Cardiac Consequences of Autonomic Dysreflexia in Spinal Cord Injury

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Abstract—Autonomic dysreflexia (AD), which describes episodic hypertension, is highly prevalent in people with spinal cord injury (SCI). In non-SCI, primary hypertension depresses cardiac contractile reserve via β-adrenergic mechanisms. In this study, we investigated whether AD contributes to the impairment in cardiac contractile function that accompanies SCI. We induced SCI in rodents and stratified them into sham, SCI, or SCI plus repetitive induction of AD. At 6-week post-SCI, we assessed cardiac function using in vivo (speckle-tracking echocardiography), ex vivo (working heart), and molecular approaches (Western blot). We also provide unique translational insight by comparing the relationship between the number of daily AD events and cardiac function in 14 individuals with cervical SCI. We found SCI and SCI plus repetitive induction of AD exhibited a reduction in left ventricular dimensions at 6-week post-SCI versus preinjury (P<0.049). Compared with sham, SCI exhibited a reduction in peak radial strain along with a down and rightward shift in the Starling curve (P<0.037), both of which were further depressed in SCI plus repetitive induction of AD (P<0.042). In response to β-adrenergic stimulation, SCI plus repetitive induction of AD exhibited an attenuated increase in contractile indices (P<0.001), despite no differences in β-receptor expression within the left ventricle. Our clinical data confirm our experimental findings by demonstrating significant associations between the number of daily AD events and markers of systolic and diastolic function along with left ventricular mechanics. Here, we provide the first evidence from a translational perspective that AD exerts insidious effects on cardiac function in rodents and humans with SCI. (Hypertension. 2016;68:00-00. DOI: 10.1161/HYPERTENSIONAHA.116.07919.)

Key Words: cardiovascular diseases ■ echocardiography ■ hypertension ■ spinal cord injuries ■ systole

Hypertension is the number one modifiable risk factor for cardiovascular disease (CVD). Hypertensive heart diseases are characterized by a constellation of abnormalities that include hypertrophic remodeling,1 perivascular and interstitial fibrosis,2 systolic and diastolic function,3 attenuated β-adrenergic responsiveness,4,5 and ultimately the clinical manifestation of heart failure.6 The exact clinical presentation of hypertensive heart disease can range from concentric remodeling with preserved ejection fraction (EF) to dilated remodeling with reduced EF. Although the classical paradigm of the progression from concentric remodeling to dilated cardiac remodeling (ie, progression to failure) suggests that such a transition does not occur without an interval myocardial infarction,7 it is now well recognized that clinical heart failure can occur in either scenario.8

Another population with a dramatically increased risk for CVD is spinal cord injury (SCI).9,10 Increased risk for CVD is particularly pronounced in those with high-lesion SCI.11 A likely contributing factor to this elevated risk is that individuals with high-lesion SCI experience repetitive and severe bouts of episodic hypertension (≤300 mm Hg) during autonomic dysreflexia (AD), which can occur in excess of 40× per day.12,13 AD occurs when there is damage to the spinal cord tissue, which induces a myriad of systemic changes, including a loss of descending sympathetic inhibition,14 changes in spinal sympathetic circuitry,15,16 and hypertsensitization of the peripheral adrenergic receptors (ARs).17,18 AD has been directly implicated in acute clinical cardiovascular events post-SCI, such as cerebral hemorrhage,19 myocardial infarction,20 and even death.21 There are also likely to be long-term deleterious consequences of AD on the cardiovascular system. Evidence supporting this postulate is that individuals with white coat hypertension (persistently elevated blood pressure [BP] in the doctor’s office, although BP is otherwise normal) are known to exhibit an increased risk for CVD.22 Moreover, by repetitively inducing AD on a daily basis in rodents with high-thoracic SCI, we have demonstrated the potential systemic consequences of episodic hypertension by reporting...
that AD impairs mesenteric endothelial function. The effects of chronic AD on the heart, however, have yet to be directly investigated. We think chronic exposure to episodic hypertension because of AD may contribute to cardiac dysfunction after SCI because both clinical and preclinical studies reveal major similarities in the cardiac phenotype that develops in both hypertensive heart disease and SCI. As such, the episodic hypertension commonly experienced in people with SCI during frequent bouts of AD may provide a potential explanation for the increased risk of heart disease in this population. Moreover, understanding how AD affects cardiac function in SCI may provide novel insight into the cardiac consequences of other conditions that are characterized by paroxysmal hypertension, such as preeclampsia or gestational hypertension, as well as providing information on the relative hypertensive stimulus required for hypertensive heart disease.

