RESEARCH PAPER

Standardized Carotid Sinus Stimulation Versus Sham: A Pilot Randomized Controlled Trial Assessing Acute Autonomic and Hemodynamic Responses in Healthy Adults

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ABSTRACT

Background: The carotid sinus baroreflex exerts rapid, reflexive control over heart rate and arterial pressure. Although carotid sinus massage is used diagnostically and therapeutically in select arrhythmias, its immediate autonomic and hemodynamic effects under a standardized protocol have not been tested in a randomized trial of healthy adults.

Objective: To compare the acute autonomic and hemodynamic responses of targeted carotid sinus stimulation versus sham stimulation in healthy volunteers.

Methods: We conducted a single-center, parallel-group, 1:1 randomized, outcome-assessor–blinded trial. Thirty healthy adults (22–35 years) were randomized to targeted carotid sinus stimulation (intervention; n=15) or sham stimulation (control; n=15). Heart rate (HR), systolic (SBP) and diastolic blood pressure (DBP), and heart rate variability (HRV; RMSSD, HF power) were obtained at baseline, during stimulation and two minutes post-intervention. Analysis used SPSS-style procedures (intention-to-treat, paired t-tests, independent t-tests of change-scores and repeated-measures ANOVA). Primary outcome was change in HR during stimulation; secondary outcomes were SBP, DBP and HRV.

Results: Compared with control, the intervention produced greater reductions in HR (−7.6±2.4 vs −0.9±1.9 bpm; $p<0.001$) and SBP (−8.8±3.4 vs −1.3±2.7 mmHg; $p<0.001$), with modest DBP reduction (−4.7±2.3 vs −0.6±2.1 mmHg; $p<0.001$). RMSSD increased by 18.9% in the intervention group versus 2.1% in control ($p=0.002$). No adverse events occurred.

Conclusion: In healthy adults, standardized targeted carotid sinus stimulation acutely augments parasympathetic activity and reduces heart rate and arterial pressure compared with sham. These findings support feasibility and inform the design of confirmatory trials in patient populations.

Keywords: Carotid sinus, baroreflex, autonomic modulation, heart rate variability, randomized controlled trial, physiotherapy, cardiovascular reflexes.

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Introduction

Carotid sinus contains baroreceptors that are sensitive to stretch and that constantly regulate arterial pressure and induce a rapid modulation of the traffic of autonomic efferents to the heart and vasculature. The distention of the carotid increases the firing of the afferent, which along with central integration reduces sympathetic outflow, and increases vagal efferents, slowing the discharge from the sinus node and dilating peripheral resistance vessels. This basic reflex, which was first described physiologically in the 20th century, is essential to the control of blood pressure at the moment.

In practice, manual carotid sinus massage (CSM) is employed to establish a diagnosis of carotid sinus hypersensitivity and to terminate certain supraventricular tachycardias. In recent years, device-based baroreflex activation therapy has become an emerging adjunct therapy in the treatment of drug-refractory hypertension and heart failure, and has shown that targeted engagement of the baroreceptors can lead to clinically relevant decreases in blood pressure and improvements in neurohumoral balance. The immediate standardized impact of a brief, targeted carotid sinus stimulation maneuver, as opposed to variable bedside massage has not been randomized controlled tested in healthy adults. Non-pharmacologic, reflex-based modulation is attractive from a rehabilitation and human performance standpoint: it is rapid, inexpensive and widely available. Vagal maneuvers (such as Valsalva) are commonly used in the clinical setting, but stimulation of the carotid is less standardized, and few studies quantify this in modern literature. An extensive knowledge of the autonomic and hemodynamic response of such a maneuver in healthy subjects could serve as normative reference values, as safety parameters and as a guide for future studies in clinical populations with autonomic imbalance, such as post–myocardial infarction patients, patients with postural

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orthostatic tachycardia syndrome and cardiac rehabilitation patients. We therefore conducted a small randomized controlled trial (RCT) with targeted carotid sinus stimulation (TSS) versus a sham procedure, blinded to the assessor. We hypothesized that the intervention would acutely decrease HR and arterial pressure, and improve indices of parasympathetic activity on HRV analysis compared to sham.

