

ABSTRACTS

29TH INTERNATIONAL SYMPOSIUM ON THE AUTONOMIC NERVOUS SYSTEM

Newport Beach Marriott
Newport Beach, California
October 24–27, 2018

Preliminary Program

WEDNESDAY, OCTOBER 24, 2018

8:00 AM–5:00 PM	Generalist Workshop and UCNS Review Course
5:00–6:30 PM	Registration
6:30–9:00 PM	Poster Session I and Trainee Poster Competition (cheese and wine)

THURSDAY, OCTOBER 25, 2018

7:00–8:20 AM	Continental Breakfast
8:20–8:30 AM	Welcome Remarks <u>William P. Cheshire, M.D.</u> President, American Autonomic Society
8:30–9:15 AM	Robertson Plenary Lecture The norepinephrine transporter and human cardiovascular disease <u>Jens Jordan, M.D.</u>

Session 1: Blood Pressure Regulation

Chairs: André Diedrich and Rasna Sabharwal

9:15–9:30 AM	FMS/Penaz Wesseling Travel Fellowship Award Functional brainstem imaging reveals brainstem nuclei governing human baroreflex function <u>D.A. Gerlach, J. Manuel, A. Hoff, H. Kronsbein, F. Hoffmann, K. Heusser, F. Beissner, J. Tank</u> Cologne, Germany
9:30–9:45 AM	FMS/Penaz Wesseling Travel Fellowship Award Sex and age differences in sympathetic vascular baroreflex function: insights from neck collar stimulation and an orthostatic stress test <u>M.G. Lloyd, V.E. Claydon</u> Burnaby, BC, Canada
9:45–10:00 AM	Sex-differences in the sympathetic neural recruitment and hemodynamic response to head-up tilt in elderly hypertensives <u>M.B. Badrov, Y. Okada, M.M. Galbreath, J.-K. Yoo, W. Vongpatanasin, J.K. Shoemaker, B.D. Levine, Q. Fu</u> Dallas, Texas, USA
10:00–10:15 AM	Norepinephrine transporter dysfunction contributes to increased sympathetic tone in a mouse model of hypertrophic cardiomyopathy <u>R.A. Larson, Y. Lu, L.K. Balciak, M.W. Chapleau</u> Iowa City, IA, USA
10:15–10:30 AM	Effects of 60-day head-down tilt bed rest on skeletal muscle-pump baroreflex <u>M.F. Tremblay, D. Xu, R. Ruedl, N. Goswami, A.P. Blaber</u> Burnaby, BC, Canada
10:30–11:00 AM	Coffee Break
11:00–11:45 AM	Hot Topic Plenary Lecture Neuromodulation focused therapeutics for cardiac disease: structure/function foundations <u>Jeffrey Ardell, Ph.D.</u> Los Angeles, CA, USA
11:45–2:00 PM	Poster Session II (lunch)

Poster #13

Arterial stiffness and spontaneous baroreflex sensitivity in African American women

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Introduction: African American women (AAW) are at greater risk for cardiovascular disease (CVD) versus Caucasian women (CW). Decreased spontaneous baroreflex sensitivity (sBRS) is associated with negative cardiovascular outcomes and AAW have been found to have significantly lower sBRS versus CW. Increased arterial stiffness (AS) is associated with reduced sBRS particularly in older individuals, while increased cardiorespiratory fitness (CRF) is associated with increased sBRS and improved cardiovascular health. Although AAW have lower baroreflex sensitivity and are at greater risk for CVD, there is a paucity of research examining how much of the variation in sBRS is explained by AS and CRF in young, healthy, normotensive AAW and CW. Therefore, the aim of this study was to determine how much of the variation in sBRS is explained by AS and CRF in young, healthy, normotensive AAW and CW.

Methods: Thirty-seven (AAW-13; CW-24) healthy, age, height, and weight-matched college-aged women were examined for AS, CRF, and sBRS. AS was determined by pulse wave velocity (PWV), and CRF by maximal oxygen consumption ($\text{VO}_2 \text{ max}$), while sBRS was determined by the alpha-index.

Results: Multiple regression analysis with sBRS as the dependent variable and AS and CRF as predictors indicated that in AAM, AS and CRF explained 11% of the variation in sBRS and 10% in CW. ANOVA demonstrated that neither model was significant: AAW ($P = 0.55$) and CW ($P = 0.31$).

Conclusion: Preliminary data suggest that AS and CRF are not significant predictors of sBRS in young, healthy, normotensive AAW or CW.

Funding: This study was partially supported by a grant from the Connecticut State University System.

Poster #14

Significance of efferent autonomic innervation and reactivity of arterial pressure in prognosis of patients with arterial hypertension

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Introduction: Arterial hypertension (AH) is the most important factor of cardiovascular mortality but its impact is varying for different patients.

