High dose group (n = 6) received 2 W/cm^2 for 2 minute with 0.7 mL microbubbles IV. Perfusion was measured before and after AVUS with contrast-enhanced ultrasound (CE-US) and power Doppler (PD-US). Peak enhancement (PE) and perfusion index (PI) were measured from each US mode. Histology after sacrifice or natural death was compared to pre/post US. Analysis of H&E and trichrome sections was evaluated for percent area of hemorrhage and findings of tissue injury and repair including inflammation, necrosis, and fibrosis. RESULTS/ANTICIPATED RESULTS: After high dose AVUS, PE, and PI of CE-US decreased from baseline by an average of 33.3% and 29.7%, respectively. Histology showed extensive tissue injury (hemorrhage, necrosis, fibrosis) in 58% of tumor cross-sectional area. Conversely, low dose AVUS increased PE and PI of CE-US by an average of 39.3% and 67.8%, respectively. Histology showed smaller areas of microhemorrhage Versus large pools of hemorrhage (only 17% area). PD-US changes were similar to CE-US. DISCUSSION/SIGNIFICANCE OF IMPACT: In summary, the opposing effects of AVUS observed at 2 doses allows for multiple roles in tumor therapy. Enhanced perfusion at a low dose may improve drug delivery or radiation therapy. Whereas, vascular disruption at high doses of AVUS may allow noninvasive ischemic therapy. Furthermore, AVUS is ripe for translation given the use its component parts clinically: low-intensity long-tone burst for physiotherapy and microbubbles as an US contrast agent. Thus, AVUS should be evaluated for translation of its differential effects into noninvasive therapies for HCC and other tumors.

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Cardiac injury due to *Streptococcus pneumoniae* invasion during severe pneumococcal pneumonia in a novel nonhuman primate model

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OBJECTIVES/SPECIFIC AIMS: The aims of this study are (1) to develop and characterize a novel nonhuman primate model of pneumococcal pneumonia that mimics human disease; and (2) determine whether *Streptococcus pneumoniae* can: (a) translocate to the heart, (b) cause adverse cardiac events, (c) induce cardiomyocyte death, and (d) lead to scar formation during severe pneumonia in baboons. METHODS/STUDY POPULATION: Six adult baboons (*Papio cynocephalus*) were surgically tethered to a monitoring system to continuously assess their heart rate, temperature, and electrocardiogram (ECG). A baseline transthoracic echocardiogram, 12-lead ECG, serum troponin-I levels, brain natriuretic peptide, and heart-type fatty acid binding protein (HFABP) levels were obtained before infection and at the end of the experiment to determine cardiovascular damage during pneumococcal pneumonia. Animals were challenged with 108 colony-forming units of *S. pneumoniae* in the right middle lobe using flexible bronchoscopy. Three baboons were rescued with ampicillin therapy (80 mg/kg/d) after the development of pneumonia. Cardiac damage was confirmed by examination of tissue sections using immunohistochemistry as well as electron and fluorescence microscopy. Western-blots and tissue staining were used to determine the presence of necroptosis (RIP3 and pMLKL) and apoptosis (Caspase-3) in the cardiac tissue. Cytokine and chemokine levels in the heart tissue were determined using Luminex technology. RESULTS/ANTICIPATED RESULTS: Four males (57%) and three (43%) females were challenged. The median age of all baboons was 11 (IQR, 10-19) years old, which corresponds to a middle-aged human. Infected baboons consistently developed severe pneumonia. All animals developed systemic inflammatory response syndrome with tachycardia, tachypnea, fever, and leukocytosis. Infection was characterized by initial leukocytosis followed by severe leukopenia on day 3 postinoculation. Non-specific ischemic alterations by ECG (ST segment and T-wave flattering) and in the premortem echocardiogram were observed. The median (IQR) levels of troponin I and HFABP at the end of the experiment were 3550 ng/mL (1717–5383) and 916.9 ng/mL (520.8–1323), respectively. Severe cardiomyopathy was observed using TEM and H&E stains in animals with severe pneumonia. Necroptosis was detected in cardiomyocytes of infected animals by the presence of pMLKL and RIP3 in cardiac tissues. Signs of cardiac remodeling indicated by disorganized collagen deposition was present in rescued animals but not in the other animals. DISCUSSION/SIGNIFICANCE OF IMPACT: We confirmed that baboons experience cardiac injury during severe pneumococcal pneumonia that is characterized by myocardial invasion, activation of necroptosis, and tissue remodeling in animals rescued by antimicrobial therapy. Cardiac damage by invading pneumococci may explain why adverse cardiac events that occur during and after pneumococcal pneumonia in adult human patients.

