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Lampert, Rachel Jamner, Lawrence Burg, Matthew et al.

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## Letters

# Triggering of Symptomatic Atrial Fibrillation by Negative Emotion



Negative emotions such as anger, anxiety, and sadness can precipitate ventricular arrhythmias (1) and myocardial infarction (2), but whether emotion may similarly trigger atrial fibrillation (AF) has not been systematically evaluated. Pharmacological autonomic manipulations alter atrial electrophysiology (3), suggesting that sympathetic arousal could trigger AF.

To evaluate whether emotion can trigger episodes of symptomatic AF, 95 patients with intermittentpersistent or paroxysmal AF who were in sinus rhythm at enrollment completed an electronic diary (eDiary) query of emotions at the end of each day, summarizing their emotions for that day, for 1 year. Patients also underwent monthly 24-h Holter monitoring, completing an eDiary twice per waking hour as prompted. With any symptoms, they recorded their heart rhythm on a standard nonlooping event monitor and completed an eDiary querying the preceding (proximal) 30 minutes (before calling in the event). Emotions reported on eDiary for the 30 minutes preceding AF were compared with those reported during 24-h monitoring during sinus rhythm (Table 1). Similarly, end-of-day emotion summaries for days preceding a day with AF were compared with end-of-day emotion summaries for the preceding days without AF (Table 2). Multiple imputations with data augmentation were performed to impute missing data for nightly and proximal diary data. After imputation, each "filled-in" data set was analyzed separately to examine the associations of AF events with proximal emotions and with end-of-day emotion summaries collected on the prior day using generalized estimating equations, and parameter estimates were averaged across data sets. Sensitivity analyses also were performed to examine robustness of conclusions to the missing data at random assumption.

Event monitors recorded 228 confirmed episodes of symptomatic AF. Of these, 163 episodes (in 34

subjects) had associated proximal recordings of emotion on eDiaries. A total of 12,597 emotion reports were completed on eDiaries during monitoring. There were 14,775 end-of-day summaries completed on eDiaries, of which 112 preceded days with episodes of AF (in 31 subjects).

There was a significant unadjusted increase in the likelihood of AF in association with endorsement of proximal sadness, anxiety, anger, and stress, with minimal difference after adjustment (Table 1). The likelihood of AF events was 85% lower after reports of happiness, and this remained significant after controlling for clinical factors and negative emotions. A "dose-response" relationship was observed, with the temporal association of AF increasing substantially as proximal emotional intensity increased (data not shown). In sensitivity analyses that incrementally weighted the probability of having an emotion in the imputation of missing data, the odds ratios for negative proximal emotions would have to be decreased by two-thirds and for happiness increased by 6 times for loss of significance to occur.

The endorsement of stress on the end-of-day emotion summaries almost doubled the likelihood of AF on the following day, with similar effects for anger. Adjustment had minimal effect (**Table 2**). A "doseresponse" relationship was observed for stress. In sensitivity analyses that incrementally weighted the probability of having an emotion in the imputation of missing data, the odds ratios for negative end-of-day emotions would have to be decreased by 5% for anger and by 20% for stress for loss of significance to occur.

On analysis of the subgroup of patients reporting at least 1 episode of AF on follow-up, results were unchanged for proximal and nightly emotions (data not shown).

In summary, this study systematically and prospectively showed that negative emotion can trigger symptomatic AF. Stress, anxiety, sadness, and anger each increased the likelihood of AF, whereas happiness was protective. These associations were seen for emotion in the period immediately preceding an AF event (proximal) and for the summary of emotions for the day preceding an episode of AF (for anger and stress).

Although previous landmark studies have drawn linkages between emotions and other cardiac events

TABLE 1 Proximal Emotions and Atrial Fibrillation				
	Unadjusted Odds Ratio Adjusted Odds Ratio	95% Confidence Interval	p Value	
Happiness	0.15	0.09-0.25	< 0.0001	
	0.12	0.06-0.22	< 0.0001	
Sadness	5.39	3.11-9.34	< 0.0001	
	5.59	3.20-9.75	< 0.0001	
Anger	3.94	2.12-7.34	< 0.0001	
	4.46	2.38-8.36	0.004	
Stress	2.92	1.52-5.59	0.001	
	3.07	1.53-6.13	0.002	
Impatience	2.92	1.52-5.59	0.001	
	3.07	1.53-6.13	0.002	
Anxiety	4.27	1.85-9.83	0.0008	
	4.41	1.80-10.78	0.001	
Hunger	0.93	0.64-1.36	0.72	
	0.98	0.68-1.40	0.90	

Odds ratios quantify the likelihood of atrial fibrillation after periods during which patients endorsed, compared with those during which they did not endorse, a particular emotion. Multivariable models adjusted for age, sex, use of betablockers, simultaneous alcohol intake, time of day, day of week (weekday/weekend), and season and included all emotions.

(1,2), data regarding preceding emotions in these earlier studies were collected up to 4 days later, resulting in the inability to exclude the potential of recall bias. In this analysis, the eDiary decreases recall bias because entries are immediate, but it does not eliminate it. However, emotions reported on the prospectively obtained, end-of-day summaries also predicted symptomatic AF on the following day. By decreasing recall bias, these data provide compelling evidence that emotions can trigger spontaneous clinical arrhythmia.

TABLE 2 End-of-Day Emotion Summary and Next-Day Atrial Fibrillation

	Unadjusted Odds Ratio Adjusted Odds Ratio	95% Confidence Interval	p Value
Good mood	0.82	0.53-1.27	0.38
	0.81	0.54-1.21	0.36
Sadness	1.22	0.78-1.89	0.39
	1.25	0.78-2.00	0.36
Anger	1.69	1.01-2.81	0.05
	1.73	1.04-2.90	0.04
Stress	1.82	1.16-2.84	0.009
	1.88	1.18-3.02	0.008
Impatience	1.44	0.98-2.11	0.07
	1.48	0.99-2.23	0.06
Worry	1.37	0.88-2.15	0.17
	1.44	0.89-2.34	0.14

Odds ratios quantify the likelihood of atrial fibrillation after periods during which patients endorsed, compared with those during which they did not endorse, a particular emotion. Multivariable models adjusted for age, sex, use of beta-blockers, simultaneous alcohol intake, day of week (weekday/weekend), and season and included all emotions.

These results have significant clinical implications for novel treatments for AF targeting the stress response. Stress reduction therapy benefits patients with coronary disease (4) and may decrease ventricular arrhythmias in patients with defibrillators (5).

Limitations include incomplete compliance (although similar to most diary-based studies). However, sensitivity analyses found the associations were robust even in the setting of nonrandom noncompliance. Because patients were not monitored continuously, the possibility that asymptomatic AF started earlier, leading to negative emotion, and then became symptomatic cannot be excluded. Finally, only symptomatic events were analyzed, because there were too few asymptomatic events recorded on Holter monitoring for meaningful analysis.

In conclusion, negative emotions including anger, anxiety, sadness, and stress trigger symptomatic AF, whereas happiness is protective. Future research should address whether stress reduction therapies can reduce recurrence of AF.

\*Rachel Lampert, MD Lawrence Jamner, PhD Matthew Burg, PhD James Dziura, PhD Cynthia Brandt, MD Haibei Liu, MPH Fangyong Li, MPH Theresa Donovan, BS Robert Soufer, MD

\*Section of Cardiology Yale University School of Medicine 789 Howard Avenue Dana 3 New Haven, Connecticut 06520

E-mail: rachel.lampert@yale.edu

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