**Center of Pressure Regularity With and Without Stochastic Resonance Stimulation in Stable and Unstable Ankles**

By: Stephen M. Glass, Scott E. Ross, Brent L. Arnold, and Christopher K. Rhea


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**Abstract:**

Chronic ankle instability (CAI) is associated with sensorimotor deficits, which may affect dynamic complexity by constraining the postural control system. Stochastic resonance stimulation (SRS) may restore sensory function and promote healthy postural control dynamics. This study used Sample entropy (SampEn) during quiet single- and double-leg stance to examine the impact of CAI on center of pressure velocity (COPV) dynamics and the effects of SRS on COPV dynamics in individuals with CAI. Group differences in baseline SampEn were observed in double-leg resultant COPV, single-leg mediolateral COPV, and single-leg resultant COPV ($P < .05$). For single-leg mediolateral and resultant COPV, SampEn in the CAI group with SRS was not different than SampEn in the control group without SRS ($P > .05$). These findings suggest that CAI is associated with changes in behavioral complexity and that SRS may restore complex COPV dynamics in individuals with CAI.

**Keywords:** Chronic ankle instability | Stochastic resonance stimulation | Center of pressure velocity | Ankle sprains | Sport-related injuries

**Article:**

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Ankle sprains are among the most common sport-related injuries. Individuals with a history of isolated or repeated ankle sprains often present with the sensation of instability, a condition known as chronic ankle instability (CAI). CAI is associated with functional performance deficits, as well as reduced health-related quality of life. This pathology is thought to be multifactorial in origin and likely involves both “functional” and “mechanical” factors. Potential mechanical causes of CAI include joint laxity, bony incongruence, and joint degeneration. Intrinsic factors include strength deficits, as well as changes in spindle cell and Golgi tendon organ function. Reliably quantifying how these deficits affect neuromuscular control is of great interest to injury and rehabilitation researchers.

Although CAI is associated with balance deficits, evidence of a link between CAI and instrumented postural control impairments is inconsistent when examining individual studies. McKeon and Hertel conducted a systematic review in which they were unable to conclude that such impairments exist, a result they attributed in part to a lack of consistent definitions of CAI. Another factor likely contributing to discrepancies among studies is the variety of measures used to assess postural control. Many variables can be derived from center of pressure (COP) measurements, some of which are more sensitive than others in detecting CAI deficits. Variables, such as COP area, COP excursion, and COP velocity, have all been reported in the ankle instability literature. These variables can be calculated using the anteroposterior/mediolateral components of COP time series or the resultant vectors. Some authors have more recently used spatiotemporal measures, such as time-to-boundary, in the assessment of CAI. Such nonlinear measures may be more sensitive to the balance deficits associated with ankle instability and have been suggested as a direction of interest for future research.

A second area of research producing conflicting results concerns the effects of interventions on postural control in CAI. Considerable interest exists in identifying interventions capable of restoring function in this population. Previous studies have shown improvement in COP measures following training interventions. However, evidence in this area has also been inconsistent. A therapy known as stochastic resonance stimulation (SRS) may hold promise as a complementary or stand-alone treatment. SRS is a process whereby signal detection within physiological systems is enhanced with the introduction of white noise. Mechanical or electrical white noise may sensitize peripheral nervous system structures, such as muscle spindles and Golgi tendon organs, to detect signals that may otherwise go undetected. SRS has been shown to elicit improvements in balance parameters in healthy participants, as well as participants with CAI. Further, SRS appears to augment the effects of balance training in CAI, in that improvements occur more quickly when compared with balance training without SRS. With one exception, previous studies investigating the effects of SRS on postural control in CAI have relied on summary measures of COP, such as path length, standard deviation, and mean displacement and velocity.

Although summary measures of COP can index balance impairments associated with CAI, these results have not been consistent across investigations. These linear outcome measures may also overlook certain functional implications of the pathology. An approach that might address these concerns involves the analysis of postural control from the perspective of nonlinear dynamics. Dynamics measures can provide an index of complexity within physiological time series. The
complexity of a biological system is a function of the inputs influencing that system and the interactions between them. In the case of postural control, we could identify proprioceptive, visual, and vestibular inputs. In a healthy physiological system, these inputs interact to produce an adaptable behavior that is optimally complex. Aging and disease are characterized by changes in complexity, whereby physiological systems become less robust in their ability to adapt to environmental constraints. Because balance depends on the integrated function of the neuromuscular system, nonlinear analyses are frequently conducted, using postural control variables. Using these nonlinear metrics, increased regularity in movement behavior has been observed in clinical conditions, such as Parkinson's disease and cerebral concussions, compared with healthy controls. We expect that balance dynamics are similarly affected in CAI.

