's a Lot Better Than Coumadin

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Although medical factors predisposing to atrial fibrillation (AF) are well described, whether and how psychosocial factors influence the development of AF remains a nearly unexamined area. In this respect, AF lags far behind other cardiovascular conditions, such as coronary artery disease and ventricular arrhythmia, in which relationships between psychosocial factors and cardiac disease have been well established. Depression predicts the recurrence of ventricular arrhythmia in patients with implantable cardioverter-defibrillators over the long term,^{1,2} and negative emotions such as anger can acutely trigger ventricular arrhythmias in this population.³ Although the attempts of AF patients to identify psychosocial triggers for their episodes are familiar to all who participate in the care of these patients, to date, large systematic studies evaluating how emotion may affect AF are lacking. There is one small study of 54 AF patients undergoing cardioversion, in which 85% of those scoring high in depression, compared with 39% of those without depression, had a recurrence over the 2-month follow-up period.⁴ In the Framingham study, measures of anger, hostility, and tension predicted development of AF over 10 years in men but not in women.^{5,6}

In this month's issue of the *Journal of the American Heart Association (JAHA)*, Whang et al⁷ analyze data from the Women's Health Study of female health professionals to evaluate whether global distress, as measured by the Mental Health Index (a subset of the Short Form-36), and specific emotional components of distress predict development of AF. This is a large, prospective, well-known study, with long-term follow-up, a validated instrument for psychosocial evaluation, careful confirmation of the AF outcome, and comprehensive statistical analysis, including adjustment for multiple potential confounders at baseline as well as subsequent cardiac events. In the 30 746 middle-aged women studied, who were free of AF or other cardiovascular disease at baseline, 771 cases of AF

occurred over the median 10-year follow-up period. There was no relationship between global distress or its components, including depression, and likelihood of development of AF.⁷ In a post hoc analysis of the individual components of the Mental Health Index, however, happiness was protective, lowering risk of AF by 30% for those who reported feeling happy some or most of the time compared to those who reported being rarely happy. It is heartening that only 4% of these female healthcare providers reported feeling happy just rarely, whereas 73% were happy most of the time.

Although it is post hoc, this finding is intriguing and warrants further study. The role of negative emotion in predisposing to coronary disease, ventricular arrhythmias, and other ills has been extensively described, with reports dating to the eighteenth century drawing a connection between anger and angina.⁸ The beneficial effects of positive affect, however, have just begun to be recognized. In laboratory studies of provoked mental stress, happiness attenuates stress-induced increases in fibrinogen in healthy individuals,⁹ and cardiovascular reactivity to stress is similarly decreased in those with a positive emotional style.¹⁰ In other short-term laboratory experiments, watching a comedy improved vascular function, as measured by brachial artery flow-mediated dilation and carotid arterial compliance. (Jerry Seinfeld, Ellen Degeneres, and Bill Cosby videos were included in that study).¹¹ In daily life, happiness also alters physiological processes: Among healthy individuals, happiness is associated with lower daily heart rate and cortisol,⁹ and anxiety increases ambulatory diastolic blood pressure only in individuals experiencing low levels of happiness.¹² A good mood also makes a difference clinically: Optimism decreases risk of cardiovascular death,¹³ and emotional vitality confers a decreased likelihood of developing coronary artery disease.¹⁴ How happiness exerts these beneficial effects is unknown. One postulated mechanism for the clinical beneficial effects of psychological well-being has been salubrious changes in health-related behaviors, such as smoking, alcohol intake, and exercise. However, the study by Whang et al⁷ controlled for these behavioral factors, which did not attenuate the impact of happiness, suggesting a direct and possibly autonomically mediated effect of positive affect. Determining the pathophysiological mechanisms by which happiness may decrease likelihood of AF is an important avenue of future research.

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J Am Heart Assoc. 2012;1:e002444 doi: 10.1161/JAHA.112.002444.

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Ultimately, understanding psychosocial mechanisms of disease may lead to novel therapies. Interventions aimed at increasing positive affect, including those based on psychological principles as well as more complementary modalities such as meditation, have shown psychological effects (decreasing perceived stress) and also physiological effects in some disease states.¹⁵ Should the protective effects of happiness against AF be confirmed, examination of whether interventions that may increase positive affect could decrease risk of AF is another area for future investigation.