In this study, we directly assessed the cardiac consequences of AD in rodents with high-thoracic SCI by repetitively induced colorectal distension (CRD), a clinically relevant and reliable AD stimulus. We also demonstrate the clinical relevance of our animal model and provide direct translational insight into our experimental findings by investigating the relationship between the number of daily AD events and cardiac function in a group of 14 individuals with cervical SCI.

Methods

Experimental Design

Experiments were conducted on 24 adult male Wistar rats (250–300 g; Harlan Laboratories). Animals were randomly assigned to 1 of 3 groups: uninjured control (CON; n=8), T3 complete SCI (SCI; n=8), or T3 complete SCI plus daily induction of AD (SCI-AD; n=8). All procedures were conducted in strict accordance with the Canadian Council for Animal Care and approved by the University of British Columbia Animal Care Committee. At pre-SCI, all animals underwent in vivo echocardiography to assess cardiac structure and function. At study termination (6-week post-SCI), animals underwent in vivo echocardiography followed by excision of the heart for ex vivo hemodynamic and histological analysis. The hearts were then immediately flash-frozen in liquid nitrogen for subsequent Western blot analysis. A separate group of animals (n=3) underwent implantation of telemetric BP monitors into the abdominal aorta to confirm our AD protocol produced an efficacious pressor response. In these animals, the telemetric devices were implanted 2 weeks before SCI. Our methods of telemetric implantation are published elsewhere. We also included 7 uninjured body mass–matched animals at the experimental end point that underwent working heart assessments and Western blot analysis.

To validate the efficacy of our animal model and to examine the clinical applicability of our findings, we also investigated the relationship between the number of daily AD events cardiac function in 14 individuals with cervical SCI (injury level=C4–C8, 4 females, aged 41±12 years, time since injury=13±9 years, mass=73±15 kg, supine mean arterial BP=85±17 mm Hg). No individual had a history of CVD, hypertension, or type II diabetes mellitus. Four individuals were taking midodrine hydrochloride for hypotension. The number of daily AD events was determined by 24-hour BP monitoring, and cardiac function was assessed using transthoracic echocardiography. The neurological level and completeness of injury was confirmed using the International Standards for Neurological Classification of SCI. Ethics approval for the clinical portion of this study was granted by the University of British Columbia Clinical Research Ethics Board.

Surgery and Animal Care

Rats were anesthetized with ketamine hydrochloride (70 mg/kg, IP; Vetalar; AVP; Langley, Canada) and medetomidine hydrochloride (0.5 mg/kg, IP; Domitor; AVP). After a dorsal midline incision at the C8–T3 vertebral levels, the dura was opened at the T2–T3 intervertebral space, and the spinal cord was completely transected using microscissors at the T3 spinal level. Complete transaction was confirmed by 2 surgeons via visual separation of the rostral and caudal stumps, and Gelfoam (Pharmacia & Upjohn Company, Pfizer, NY) was placed between the stumps to achieve hemostasis. This procedure is well characterized in our laboratory.25–35