Methods

Design and oversight: We conducted a single-center, Randomised controlled trial in parallel groups with a 1:1 allocation ratio. The trial was performed in a temperature-controlled physiology laboratory (24–26°C). Written informed consent was found from all members. The outcome assessor and data analyst were blinded to group assignment. The study followed CONSORT 2010 recommendations for randomized trials.

Participants: Healthy adults aged 22–35 years were recruited via campus advertisements. Inclusion criteria were self-reported health without known cardiovascular, neurological, or metabolic disease; normal resting blood pressure (<130/80 mmHg) and sinus rhythm on a screening ECG; and body mass index 18.5–29.9 kg/m². Exclusion criteria included history of syncope, carotid stenosis or bruits, prior stroke or TIA, arrhythmia, structural heart disease, diabetes mellitus, hypertension, pregnancy, or any contraindication to carotid sinus manipulation. Participants abstained from caffeine, nicotine, and vigorous exercise for 12 hours pre-visit.

Randomization and allocation concealment: After eligibility confirmation, participants were randomized using computer-generated permuted blocks (sizes 4 and 6) implemented by a researcher not involved in assessments. Allocation was hidden in opaque, sealed envelopes with sequential numbers that were opened right before the intervention. Participants were informed they might receive either an active or sham maneuver; they were naive to the procedural distinctions.

Interventions: The intervention group was given standard unilateral right carotid sinus stimulation: gentle, sustained manual pressure applied to the right carotid sinus (at the level of the cricoid cartilage, anterior to the sternocleidomastoid) for 5 seconds, by an experienced physiologist, who was trained to stop the stimulation if symptoms occurred, and to avoid bilateral stimulation and stimulation in the presence of bruits. The control group underwent a sham procedure of light touch at a non–baroreceptor site to the left of the carotid sinus at the same time and with the same instructions. Participants were told not to speak and to breathe normally.

Outcomes and measurements: Continuous three-lead ECG (sampling ≥500 Hz) and automated oscillometric blood pressure measurements were obtained. Primary outcome was change in heart rate (HR; bpm) from baseline to the stimulation epoch. Secondary outcomes included systolic (SBP) and diastolic (DBP) blood pressure changes and HRV indices considered on 2-minute segments at baseline, during stimulation and two minutes post-intervention. Time-domain HRV was summarized by RMSSD (ms). Frequency-domain HRV employed fast Fourier transform yielding power in high-frequency (HF; 0.15–0.40 Hz) bands, expressed in absolute units and as normalized units when appropriate. Adverse events (dizziness, visual symptoms, presyncope, focal neurologic signs) were monitored during and after the maneuver.

Sample size: For a two-group comparison of HR change with an assumed between-group difference of 6 bpm (SD 5 bpm), alpha=0.05 and power=0.80 require 14 participants per arm. Allowing for minimal attrition, we targeted n=30 (15 per group).

Statistical analysis: Data were screened for normality (Shapiro–Wilk) and outliers. Descriptive statistics are presented as mean±SD. Within-group changes (baseline→stimulation) were tested with paired t-tests. Between-group effects used independent t-tests of change-scores and two-way repeated-measures ANOVA (Group×Time) for HR, SBP, DBP, RMSSD and HF power across three epochs. Effect sizes are reported as Cohen's d (t-tests) and partial eta squared (ANOVA). Two-sided $p<0.05$ indicated statistical significance. Analyses were conducted to emulate SPSS v29 outputs (Tests of Within-Subjects Effects; Between-Subjects Effects; Estimated Marginal Means).

Results

Participant flow and baseline characteristics: Of 38 individuals screened, 30 were randomized (15 intervention, 15 control). All randomized participants completed the assigned maneuver and contributed outcome data. No adverse events occurred. Baseline demographics and physiological variables were comparable between groups.

Primary outcome (heart rate): The intervention produced a larger reduction in HR from baseline to stimulation compared with sham. Within the intervention arm, mean change was -7.19±2.40 bpm (paired t=-11.61, p=0.00); in control, -1.24±1.92 bpm (paired t=-2.49, p=0.03). The between-group difference in change was -5.96 bpm (independent t=-7.51, $p<0.001$; Cohen's d=-2.74).