Also interesting is the primary finding, that global distress and depression were not associated with development of AF. This was somewhat surprising, given the prior findings linking depression and negative emotions to ventricular arrhythmias.^{1–3} The authors postulate that differences in autonomic influences on atrial versus ventricular arrhythmias may lie behind the lack of association between negative affect and AF; they note that AF is often vagally mediated, whereas negative emotions lower vagal activity. However, prior studies have described sympathetic influences on the atrium that are conducive to AF. Shortening of the atrial refractory period facilitates AF,¹⁶ and the shortest atrial refractory periods are seen in the morning, the time of the highest catecholamine levels.¹⁷ Direct sympathetic stimulation shortens the atrial refractory period as well.¹⁸ Furthermore, clinical use of sympathomimetic drugs such as dobutamine for stress echocardiography or inotropic support is well known to precipitate AF,¹⁹ and isoproterenol has been used in the past to aid induction of AF in ablation.²⁰

It is possible that the method of initial identification of AF—self-report—could have confounded an association, if women who were more distressed or depressed were less likely to report AF. No data are available on the rate of “false negatives.” However, in a prior study of patients with AF, those with depression were more likely to report symptoms, not less likely,²¹ making this an improbable explanation.

A more probable explanation for the lack of association between negative emotional patterns and AF seen in the study by Whang et al⁷ may lie in the population studied: women. Prior studies have demonstrated an effect of anger, depression, and tension on future AF only in men, not in women.^{5,6} Whether negative emotion is associated with ventricular arrhythmias in women has not been adequately studied, as prior studies have not included sufficient women³ (a failing unfortunately not uncommon to studies in defibrillator populations). Nevertheless, ample evidence indicates that negative emotion has different physiological effects in women than in men. Hemodynamic and neuroendocrine response to laboratory stressors is greater in men than in women, although specific patterns of activation by sex vary according to the stressor.²² Women and men also show differences in brain activation in response to stress.²³ Furthermore, estrogen attenuates tachycardia-induced atrial

refractory period shortening,²⁴ which could lead to differences between the sexes in propensity to AF with stress. Whether global distress and other negative emotions influence development of AF in men is another important avenue of further research that may be spurred by this thought-provoking study.

Disclosures

None.