Repetitive Induction of AD

Starting at 14-day post-SCI, the SCI-AD group received six 10-minute bouts of CRD 5 days per week for 4 weeks. Bouts 1 to 3 occurred immediately after each other followed by a 15-minute break after which a further 3 bouts were completed. To initiate CRD, a small deflated plastic balloon (the balloon tip of a Swan-Ganz catheter; 10 mm in length) was inserted rectally for a distance of 1.5 cm, according to standard procedures. After 10 minutes of hemodynamic stabilization, the first bout of CRD was initiated. For this, the balloon was infused with 2 mL of air for 10 s, and distension was maintained for 10 minutes. At the end of the 10 minutes, the balloon was deflated, and the CRD procedure was immediately repeated. We found this deflation and reinflation of the balloon was necessary because our telemetric BP data consistently indicated that the pressor response to CRD gradually subsided during a 10-minute period such that by 10-minute post-infusion, the BP was no longer different from baseline. On reinflation, however, the pressor response returned. An example BP trace during 3 bouts of repeated AD is displayed in Figure 1. All CRD procedures were performed in freely moving unanesthetized animals within their home cages.

In Vivo Echocardiography Rodent

Echocardiography was performed with a commercially available imaging system (Vivid 7, GE Healthcare; Milwaukee, WI) and 11.5 MHz pediatric sector transducer, as described previously in our laboratory.25 Briefly, rats were anesthetized with isoflurane (initial chamber induction at 4% isoflurane with 2 L/min oxygen, followed by maintenance on a Bain system at 1.5%–2% isoflurane with 1.5–2 L/min oxygen), placed in dorsal recumbency, and secured to a custom-made rodent echo platform that was able to tilt laterally to aid image acquisition. Body temperature was monitored using a rectal probe and maintained via a recirculating water-filled heating mattress at 36.5°C and 37.5°C. The heart rate was maintained between 300 and 350 bpm. Standard measures of left ventricular (LV) structure and function were assessed using M-mode echocardiography averaged

Figure 1. Example blood pressure (BP) trace obtained from 1 animal during our repetitive colorectal distension (CRD) protocol. Note that the pressor response to CRD gradually diminished during the CRD bout despite no leak, and the balloon remaining inflated. For this reason, we completely deflated and reinflated the balloon with 2 mL of air every 10 min to ensure that an efficacious pressor response was maintained throughout the 3 bouts of CRD.
across 5 cycles at end expiration from the parasternal short-axis view. Radial strain, an in vivo approximation of contractile function that is angle of insonation independent,\(^1\) was derived from 2-dimensional speckle-tracking analysis of parasternal short-axis images at the level of the papillary muscle according to standard guidelines,\(^2\) using commercially available software (EchoPAC PC; GE Medical Systems, Milwaukee, WI). Radial strain was normalized to percentage of cardiac cycle using linear interpolation to account for between-group differences in heart rate. An average of 5 cardiac cycles with a minimum frame rate of 90 frames per second was used for analysis.

**In Vivo Echocardiography Human**

Imaging was performed on the same commercially available system as the rodents but with a different probe (dual harmonic 1.7/3.4 MHz transducer). Indices of LV structure were measured at end diastole (d) and end systole (s) from the parasternal long-axis view. Relative wall thickness (RWT) was indexed to body surface area and calculated as \((2 \times \text{LVPWd}/\text{LVId})\), where LVPWd represents the LV posterior wall thickness in diastole and LVId represents the LV internal diameter during diastole. Modified single-plane Simpson method was used to analyze apical 4-chamber views to determine end-diastolic volume and end-systolic volume, and for the subsequent calculation of stroke volume, cardiac output, and EF. Global diastolic function ratio (function of early-to-late transmitral filling; E/A ratio) was determined from pulsed-wave Doppler at the tips of the mitral valve leaflet. Radial and longitudinal strain was determined as outlined above using the same software as described previously by our group\(^3\) and according to the established guidelines.\(^4\) Because of insufficient image quality in 2 individuals, strain data are provided for 12 individuals only.