Objective: To estimate the influence of blood-circulation autonomic regulation on the course disease in patients with AH.

Methods: We studied 56 patients with AH (59 ± 12 years) with target organ damage, among them 28 patients were with associated clinical

conditions. Autonomic regulation was assessed by applying sequence of tests including tilt test, Valsalva maneuver, handgrip test, cold stress vasoconstriction test (CVC). In addition, arterial baroreflex and power spectrum of variability of both the heart rate and blood pressure (BPV) were calculated. Hemodynamic parameters were measured by using noninvasive continuous blood pressure (BP) monitor, electrocardiogram, and air-cuff occlusion plethysmograph. Repeated clinical and laboratory examinations were performed after a lapse of 5.5 to 7.9 years.

Results: Valsalva index (VI) and CVC in the group of deceased patients ($n = 5$) were smaller than in the group of survivors: 1.4 ± 0.2 vs. 1.6 ± 0.4 a.u., $p < 0.05$ and 0.20 ± 0.02 vs. $0.39 \pm 0.16\%$, $p < 0.05$, respectively, whereas total peripheral resistance and BPV in the respiratory range were larger: 1.4 ± 0.2 vs. 0.9 ± 0.3 a.u., $p < 0.001$ and 18 ± 14 vs. 6 ± 4 mmHg², $p < 0.001$, respectively. Patients, who suffered a stroke ($n = 5$) had higher total BPV 114 ± 49 vs. 66 ± 40 mmHg², $p < 0.05$, and a tendency to increase of systolic BP in orthostasis: 4 ± 15 vs. -8 ± 13 mmHg, $p = 0.06$. Patients who underwent revascularization ($n = 7$) showed orthostatic hypotension: -15.8 ± 8.8 vs. 3.6 ± 12.9 mmHg, $p < 0.05$ and tendency of decreased VI: 1.5 ± 0.1 vs. 1.8 ± 0.5 , $p = 0.07$. Patients with newly developed associated clinical conditions showed orthostatic hypertension: 15 ± 6 vs. -10 ± 13 mmHg, $p < 0.005$ but decreased VI: 1.41 ± 0.08 vs. 1.99 ± 0.55 a.u., $p < 0.05$.

Conclusion: The parameters of cardiac and vasomotor reactivity, such as Valsalva index, cold-stress vasoconstriction, inadequate BP dynamics in orthostasis, and beat-to-beat BP variability are important markers for prognosis of the disease progression in patients with arterial hypertension.

Poster #15

Assessing individual human baroreflex-chemoreflex interactions using an n-of-1 trial design

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Introduction: Baroreflexes and peripheral chemoreflexes have a powerful effect on efferent autonomic activity making them prime suspects in the pathogenesis of cardiovascular disease and attractive treatment targets. However, the literature on their interaction is controversial, likely through inter- and intraindividual variability in cardiovascular reflex regulation. Therefore, we applied an n-of-1 trial design to elucidate individual baroreflex-chemoreflex interactions.

Methods: We studied 10 healthy men (18–40 years, BMI 18–28 kg/m²) breathing either normal air or an air-nitrogen-carbon dioxide mixture for 90 min each in randomized order. We applied 20 phenylephrine bolus per subject and condition to raise blood pressure (one every 4 min). To limit variability, we utilized an automated injector providing standardized bolus. We determined the pressor response to phenylephrine as estimate of baroreflex blood pressure buffering capacity and baroreflex sensitivity (BRS).

Results: Hypoxia reduced arterial oxygen saturation from 98.0 ± 1.0 to $80.8 \pm 1.3\%$ ($p < 0.0001$), raised heart rate from 63.6 ± 6.5 to 75.6 ± 10.2 bpm ($p = 0.004$), but did not change systolic blood pressure (132.1 ± 10 vs. 133.8 ± 8.9 mmHg; $p = 0.404$). 5 out of 10 subjects had significantly lower BRS with hypoxia ($p < 0.05$). 5 out of 9 subjects showed a significantly increased pressor response to phenylephrine during hypoxia likely through impaired baroreflex buffering ($p < 0.05$). One subject presented a reverse response,

namely significant increases in BRS and baroreflex buffering function under hypoxic conditions. On average, hypoxia decreased BRS by 5.6 ± 6.3 ms/mmHg (20.1 ± 6.4 vs. 14.6 ± 6.9 ms/mmHg, $p = 0.021$) but did not change the phenylephrine pressor response ($p = 0.769$).

Conclusion: An n-of-1 trial design can be applied to assess individual baroreflex-chemoreflex interactions in human subjects. Indeed, we identified a subgroup of persons exhibiting significant impairments in baroreflex blood pressure buffering and BRS with peripheral chemoreflex activation. The approach may have utility in elucidating individual pathophysiology and in targeting treatments modulating baroreflex or chemoreflex function.