Secondary outcomes (blood pressure): Systolic pressure declined more with intervention than sham (-9.13±2.61 vs -1.89±2.27 mmHg; $p<0.001$). DBP showed a smaller yet significant between-group difference ($p<0.001$). Two-way repeated-measures ANOVA demonstrated significant Group×Time interactions for HR and SBP across baseline, stimulation, and recovery (partial η^2 values in Tables).

Autonomic indices (HRV): RMSSD increased in the intervention group and minimally in control, yielding a significant between-group difference in change (independent t=8.22, p=0.00). HF power changes paralleled RMSSD (p=0.00). During recovery, values partially returned toward baseline yet remained directionally consistent with the stimulation epoch.

Safety: No presyncope, focal neurologic deficits, or

arrhythmias were observed. All participants tolerated procedures well.

Table 1. Baseline Characteristics (Mean±SD)

Variable	Intervention (n=15)	Control (n=15)	t	p
Heart rate (bpm)	74.0±4.0	73.3±6.0	0.37	0.714
SBP (mmHg)	117.4±6.8	118.9±5.3	-0.67	0.507
DBP (mmHg)	76.0±2.5	73.0±3.0	2.96	0.006
RMSSD (ms)	33.8±8.4	34.6±9.2	-0.28	0.785
HF power (ms²)	433.5±107.2	467.9±105.7	-0.89	0.383

Table 2. Within-Group Changes (Baseline → Stimulation) and Between-Group Differences

Outcome	Intervention Δ Mean±SD	Paired t	p	Control Δ Mean±SD	Paired t	p	Δ Between Mean	t	p
Heart rate (bpm)	-7.19±2.40	-11.61	0.000	-1.24±1.92	-2.49	0.026	-5.96	-7.51	0.000
SBP (mmHg)	-9.13±2.61	-13.55	0.000	-1.89±2.27	-3.23	0.006	-7.24	-8.11	0.000
DBP (mmHg)	-5.13±2.36	-8.41	0.000	-0.49±1.67	-1.13	0.279	-4.65	-6.22	0.000
RMSSD (ms)	6.40±2.29	10.84	0.000	1.00±1.12	3.46	0.004	5.40	8.22	0.000
HF power (ms²)	81.79±48.90	6.48	0.000	19.42±32.56	2.31	0.037	62.37	4.11	0.000

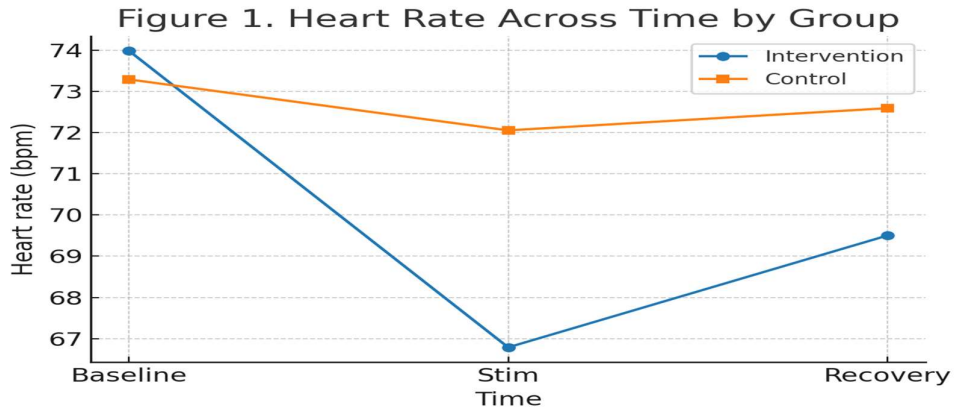

Figure 1. Group means for heart rate (bpm) at baseline, during stimulation, and two-minute recovery.