**Ex Vivo Working Heart**

Rats were deeply anaesthetized with isoflurane, and hearts were excised and cleaned in ice-cold oxygenated Chenoweth–Koelle solution. Hearts were quickly hung and perfused with oxygenated Chenoweth–Koelle buffer. LV pressure was measured via a transducer attached to a 20-gauge needle inserted through the apex of the heart. Hearts were paced at 300 bpm. Left atrial filling pressure was initially maintained at 7 mmHg and then gradually stepped up and down (±1 mmHg) every 3 minutes to cover the physiological range. LV developed pressure and the rates of contraction (+dP/dt) and relaxation (−dP/dt) were measured continuously. Function curves were repeated 3× for each animal. The final 20 beats from each left atrial filling pressure were extracted using a custom program and stored for off-line analyses. Next, we tested contractile reserve by elevating cardiac inotropic via isoproterenol infusion at a concentration of \((1 \times 10^{-7} \text{mmol/L})\) and repeating the function curves. We chose this concentration because we have previously found that this generates the greatest change in +dP/dt.\(^2\) At the end of the experiments, the great vessels were dissected, and the heart was weighed after which the heart was flash-frozen over liquid nitrogen and stored at −80°C.

**Western Blot**

Fifty milligrams of tissue was dissected from the LV free wall at the midheart level (ie, half way between the base and the apex) and diluted in 400 μL of homogenizing buffer. Samples were coalesced using a custom-built homogenizer and sonicated until sufficiently uniform. Protein concentration within each sample was determined using the Bradford assay (Sigma-Aldrich, Inc, St. Louis, MO) with bovine serum albumin as the standard. On the basis of the Bradford assay, 10 mg of protein for each sample was then separated by 10% SDS-PAGE and transferred onto nitrocellulose membranes. Membranes were first blocked using 5% nonfat dry milk in Tris-buffered saline–Tween (pH 7.6, 20 mmol/L Tris HCl, 137 mmol/L NaCl, and 0.2% Tween 20) and then probed with a polyclonal antibody against either β1 (Santa Cruz Biotechnologies sc-568; 1:500) or β2 (Santa Cruz Biotechnologies sc-569; 1:500)–ARs at 4°C overnight. After a 30-minute wash in Tris-buffered saline–Tween, membranes were incubated with secondary antibodies and detected using an enhanced chemiluminescence detection reagent (GE Healthcare, Baie d’Urfe QC) according to the manufacturer’s guidelines. Membranes were then stripped and reprobed using a polyclonal primary antibody against GADPH (Santa Cruz Biotechnologies sc-25778; 1:2000), followed by incubation with secondary antibody, and detected according to the above procedures.

**Twenty-Four-Hour Ambulatory BP Monitoring (Human)**

BP monitoring was performed for a 24-hour period using the Meditech Card(Xplore device (Meditech, Budapest, Hungary). The device was fixed with appropriate cuff sizes to the nondominant arm and preprogrammed to record BP and heart rate every 15 minutes from 8 am until 7 pm, and every 60 minutes at all other times (to avoid sleep disruption). Participants were additionally able to self-initiate a measurement if they experienced symptoms of AD. Baseline BP was defined as the average of 3 consecutive resting BPs while seated in the morning (preprogrammed BP measures). Baseline BP was used to assess the number of AD during the day, where AD was defined as an increase in systolic BP >20 mmHg from baseline. This protocol is similar to what we have used previously in the clinical SCI population.\(^5\)

**Statistical Analyses**

Between-group differences for in vivo echocardiography and β-AR protein expression were assessed using a 2-factor repeated-measure ANOVA, with 1 factor for time/receptor and 1 factor for group. Between-group differences in peak radial strain at study termination were analyzed with a 1-way ANOVA. Normalized radial strain was analyzed using a 2-factor repeated-measure ANOVA, with 1 factor for percentage cardiac cycle and 1 factor for group. Working heart data were analyzed using mixed-model regression to compare differences in response variable (ie, LV developed pressure/+dP/dt−/dP/dt) by left atrial filling pressure, using group as the independent variable. For the clinical data, multiple linear regression was performed between the number of AD events, age, and selected cardiac indicator. Post hoc testing was conducted with a Bonferroni correction. Statistical analyses were conducted using STATIA 12.0. Significance was set at \(P<0.05\).

