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Stress-induced cardiac arrhythmias: The heart–brain interaction

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There exists a complex and dynamic interaction between the heart and brain especially in the setting of negative emotions. Stress, anger, and depression have all been shown to have a significant impact on cardiac arrhythmogenesis. Not only does negatively charged emotion result in coronary ischemia, platelet activation, vasoconstriction, alteration in hemodynamics and catecholamine release but it also has a significant effect on atrial and ventricular electrical indices [1–4] (Fig.). This is not where the story ends though, as it appears that cardiac afferent feedback mechanisms result in changes in the cortical regions, insula and anterior cingulate cortices in the brain [5].

Certain people are more aware of their heart beat and the presence of arrhythmias than others. This is likely as a result of enhanced afferent feedback to the anterior cingulate and insula cortices. Heart beat evoked potentials measured via electroencephalogram have been identified as a result of cardiac afferent feedback [5]. Negative emotion has an asymmetric effect on cortical activity resulting in activation of the right hemisphere more than the left. This feedback mechanism from cardiac afferents travels via the nucleus solitarius and likely other afferent pathways to the medulla, parabrachial nucleus, hypothalamus, and thalamus [6]. There does not appear to be one arrhythmia center in the brain but rather multiple areas that respond to and meet the behavioral demands. Stress results in an inhomogeneity of repolarization associated with a change in the left temporal region heart beat evoked potentials and an increase in T-wave amplitude [5].

Why this does happen and why are some people more susceptible to this? The autonomic nervous system (ANS) plays a critical role in modulating the neuro-cardiac axis and determines how a person responds to certain triggers. Even in the setting of a structurally normal heart, we can identify changes in the neuro-cardiac axis in response to stress and anger but it appears when there is a substrate for arrhythmia these effects can be detrimental [1,7,8]. There clearly is a difference between some people being more susceptible to the effects of ANS activation, irrespective of whether a structural abnormality is present [1]. Is this as a result of discrete differences in the ANS, different personality types, a specific, as yet unidentified change at a cellular level or a combination of all of these factors? We know that abnormal fluctuations of cellular ionic fluxes in certain in the setting of Long QT or

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catecholaminergic polymorphic ventricular tachycardia are more susceptible to changes in sympathetic input. Conversely, others are affected by increases in parasympathetic tone such as Brugada syndrome or Long QT type 3. But why, in the absence of an obvious identifiable genetic or cellular susceptibility, are certain people more at risk of stress- and anger-triggered arrhythmias that put them at risk of sudden death?

It is well established there is a difference between the genders with certain disease processes such as ischemic heart disease [9] and now it is becoming apparent that there are differences in gender and the risk of arrhythmogenesis [10]. As outlined by Dr. Lampert in this issue of the journal [11], there is a significant lack of data on women regarding stress and ventricular arrhythmias, and it is important to pursue more research in this area. We are yet to clearly identify why the ANS behaves heterogeneously in certain patients, even in the absence of structural heart disease.

It is not clear how best to screen patients for anger and stress-induced events. Assessing excessive sympathetic input has been largely performed by traditional methods such as heart rate variability, T wave alternans, skin conductance, hemodynamic changes, and baroreceptor sensitivity. Heart rate variability proved to be an important predictor of mortality post-myocardial infarction [12]. T wave alternans is a beat to beat variation of the T wave associated with dispersion of repolarisation heterogeneity. It occurs as a result of fluctuations of ionic currents that are at a microvolt level that may not be visible to the eye. Rapid heart rates can result in overloading of the sodium–calcium exchange mechanism which can cause alternans of calcium cycling.

Other surrogates used in the assessment of vagal activity such as heart rate response to blockade of muscarinic receptors, and post-exercise heart rate recovery are indirect ways of assessing parasympathetic activity. Functional MRI is a very elegant way of assessing the heart–brain interaction in response to stress, but this is more of scientific interest rather than a diagnostic management tool [13].

We know that negative emotion results in release of catecholamines, increase in sympathetic input and decrease in parasympathetic tone. This imbalance in the ANS has all been shown to occur as a result of cardiac pathology when the exposure is a result of a chronic or persistent imbalance [14]. Structural changes in the stellate ganglion and cardiac nervous system occurs as a result of chronic increases in sympathetic input and results in arrhythmogenesis [15]. Removal of this excessive input to the heart by either thoracic epidural anesthesia or surgical extrication of the sympathetic paravertebral chain from the stellate ganglion to T4 has an anti-fibrillatory effect.

Stress and anger not only impact ventricular arrhythmias but also atrial arrhythmias. Many studies in relation to stress events and arrhythmias are subject to recall bias but Lampert et al., [16] performed a prospective study demonstrating that negative emotional triggers were identified as triggers of atrial fibrillation. Reducing sympathetic drive in atrial fibrillation and enhancing parasympathetic effects have been shown to reduce atrial arrhythmogenesis [17]. It is a balance though, as excessive vagal input can also result in changes in atrial effective refractory periods, atrial fibrillation induction and duration [18].

Interestingly, not only does stress increase the frequency of cardiac arrhythmias but also the lethality of ventricular arrhythmias [7]. So focussing on prevention or treatment of stress, anger, and depression could be paramount to the electrophysiologists' management of their patients. Whether psychological interventions can result in less arrhythmias is not clear but there are small studies to suggest that it may [19,20]. Referring our patients for alternative therapies may become daily practice but is this something that our health service should provide or an optional extra for our patients? Can we afford to provide this for our patients and would it result in a reduction in admissions as a result of reduction in arrhythmic events [21]? Perhaps at a national level, current introductions in yoga and mindfulness/meditation education in schools could in the future result in people who are less susceptible to sudden cardiac death from negative emotion [22]. Larger, randomized, prospective trials are needed to understand this area to enable identifying who is at risk and if treating them with psychological interventions could result in reductions in arrhythmia burden and lethality.

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Fig.

Brain–heart interactions and how stress results in a dynamic alteration in afferent and efferent cardiac signaling. EADs, early after-depolarizations; DADs, delayed after-depolarizations; VT/VF, ventricular tachycardia/ventricular fibrillation; CPVT, catecholaminergic polymorphic ventricular tachycardia, DOR, dispersion of repolarization. Authors thank Rajesh Kumar, Ph.D., (UCLA) for the fMRI brain image and Ravi Dave, M.D., (UCLA) for the ventriculogram image.