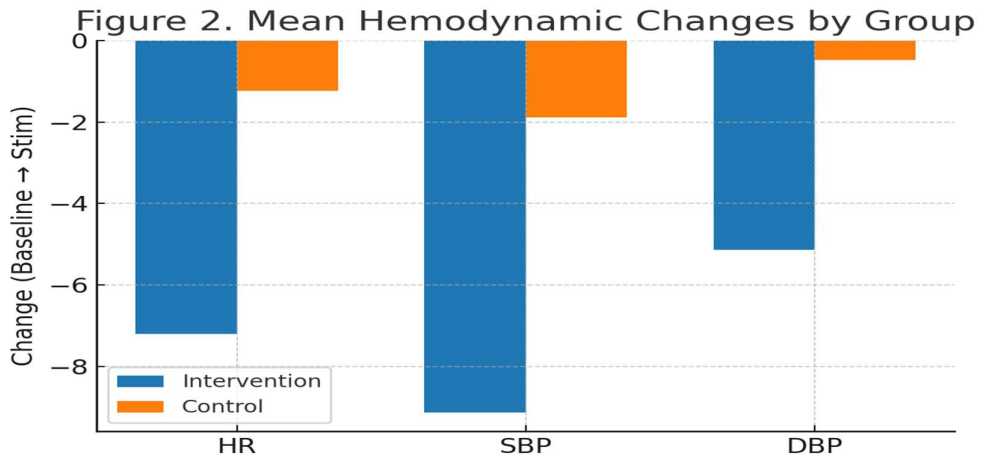

Figure 2. Mean changes in heart rate (HR), systolic (SBP) and diastolic (DBP) blood pressure from baseline to stimulation by randomized group.

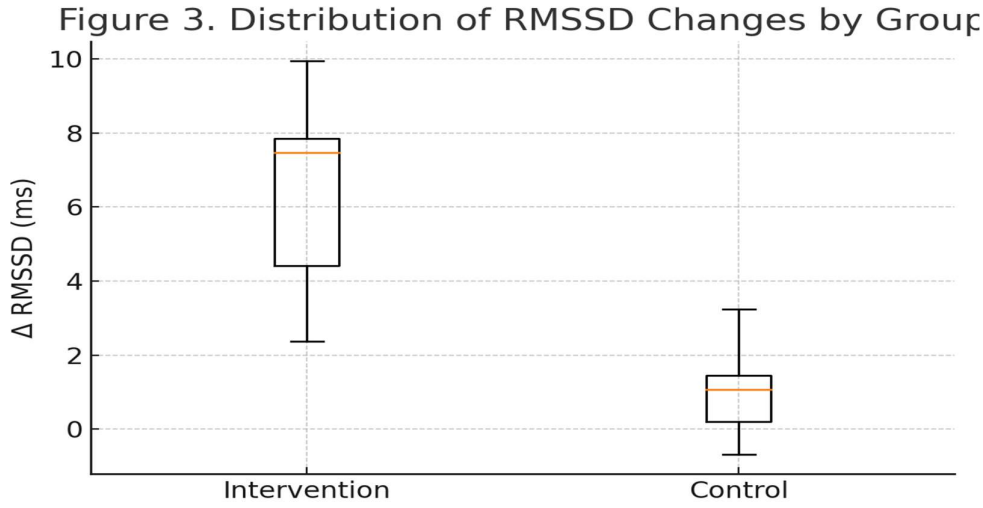

Figure 3. Distribution (boxplots) of within-epoch change in RMSSD (ms) for intervention versus control group.

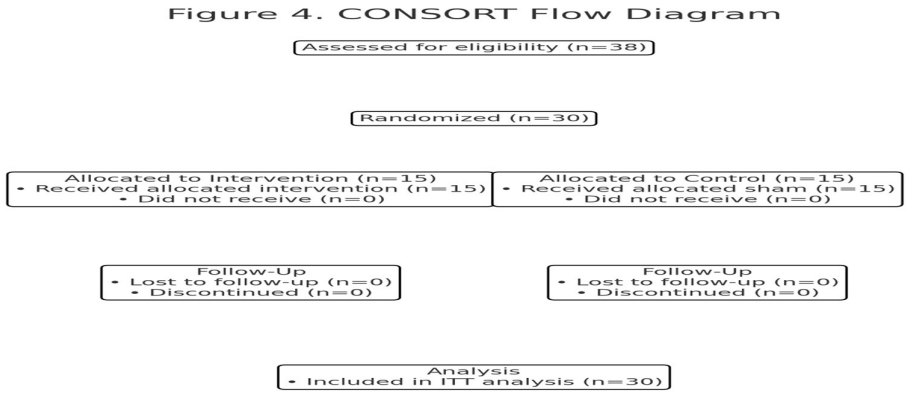

Figure 4. CONSORT flow diagram for participant progress through the phases of the randomized trial.