**Results**

**Chronic Repetitive AD Does Not Exacerbate SCI-Induced Impairments in Cardiac Structure**

Echocardiography-derived cardiac parameters for SCI- and SCI-AD pre-SCI and 6-week post-SCI are shown in Figure 2. There was a main effect for time on end-diastolic volume, stroke volume, LVPWT, and RWT (all \(P<0.0488\)) but no significant group or interaction effects. There were no significant differences in end-systolic volume or EF across time or between groups. There were no differences between SCI and SCI-AD at the experimental end point for body mass (365±26 g versus 385±31 g, respectively) or heart mass (1.21±0.06 g versus 1.18±0.13 g, respectively). Body mass and heart mass in both the SCI groups were not different from control (390±23 and 1.14±0.07 g, respectively).

**Chronic Repetitive AD Further Impairs LV Mechanics Beyond SCI Alone**

Peak radial strain was reduced in SCI (n=6) and SCI-AD (n=5) compared with sham (\(P<0.001\)) but was not different between SCI groups. When normalized for percentage of cardiac cycle, SCI-AD exhibited reduced radial strain between 20% to 33% and 27% to 68% of the cardiac cycle relative to SCI and CON, respectively (all \(P<0.042\); Figure 3). SCI also exhibited a lower radial strain between 37% and 76% of the cardiac cycle relative to CON (all \(P<0.037\)).
Chronic Repetitive AD Exacerbates Basal Cardiac Contractile Dysfunction

Modified Starling curves for SCI and SCI-AD obtained during the working heart preparation alone or under β-adrenergic stimulation with isoproterenol are shown in Figure 4. Compared with CON, the magnitude of increase in LV developed pressure in response to stepped increases in left atrial filling pressure was attenuated in SCI (P = 0.017) and was further attenuated in SCI-AD versus SCI (P = 0.055). Similarly, the degree of increase in +dP/dt was also attenuated in SCI versus CON (P = 0.001) and further attenuated in SCI-AD versus SCI (P = 0.017). For −dP/dt, however, the magnitude of increase was only attenuated in SCI-AD versus CON (P = 0.005).

Chronic Repetitive AD Depresses β-AR Responsiveness but Does Not Alter β-AR Protein Content

Under β-adrenergic stimulation with isoproterenol, the magnitude of increase in LV developed pressure, +dP/dt, and −dP/dt was attenuated in SCI-AD versus SCI and CON (all P < 0.001; Figure 4D through 4F). Western blot analysis revealed no significant changes in β1- or β2-AR expression in the LV in either SCI or SCI-AD (Figure 5; all P > 0.64).

Clinical Findings

The number of daily AD events ranged from 1 to 16, with an average of 8 events. Daily average systolic BP ranged from 90 to 130 mm Hg, with an average of 107 mm Hg.
In multiple regression analyses adjusted for age and average systolic BP, number of daily AD events was inversely related to EF ($r^2=0.78$, $P<0.001$), early filling velocity during diastole ($r^2=0.48$, $P=0.051$), basal radial strain ($r^2=0.58$, $P=0.037$, $n=12$), and positively related to longitudinal strain ($r^2=0.53$, $P=0.042$, $n=12$) and RWT ($r^2=0.54$, $P=0.035$). Age was only a significant predictor for EF ($P=0.038$). Daily average systolic BP was only a significant predictor for RWT ($P=0.024$). Regression analyses for the unadjusted models (ie, number of AD events on cardiac indices) for selected cardiac indices are summarized in Figure 6.