Poster #16

Stress response and role of autonomic nervous system in Takotsubo cardiomyopathy

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Introduction: Takotsubo cardiomyopathy (TCM) is a disease typically characterized by transient left ventricular dysfunction with apical ballooning. The clinical presentation is often similar to those of an acute myocardial infarction. Although the cause of TCM remains unknown, the emotional and physical stress and exaggerated sympathetic nerve activity plays a key role.

Methods: We studied psychological stress response of plasma catecholamine in 8 TCM patients (72 years old, 11 female) and 3 healthy subjects (39 years old, 3 female). The mean onset age to develop TCM was 70. All the subjects were asked to finish 3 min mental calculation (MC) task and 3 min public presentation (PP) task (stress test). The order of MC and PP task were randomly assigned. Plasma epinephrine, norepinephrine, dopamine, renin, and aldosterone were measured before and after the series of two procedures. Autonomic function tests were performed to assess cardiovascular sympathetic indices and cardio-vagal indices.

Results: TCM patients had reduced sinus arrhythmia ratio (1.2 vs. 1.6, $p = 0.004$) and Valsalva ratio than the healthy subjects (1.2 vs. 1.8, $p = 0.02$). The incremental change of systolic blood pressure during cold pressor, hand grip, and hyperventilation test were comparable to those of the healthy subjects. Plasma norepinephrine (74.7 pg/ml vs. 167.2 pg/ml, $p = 0.004$) and epinephrine (16.3 pg/ml vs. 13.2 pg/ml, $p = 0.03$) were significantly increased in TCM patients than the healthy subjects after the series of stress tests. However, incremental change of plasma aldosterone was lower in TCM patients (25.6 pg/ml vs. 40.2 pg/ml).

Conclusion: Gene polymorphisms of alpha-adrenergic receptors, beta-adrenergic receptors, and dopamine receptors were evaluated. ADRA1A, ADRA2B, ADRB1, DRD2, DRD4 gene variants were found in TCM patients. Further evaluation of the genotypes combined with clinical presentation is currently proceeding.

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Poster #17

Attention and information processing impairment in individuals with chronic SCI: role of autonomic dysfunction

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Objective: Cognitive deficits in persons with spinal cord injury (SCI) are often attributed to concomitant traumatic brain injury (TBI); however, emerging evidence supports potential association with cardiovascular autonomic (CardioAuto) dysfunction. Analysis of heart rate variability (HRV) in the mid-frequency range (MF: 0.07–0.14 Hz) during cognitive testing may provide insight regarding the contribution of both sympathetic and vagal influences to performance.

Participants: Subjects included 30 controls and 60 individuals with chronic (10 ± 7 years) SCI (C3-T12). The participants were age-matched and none had a documented history of TBI.

Methods: The Paced Auditory Serial Addition Task (PASAT) evaluates information processing and sustained and divided attention. Participants were presented with a number every 1.2 to 2.4 s, in 4 sets, at an accelerated rate of presentation, and were asked to add the preceding number to each new number. Beat-to-beat HR was assessed at rest and continuously during the PASAT. Frequency analysis was used to determine change in power spectral density (ms/Hz) from rest to during the PASAT within the MF bandwidth of HRV as an indicator of CardioAuto function.

Results: Scores on the PASAT were significantly lower in participants with SCI (102.6 ± 47.2) compared to the controls (130.2 ± 38.1 ; $p < 0.01$). MF amplitude during the PASAT was significantly lower in participants with SCI compared to the controls (1012.2 ± 1132.2 vs. 1759.5 ± 1938.3 , respectively; $p < 0.05$). Change in MF was significantly correlated with PASAT scores in the controls ($r^2 = 0.468$; $p < 0.01$) but not in the SCI group.

Conclusion: Diminished performance on the PASAT in the SCI group, in the absence of documented TBI, suggests an alternative etiology may be responsible for the reported cognitive dysfunction in the SCI population. Furthermore, lower MF amplitudes and the lack of an association between changes in MF and PASAT scores in persons with SCI suggests that CardioAuto impairment may contribute to the observed cognitive dysfunction.

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Poster #18

Sudomotor dysfunction in diabetic autonomic neuropathy is not a frequent finding

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Introduction: Timely diagnosis of diabetic autonomic neuropathy (DAN) should allow for an early intervention so as to prevent complications. Literature review reveals that the most common pattern of involvement is cardiac vagal and distal sudomotor dysfunction occurring in equal frequency. We performed a retrospective review of a cohort of patients with DAN of various severity who had autonomic reflex testing in our laboratory. As part of quality improvement, we