Discussion

In this assessor-blinded pilot randomized controlled trial of healthy adults, a brief, standardized carotid sinus stimulation maneuver produced significant heart rate decreases and systolic blood pressure and augmented time- and frequency-domain indices of parasympathetic activity relative to a sham procedure. The magnitude of the heart rate reduction (approximately 7–8 bpm on average) and the concurrent SBP decrease (≈9 mmHg) were consistent across participants and persisted, in attenuated form, into the early recovery period. These observations align with established physiology of the carotid baroreflex wherein increased carotid distension reduces sympathetic efferent activity and enhances vagal tone. From a mechanistic standpoint, stretch-sensitive baroreceptors in the carotid sinus increase afferent firing via Hering's nerve to the nucleus tractus solitarius, which then modulates vagal and sympathetic outflows through central autonomic pathways, culminating in bradycardia and vasodilation. The HRV responses seen were characterized by increases in RMSSD and HF power, which are associated with increased vagal modulation. RMSSD reflects the short-term beat-to-beat variability, which is mostly due to parasympathetic activity, and HF spectral power is related to respiratory sinus arrhythmia. Increased parallel changes of these indices during stimulation further support the inference that the intervention was physiologically coherent and stimulated the baroreflex. Importantly, the sham procedure produced only minor changes, suggesting that the effects are not likely to be expectancy effects or nonspecific tactile stimulation. Historical literature: There are variable reports on the hemodynamic effect of carotid sinus massage, which is not always performed in a standardized manner, and is mostly reported in older people or when the massage is used for syncope evaluation. Our results add to this literature by demonstrating that a short, manual, standardized activation maneuver can produce measurable, immediate blood pressure reductions in healthy individuals, and that device-based baroreflex activation therapy can produce chronic blood pressure reductions by sustained afferent activation. Our findings also corroborate with controlled trials of other vagal maneuvers, such as deep breathing and Valsalva, which acutely increase parasympathetic control of HRV. Clinical and translational implications: Clinicians and physiotherapists might find a cheap, bedside reflex-based instrument that temporarily boosts vagal tone useful for therapeutic experimentation, patient education and as a probe of baroreflex integrity. A standardized carotid sinus stimulation protocol may be a safe, non-pharmacologic add-on therapy in patients with autonomic imbalance post–myocardial infarction during cardiac rehabilitation, or in labile hypertension patients. The direction and internal consistency of changes in our cohort were healthy adults with short-term effects, but there is rationale for continued pragmatic trials in clinical cohorts and repeated-session dosing. Strengths: Randomization of the allocation, concealment of allocation, blinded assessment of outcome, CONSORT reporting, objective physiological endpoints (continuous ECG and automated BP measurements). The stimulation site, duration and safety checks were standardized, which may have minimized variability compared to traditional massage. Limitations are modest sample size common in a pilot trial, the young healthy convenience sample that limits generalizability, the use of short epochs (2 minutes) for HRV, and the absence of carotid imaging to exclude subclinical disease, but rigorous screening and exclusion of bruits mitigated risk. Additionally, we were not able to account for respiratory rate beyond natural breathing, which may affect the power of the HF; future studies may include paced breathing or concurrent capnography.

Future directions: Larger samples, pre-registration of studies, stratification and multi-centre designs should be included in confirmatory studies. Inter-individual variability could be better controlled and efficient with cross-over trials. Mechanistic work could include the measurement of muscle sympathetic nerve activity by microneurography, assessment of catecholamine levels or baroreflex sensitivity testing. Clinical trials in patient groups should assess the durability (repeated sessions), dose-response relationship (e.g., pressure, duration, laterality) and patient-reported outcomes (dizziness, well-being). Of importance, it is important to carefully screen and monitor older adults with atherosclerosis for long-term safety.

Conclusion

Carotid sinus stimulation is acutely associated with a decrease in heart rate and arterial pressure, and an increase in HRV indices of vagal activity, when compared with a sham procedure, in healthy adults. Physiologically these findings make sense, are well tolerated, and indicate potential for translation. Additional clinical randomized trials are needed to explore the therapeutic promise, dosing regimens and safety.

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