**Discussion**

We report for the first time that repetitive over induction of AD in SCI impairs LV contractility beyond what is typically observed after SCI. Furthermore, our pharmacological and molecular biological data suggest that AD desensitizes $\beta$-AR and thus may share similar mechanisms to $\beta$-AR dysfunction observed in primary hypertension. Importantly, we also demonstrate that our findings in the rodent model translate to the clinical population because we found significant associations between the number of daily AD events and markers of systolic and diastolic function along with LV mechanics. Together these findings provide a direct link between AD and...
cardiac dysfunction, represent a potential mechanism for the accelerated development of heart disease after SCI, and validate an animal model for subsequent studies to investigate the effects of SCI and AD on cardiovascular outcomes.

The major finding of the current experiment is that AD induces a similar attenuation of β-AR responsiveness to isoproterenol as that which occurs in primary hypertension, suggesting a lack of contractile reserve. That we observed no decrease in β-AR receptor expression within samples of the LV in either SCI or SCI-AD relative to CON supports the contention that AD reduces the sensitivity of the cardiac β-ARs.

From a clinical point of view, the finding that AD causes β-AR dysfunction has important consequences because β-AR dysfunction is known to precede the development of overt cardiomyopathy and has been established as a critical target to reverse heart failure. Because essential hypertension...
has been linked to elevated sympathetic drive, others have suggested that cardiac impairments may in fact be a result of catecholamine-induced β-AR desensitization. This argument is supported and extended by the current experiments because we have previously shown that our animal model of induced AD is known to result in episodic hypertension secondary to increased renal sympathetic nerve activity. Furthermore, both preclinical and clinical studies have demonstrated increased levels of circulating catecholamines during episodes of AD. Thus, we posit a potential mechanism, whereby the increase in sympathetic firing during AD results in aberrant spikes of circulating catecholamines, which ultimately lead to β-AR desensitization and impaired inotropic reserve.

A second major finding of this study is that our traditional ex vivo techniques and our novel assessment of in vivo radial strain both indicate that basal contractility is reduced in SCI and further reduced in SCI-AD. Remarkably, our clinical data, which also demonstrate that those with a higher daily incidence of AD exhibit impaired systolic and diastolic cardiac function along with reduced longitudinal and radial strain, imply that our experimental findings extend to the clinic. In hypertension, basal contractility (characterized mostly by reduced EF) can be either preserved or reduced. Typically, reduced EF is associated with an eccentrically remodeled (ie, dilated) ventricle, and preserved ejection is associated with a concentrically remodeled ventricle. In this study, our rodent data revealed preserved EF in SCI and SCI-AD. In our human data, although we found more AD was associated with lower EF, no individual met the clinical cutoff for defining low EF (ie, <50%). Interestingly, both our rodent and clinical data indicate that AD exacerbates SCI-induced reductions in LV strain. That EF seems relatively well preserved in rodents and humans with SCI in the face of reduced LV radial and longitudinal strain is likely because of LV strain being more sensitive to detect early impairments in contractile function in the setting of preserved ejection. In this respect, recent evidence in primary hypertension suggests that the development of short-axis dysfunction (ie, reduced radial) may indicate the transition point from hypertensive heart disease to heart failure. Thus, a natural extension of this work would be to investigate whether longer duration induction of AD in rodents is associated with reduced EF.

Our third major finding was that repetitive AD did not reverse or exacerbate inward concentric remodeling of the LV after SCI in rodents but did seem to in humans, as evidenced by a significant positive association between the number of AD events and RWT. This differential response in our rodent study and clinical comparison may be because of the relatively short nature of the induced AD stimulus in rodents, which induced functional changes but may have been too brief to induce structural changes. Inward remodeling post-SCI is due primarily to the dramatic loss of preload, which occurs secondary to decentralization of vasculature. Some have suggested that this inward remodeling may be compensatory to maintain LV wall stress. However, we, and others, have clearly demonstrated that such atrophic remodeling is associated with fibrotic remodeling of the extracellular matrix, which likely exacerbates impaired contractile function, and thus increases the risk of heart failure. It is interesting to note that the repetitive elevations in arterial BP that occurred during AD did not seem to produce long-term cardiac benefits from enhanced preload, likely because we have previously shown that repetitive CRD does not influence resting arterial BP. Thus, the transient nature of such elevations in arterial BP during CRD is likely offset by the chronic hypotension, which occurs in our injury model.