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Central autonomic network dysfunction implicated in alcohol-related intimate partner violence

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OBJECTIVES/SPECIFIC AIMS: Most incidents of partner violence occur when one or both partners have been drinking, however, the mechanism through which this association exists is unclear. The neural circuits that support self-regulation of emotion and social behavior, as well as autonomic influences on the heart, are co-localized in the brain and represent an integrated bidirectional regulatory system. These physiological regulatory processes are mediated by a neural substrate known as the central autonomic network which includes the peripheral autonomic nervous system. The central autonomic network modulates biobehavioral resources in emotion by flexibly responding to physiological arousal in response to changing situational demands, and serves a fundamental role in emotion regulation and goal-directed motor behavior, and this circuit can be indexed with heart rate variability (HRV). METHODS/STUDY POPULATION: In total, 17 distressed violent (DV) partners (11 females, 6 males) were matched to a sample of distressed nonviolent (DNV) partners (7 female, 6 males) were matched on age, sex, and relationship satisfaction and participated in a placebo-controlled alcohol administration study with an emotion-regulation task during which electroencephalography, HRV, and galvanic skin response (GSR) measures were collected. In the alcohol condition, participants were administered a mixture of 100 proof vodka and cranberry juice calculated to raise their blood alcohol concentration to 0.08%. In the placebo condition, participants consumed a volume of juice equivalent to that consumed in the alcohol condition, but without alcohol. Alcohol and placebo conditions were counter-balanced across participants as were the presentation the blocks of evocative and neutral partner stimuli and emotion-regulation condition (watch vs. do not react). RESULTS/ANTICIPATED RESULTS: Results show that DV partners show greater cortical arousal than DNV partners on measures event-related spectral perturbations, which are mean log event-loced deviations from baseline-mean power at each frequency of the electroencephalography power spectra, when intoxicated and viewing evocative partner stimuli in the "do not react" emotion regulation condition. Results also show a statistically significant 2 (alcohol vs. placebo) × 2 (watch vs. do not react) × 2 (DV partners vs. DNV partners) interaction of the respiratory sinus arrhythmia measure of HRV when viewing evocative partner behavior ($F = 7.102$, $p = 0.019$, partial $\eta^2 = 0.353$). Findings indicate that DV partners have lower HRV than DNV partners across conditions, but particularly when acutely intoxicated and trying not to react to their partners' evocative behavior. Similarly, results also show a statistically significantly 2 (alcohol vs. placebo) × 2 (watch vs. do not react) × 2 (DV partners vs. DNV partners) interaction on GSR ($F = 71.452$, $p = 0.000$, partial $\eta^2 = 0.749$). GSR findings indicate that DV partners also have lower GSR when acutely intoxicated and trying not to react to their partners' evocative behavior. DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest that increases in intimate partner violence under acute alcohol intoxication may be the result of dysfunction of the central autonomic network, especially when DV partners are trying to suppress a behavioral response to their partners' evocative behavior in conflict. The neurophysiological patterns evidenced by DV partners is consistent with a state of vigilance to threat, and reduced ability inhibit prepotent, but inappropriate responses. They also suggest that HRV may be an important target for intervention with partner with a history of intimate partner violence. One method may be heart rate variability biofeedback which has been shown to increase parasympathetic nervous system functioning, autonomic stability, and emotion regulation.

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Characterizing specialized pro-resolving lipid mediators and synthesis pathways in veterans with peripheral artery disease

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OBJECTIVES/SPECIFIC AIMS: Specialized pro-resolving lipid mediators (SPM) actively counter proinflammatory cascades. A deficit of SPMs is one possible mechanism through which inflammation leads to the development of atherosclerotic disease. The purpose of this study is to characterize the profiles

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