Sample entropy (SampEn) is a nonlinear variability measure that provides an index of complexity by searching for repetitions or "matches" of patterns within a time series. Clinically, SampEn may reflect the sensory or mechanical deficits constraining the neuromotor system. A greater number of pattern repetitions indicates that the human movement signal under investigation is relatively more regular. Regular/irregular in this context refers to the presence of repeated patterns in a time series and should not be interpreted to denote normal/abnormal. Movement behaviors may become overly regular or overly irregular in the presence of clinical pathology. On the basis of previous research showing that populations with balance deficits exhibit increased regularity in COP time series, we postulated that CAI would similarly lead to increased postural control regularity relative to a group with stable ankles.

SampEn is relatively robust to time series length and measurement noise. These qualities make it particularly useful for experimental COP data collected from clinical populations, as the data sets are frequently short and noisy. However, COP displacement signals often exhibit drift, or nonstationarity; in other words, a trend line drawn through the time series would have a positive or negative slope, as opposed to being flat. In the case of COP displacement, drift can result in differences in the mean magnitudes of small windows of data within the time series. This creates problems for SampEn, as matches cannot be counted for patterns repeated at different magnitudes. For example, the difference between successive points in the 1-2-3 sequence is identical to that in the 7-8-9 sequence. However, SampEn would not register this as a match because the second sequence occurs at a different magnitude. Thus, nonstationary signals can result in a false-negative when calculating SampEn. Concerns regarding nonstationarity can be addressed by analyzing the increment data, such as COP velocity, which effectively removes the drift that is often characteristic of displacement data. Moreover, the utility of the velocity variable is not limited to methodological convenience--the case has also been made that the neuromotor system attends specifically to COP velocity during quiet stance; therefore, it is more appropriate than displacement in the analysis of postural control.

Our first objective in this investigation was to calculate SampEn by using COP velocity data to determine its effectiveness in differentiating between stable and unstable ankle groups. Clinically, SampEn may reflect the underlying constraints associated with CAI and how a therapeutic intervention with SRS may correct deficits with CAI. We hypothesized that COP velocity dynamics in the CAI group would be characterized by lower SampEn values relative to healthy controls. The second purpose of our study was to examine the effects of SRS administered at an individually optimized intensity on COP dynamics in individuals with CAI.
We conjectured that SRS would increase SampEn values in the CAI group to levels indistinguishable from the control group. These hypotheses were based on the group and condition entropy differences observed in a previous study examining the effect of stochastic resonance on postural control in a clinical population. 

**METHOD**

**Participants**

This investigation was a secondary analysis of data previously collected as part of a study examining the effects of SRS on balance. Institutional review board was obtained for this study and all participants provided written informed consent prior to participation. In the current study, 24 participants were analyzed as members of the CAI group (n = 12) or stable group (n = 12). Twelve individuals with CAI (6 men, 6 women; mean age = 23 ± 3 years, mean height = 174 ± 8 cm; mean mass = 69 ± 10 kg) and 12 individuals with stable ankles (6 men, 6 women; mean age = 22 ± 2 years; mean height = 170 ± 7 cm, mean mass = 64 ± 10 kg) participated in this study. To be included in the CAI group, participants had to report a minimum of 2 episodes of "giving way" within 12 months prior to this study. On average, the participants had 2 giving-way sensations per month. In addition, participants had to self-report a history of ankle sprains. Our participants had a history of 3.5 ankle sprains. Mechanical instability was not an inclusion or exclusion criterion.