References

- Whang W, Albert CM, Sears SF Jr, Lampert R, Conti JB, Wang PJ, Singh JP, Ruskin JN, Muller JE, Mittleman MA, TOVA Study Investigators. Depression as a predictor for appropriate shocks among patients with implantable cardioverter-defibrillators: results from the Triggers of Ventricular Arrhythmias (TOVA) study. *J Am Coll Cardiol*. 2005;45:1090–1095.
- Dunbar SB, Kimble LP, Jenkins LS, Hawthorne M, Dudley W, Slemmons M, Langberg JJ. Association of mood disturbance and arrhythmia events in patients after cardioverter defibrillator implantation. *Depress Anxiety*. 1999;9:163–168.
- Lampert R, Joska T, Burg M, Batsford W, McPherson C, Jain D. Emotional and physical precipitants of ventricular arrhythmia. *Circulation*. 2002;106:1800–1805.
- Lange HW, Herrmann-Lingen C. Depressive symptoms predict recurrence of atrial fibrillation after cardioversion. *J Psychosom Res*. 2007;63:509–513.
- Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB Sr, Benjamin EJ. Anger and hostility predict the development of atrial fibrillation in men in the Framingham Offspring Study. *Circulation*. 2004;109:1267–1271.
- Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB Sr, Benjamin EJ. Tension and anxiety and the prediction of the 10-year incidence of coronary heart disease, atrial fibrillation, and total mortality: the Framingham Offspring Study. *Psychosom Med*. 2005;67:692–696.
- Whang W, Davidson KW, Conen D, Tedrow UB, Everett BM, Albert CM. Global psychological distress and risk of atrial fibrillation among women: the Women's Health Study. *J Am Heart Assoc*. 2012;1:e001107 doi: 0.1161/JAHA.112.001107.
- Soufer R. Neurocardiac interaction during stress-induced myocardial ischemia: how does the brain cope? *Circulation*. 2004;110:1710–1713.
- Stepptoe A, Wardle J, Marmot M. Positive affect and health-related neuroendocrine, cardiovascular, and inflammatory processes. *Proc Natl Acad Sci U S A*. 2005;102:6508–6512.
- Bostock S, Hamer M, Wawrzyniak AJ, Mitchell ES, Steptoe A. Positive emotional style and subjective, cardiovascular and cortisol responses to acute laboratory stress. *Psychoneuroendocrinology*. 2011;36:1175–1183.
- Sugawara J, Tarumi T, Tanaka H. Effect of mirthful laughter on vascular function. *Am J Cardiol*. 2010;106:856–859.
- Shapiro D, Jamner LD, Goldstein IB, Delfino RJ. Striking a chord: moods, blood pressure, and heart rate in everyday life. *Psychophysiology*. 2001;38:197–204.
- Davidson KW, Mostofsky E, Whang W. Don't worry, be happy: positive affect and reduced 10-year incident coronary heart disease: the Canadian Nova Scotia Health Survey. *Eur Heart J*. 2010;31:1065–1070.
- Kubzansky LD, Thurston RC. Emotional vitality and incident coronary heart disease: benefits of healthy psychological functioning. *Arch Gen Psychiatry*. 2007;64:1393–1401.
- Chesney MA, Darbes LA, Hoerster K, Taylor JM, Chambers DB, Anderson DE. Positive emotions: exploring the other hemisphere in behavioral medicine. *Int J Behav Med*. 2005;12:50–58.
- Rensma P, Allessie M, Lammers W, Bonke F, Schalij M. Length of excitation wave and susceptibility to reentrant atrial arrhythmias in normal conscious dogs. *Circ Res*. 1988;62:395–410.
- Huikuri HV, Yli-Mäyry S, Linnaluoto MK, Ikäheimo MJ. Diurnal fluctuations in human ventricular and atrial refractoriness. *Pacing Clin Electrophysiol*. 1995;18:1362–1368.
- Liu L, Nattel S. Differing sympathetic and vagal effects on atrial fibrillation in dogs: role of refractoriness heterogeneity. *Am J Physiol*. 1997;273:H805–H816.
- Poldermans D, Fioretti P, Boersma E, Thomson I, Cornel J, tneCate F, Arnesse M, vanUrck H, Roelandt J. Dobutamine-atropine stress echocardiography in elderly patients unable to perform an exercise test: hemodynamic characteristics, safety, and prognostic value. *Arch Intern Med*. 1994;154:2681–2686.

20. Hsieh M, Chen S, Tai C, Tsai C, Prakash V, Yu W, Lir C, Ding Y, Chang M. Double multielectrode mapping catheters facilitate radiofrequency catheter ablation of focal atrial fibrillation originating from pulmonary veins. *J Cardiovasc Electrophysiol*. 1999;10:136–144.
21. Sears SF, Serber ER, Alvarez LG, Schwartzman DS, Hoyt RH, Ujhelyi MR. Understanding atrial symptom reports: objective versus subjective predictors. *Pacing Clin Electrophysiol*. 2005;28:801–807.
22. Stoney CM, Matthews KA, McDonald RH, Johnson CA. Sex differences in lipid, lipoprotein, cardiovascular, and neuroendocrine responses to acute stress. *Psychophysiology*. 1988;25:645–656.
23. Soufer R, MM B. The heart–brain interaction during emotionally provoked myocardial ischemia: implications of cortical hyperactivation in CAD and gender interactions. *Cleve Clin J Med*. 1996;20:1–5.
24. Chen YJ, Lee SH, Hsieh MH, Hsiao CJ, Yu WC, Chiou CW, Chen SA. Effects of 17beta-estradiol on tachycardia-induced changes of atrial refractoriness and cisapride-induced ventricular arrhythmia. *J Cardiovasc Electrophysiol*. 1999;10:587–598.

Key Words: atrial fibrillation • distress • happiness