In this study, we chose to induce AD for 60 minutes per day for a 4-week period beginning at 14-day post-SCI. The rationale for the 14-day start point is based on our previous rodent experiments that demonstrate that reorganization of spinal sympathetic pathways, which are critical for the AD reflex to function, is not developed until ≈ 14-day post-SCI. Indeed, although AD can occur acutely post injury (because of acute loss of sympathoinhibition), telemetric studies performed in rodents by our laboratory and others reveal that both spontaneous AD and the pressor response to CRD only begin to manifest at 14-day post-SCI. The rationale for the 60-minute time period of induced AD for 4 weeks was chosen to represent a chronic intervention because it was double the stimulus of our previous study, which revealed that 30 minutes per day of induced AD for 14-day post-SCI impaired endothelial function, and because 4 weeks in a rodent approximates 2 years in humans. Moreover, 60 minutes per day represents the maximum time it takes for most individuals with SCI to complete their bowel routines. That we did not find any structural alterations in the heart of our SCI animals exposed to repetitive AD (but did in our humans with SCI), however, suggests that a 4-week AD induction period may have been too brief. Thus, a natural extension of this study would be to investigate the true long-term consequences of chronic AD on cardiovascular outcomes in rodents with SCI.

In conclusion, we provide the first critical evidence linking episodic hypertension to the development of cardiac dysfunction after SCI. That we observed impairments in inotropic reserve with no change in β-AR receptor content suggests a scenario, whereby the transient and dramatic elevation in sympathetic activity during AD causes an exaggerated release of catecholamines, which ultimately serves to reduce β-AR sensitivity. Our clinical comparison indicates that the present rodent findings may extend to the clinical SCI population and represents a critical step in revealing the underlying mechanisms responsible for this population's dramatic risk of heart disease.

**Perspectives**

Heart disease is a leading cause of death in people with SCI. AD, which describes episodic hypertension, is highly prevalent in people with SCI and can occur in excess of 40× per day. Although severe acute consequences of AD have been consistently reported, such as stroke and myocardial infarction, the long-term consequences of AD on the heart remain unclear. In this translational study, we experimentally and repetitively induced AD in rodents with chronic SCI and conducted regression analyses between the number of daily AD events and selected cardiac indices in humans with SCI. We had the novel finding that AD exacerbates the SCI-induced impairments in cardiac contractility and depresses inotropic reserve via a reduction in the sensitivity.
of the β-ARs. Although currently studied in the field of SCI, it is likely that our findings, which mirror the cardiac consequences of essential hypertension, provide novel insight into the mechanisms of increased CVD risk in other conditions characterized by episodic hypertension, such as white coat hypertension. Moreover, our study further highlights the critical need to appropriately manage AD in the clinical SCI population.

Disclosures

None.

References

Cardiac Effects of Episodic Hypertension in SCI

Novelty and Significance

What Is New?

- Exposure to autonomic dysreflexia after spinal cord injury impairs cardiac contractile function likely via desensitization of the cardiac β-receptors.

What Is Relevant?

- Our findings with autonomic dysreflexia mimic which occurs in primary hypertension suggesting that the relative hypertensive stimulus required for cardiac remodeling may be lower than is presently thought.

- Our findings also highlight the potential deleterious effects of autonomic dysreflexia and, therefore, open a new avenue of research to investigate the cardiac consequences of other pathologies that induce episodic hypertension.

Summary

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