**Protocol**

Optimal SRS intensity was individually determined for each participant in a double-leg stance. Each participant received SRS administered via subsensory mechanical stimulation, using a custom-built stimulation device (Afferent Corporation, Providence, Rhode Island), with coin-sized vibrating terminals, called *tactors*, placed midway between the origin and insertion sites of the peroneus longus, the gastrocnemius, and the anterior and posterior tibialis muscles. For testing, we used the unstable limb of the CAI group and the matched control limb for participants with stable ankles. Stimulation was administered at a percentage of sensory threshold (25%, 50%, 75%, or 90%) and a control level (0%) as the participants performed 3 trials of 20-second, quiet double-leg stance. Treatment conditions were administered in a distinct, predetermined order among participants so that the effects of fatigue or training would be evenly distributed throughout the testing order. Because stimulation was subsensory, participants were blinded to the stimulation condition. The stochastic resonance intensity that decreased the COP velocity the most, compared with the control condition, was defined as the optimal intensity. This intensity, which was associated with a given participant's minimal COP velocity in double-leg stance, was then administered during a single-leg stance protocol. The single-leg stance protocol required participants to perform 20-second trials of quiet single-leg stance on the unstable side or a matched control limb for participants with stable ankles. Participants completed 3 trials per treatment condition (*SRS*<sub>on</sub> = optimal intensity; *SRS*<sub>off</sub> = control condition with no stimulation). Failed trials resulted in a retest. The order of testing was a block-randomized design.

**Data Collection and Processing**
All balance assessments occurred on an AMTI Accu-way force plate (Advanced Mechanical Technology Inc, Watertown, Massachusetts). Signals from the plate were sampled at a rate of 50 Hz. Raw COP coordinates for anteroposterior (AP) and mediolateral (ML) components were computed in Balance Clinic Software (Advanced Mechanical Technology Inc) and exported to spreadsheets for data analysis.

LabVIEW software (National Instruments, Austin, Texas) was used to compute a resultant vector of AP and ML components. Next, data were differenced and divided by the sampling frequency to create AP and ML component time series (APCOPV and MLCOPV, respectively), as well as resultant time series (RCOPV). SampEn was then calculated for each velocity time series with a custom MATLAB script (The Mathworks Inc, Natick, Massachusetts). SampEn calculates the probability of template matches occurring within a time series, where a template is a small window of data points (length, \( m \)), compared with subsequent windows of the same length. A "match" is counted when data points in 2 templates lie within a given error tolerance of each other. The error tolerance is referred to as the radius and is denoted as \( r \). The final measure quantifies the likelihood that a match for templates of length \( m \) will remain a match when the length of the template is incremented to \( m + 1 \). This provides an index of regularity, with lower values reflecting more regular behavior. Thus, SampEn required us to specify a template length \( m \) and radius \( r \). Using a technique previously described for determining SampEn parameters,\(^{35}\) an \( m \) of 3 and an \( r \) of \((0.3 \times SD)\) were selected, where \( SD \) is the standard deviation of the time series being analyzed.

**Statistical Analysis**

IBM SPSS Statistics version 20.0 (SPSS Inc, Chicago, Illinois) was used for data analysis. An alpha level was set a priori at \( P = 0.05 \) to indicate statistical significance. Data used in the analysis for double- and single-leg stance included SRS\textsubscript{on} (optimal intensity) and SRS\textsubscript{off} (control). Mean imputation\(^{36}\) was performed for 2 participants identified as outliers--1 from the stable group in single-leg stance and 1 from the CAI group in double-leg stance. This procedure was chosen to minimize loss of power due to limited sample size and small expected effect sizes. Group means for SampEn were analyzed using \( t \) tests for planned comparisons, with an a priori alpha of 0.05. Consistent with previously published guidelines for multiple comparisons in sports medicine research, no Type I error adjustments were made for multiple effects.\(^{37}\) Cohen's effect size \( d \) values were computed for planned comparisons. Effect sizes of 0.20, 0.50, and 0.80 were considered small, medium, and large, respectively.\(^{38}\)

We first were interested in comparing the CAI and stable groups without SRS and, second, in evaluating the effects of SRS treatment in the CAI group. Of note, differences in algorithms, hardware, filtering, and parameter specifications make it difficult to establish normative data for nonlinear measures. Instead, a normative benchmark is frequently estimated by comparison with a group of young, healthy adults\(^{39}\) participating in the same study with the same equipment and data processing techniques. Therefore, the most appropriate mean comparison for evaluating the treatment effect of SRS in the CAI group was that of the stable group in the SRS\textsubscript{off}condition. Finally, because dynamic complexity is usually assumed to be optimal in young, healthy adults, establishing the effects of SRS in the control group was an exploratory question.
RESULTS

The means and standard errors for each variable are depicted in Figures 1-2. Tables 1-2 show $t$ statistics, with associated $P$ values and effect sizes (Cohen's $d$) for mean differences. For all significant differences, SampEn was lower in the CAI group, compared with the stable group. A group difference was found in baseline SampEn RCOPV during double-leg stance. This RCOPV difference for double-leg stance remained significant when comparing the CAI group during SRS$_{on}$ with the stable group during SRS$_{off}$. In single-leg stance, group differences were observed in baseline SampEn for MLCOPV and RCOPV. However, differences in single-leg stance were not found between the CAI group during SRS$_{on}$ and the stable group during SRS$_{off}$. Finally, no significant treatment effects were observed in the stable group.

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Figure 1. Group mean and standard error values for Sample entropy (SampEn) values during double leg stance. Within each graph (A-C), the stochastic resonance stimulation (SRS$_{on}$) condition is shown on the left and the SRS$_{off}$ condition is shown on the right. Solid lines represent the stable group. Dashed lines represent the chronic ankle instability (CAI) group. Group differences are indicated by an asterisk (*), treatment condition differences are indicated by a dagger (†), and differences between the CAI SRS$_{on}$ and stable SRS$_{off}$ groups are indicated by a double dagger (‡) all $P < .05$. Abbreviations: APCOPV, anteroposterior center of pressure velocity; MLCOPV, mediolateral center of pressure velocity; RCOPV, resultant time series center of pressure velocity.
DISCUSSION

The most significant finding of the current study was the convergence of SampEn values for MLCOPV and RCOPV during single-leg stance, which resulted in a nonsignificant difference between the CAI group during SRS_on, compared with the stable group during SRS_off. Although the within-treatment effects observed in single-leg stance did not reach statistical significance, we argue that our study was underpowered. The observed changes may reflect meaningful improvement in COP dynamics in the CAI group in comparison with the control group.

In a study of COP measures in CAI conducted by Ross et al, the ML variables tended to outperform the AP variables in discriminating between CAI and healthy groups in quiet single-leg stance. This discriminate ability may result from a loss of postural control in the ML direction following injury of the lateral ankle ligaments, which aid to restrain excessive frontal plane motion (ie, ML motion). Of note, although Ross et al study showed AP linear measures to be fairly effective at discriminating between groups, the current results suggest that the same is not true for SampEn. This might be a reflection of increased AP movement serving a
compensatory function, which would explain why complexity in this plane appears to be less affected by pathology during single-leg stance. Thus, SampEn may provide complementary information regarding the quality of postural control that would not necessarily be detected by summary statistics.

The relatively low values of SampEn may indicate a constrained, rigid pattern of behavior. Conversely, higher values may be interpreted as an indication of increased exploratory behavior or as a progressive loss of control. To appropriately interpret SampEn, a healthy control group is typically included to index functional behavior in a particular context. We interpreted the lower SampEn, and thus increased regularity of single-leg MLCOPV and RCO PV, to reflect the sensorimotor constraints associated with CAI. For example, deficits in muscle spindle and Golgi tendon organ function may prevent an individual with CAI from sensing, and therefore responding to, subtle changes in posture. A previous study has shown that MLCOPV is increased in CAI during single-leg stance. However, the current study suggests that sensorimotor constraints in CAI may be associated with rigid behavioral patterns, which limit an individual's ability to adapt to environmental demands. We should also note that, although deficits in sensory or motor function are likely a factor, these rigid patterns may also reflect a compensatory adaptation by which individuals with CAI attempt to reduce instability.

<table>
<thead>
<tr>
<th>COMPARISON</th>
<th>COP COMPONENT</th>
<th>t</th>
<th>df</th>
<th>P</th>
<th>EFFECT SIZE</th>
<th>LOWER LIMIT</th>
<th>UPPER LIMIT</th>
<th>95% CONFIDENCE INTERVAL</th>
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<td>.011</td>
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<td>0.20</td>
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Abbreviations: AP, anteroposterior; CAI, chronic ankle instability; COP, center of pressure; ML, mediolateral; R, results; SRS, stochastic resonance stimulation control condition with no stimulation; SRS_stable, stochastic resonance stimulation optimal intensity.

*Group and treatment comparisons for Sample entropy (SampEn) during double-leg stance. Positive effect sizes (SampEn in the group comparisons indicate higher SampEn values in the stable group. In the treatment condition comparisons, positive and negative effect sizes indicate increases and decreases in SampEn, respectively. The lower and upper limits of the 95% confidence intervals denote mean differences in SampEn.

*Statistically significant (P < .05).
In absolute value terms, the differences observed in SampEn in the current study are modest. However, SampEn values fall within a relatively narrow range—between 0 and 2. In addition, previous research has shown small differences in SampEn to be clinically meaningful.\textsuperscript{31,40} For example, Donker et al\textsuperscript{29} observed a difference in SampEn of 0.3 in a study comparing normally developing children and children with cerebral palsy. As a peripheral nervous system pathology, CAI may have less of an effect on postural control dynamics and thus on SampEn. Considering the difficulty in consistently quantifying functional deficits in CAI, SampEn differences as small as 0.05 to 0.1 may be an important finding. The 95% confidence intervals shown in Tables 1-2 depict the small range for mean SampEn differences among groups and conditions. However, the confidence intervals for statistically significant comparisons do not cross zero, suggesting that a true difference was observed. Effect sizes for the associated comparisons are nearly all "large" by Cohen’s $d$ standards and would represent meaningful clinical changes.

Sensory deficits may respond to individually optimized SRS therapy. Previous studies have shown improvements in instrumented measures of postural control with SRS.\textsuperscript{17,41} One such study conducted by Costa et al\textsuperscript{28} examined the effect of SRS therapy on the dynamics of double-leg COP in young and older adult participants. Their investigation used multiscale entropy, which applies SampEn over a variety of time scales. In the treatment condition, the older adult participants showed increased multiscale entropy for COP displacement and velocity in both the AP and ML directions, reflecting increased complexity. Only 1 significant treatment effect was
identified in the current study (double-leg MLCOPV in the CAI group). However, in contrast to the work of Costa et al,28 our results show that the treatment effect of SRS may depend on the variable analyzed and the stance condition. It is also important to note that the participants examined in the Costa et al28 article consisted of a population with significant balance deficits (older adults with fall risk), whereas the current study focused on a population that did not have a history of falling. Thus, it is plausible that SRS therapy may have an enhanced effect on populations with larger sensory deficits.

In double-leg stance, an ankle group difference was observed in SampEn for RCOPV. Previously identified deficits in force plate measures of postural control associated with CAI have generally been limited to single-leg standing.11,12 COP summary measures during double-leg stance may not be sensitive enough to detect balance impairments in CAI,42 particularly in the frontal plane, where the base of support is much wider, compared with single-leg stance. One previous study has shown that SampEn of AP COP displacement is capable of differentiating between stable and unstable ankle groups during double-leg stance.19 Our data show a significant group effect of CAI on SampEn in double-leg RCOPV. It is difficult to interpret this finding in light of the divergent effects of stochastic resonance on the 2 groups for RCOPV during double-leg stance. Future research should investigate the effects of SRS on postural complexity when stimulation is optimized independently for each limb.

An exploratory purpose of the current investigation was to examine the effects of SRS on postural control dynamics in young, healthy adults. Our exploratory analysis indicates that SRS did not have a treatment effect on participants with stable ankles. Two explanations might account for this finding. First, it may be the case that supplementary stimulation cannot increase sensorimotor function, and thus COP complexity, in the absence of any deficits. This notion is suggested by Costa et al,28 who observed no changes in multiscale entropy in a young control group. Second, the risk factors for development of CAI are unknown. It is possible that deficits in postural control dynamics may exist without subjective sensations of instability. With small sample sizes, as in the current study, any theoretically at-risk participants assigned to the control group could have adversely affected the data. Sample size was a limitation of the current study. In addition to our sample sizes, the retrospective design of this investigation limits the conclusions that can be drawn.

SampEn may be a useful complementary analysis for this clinical CAI population, in which research using traditional COP measures has been inconsistent. Nonlinear metrics may provide valuable information regarding the clinical impact of CAI and the effectiveness of treatment strategies. These preliminary findings warrant additional research designed to identify appropriate parameters and testing protocols to increase the sensitivity of SampEn in detecting balance deficits in CAI. Future studies using larger sample sizes should seek to identify these parameters, as well as factors that predict individual responses to SRS therapy, using both linear and nonlinear measures. Prospective designs will also be necessary to determine the response to SRS treatment over time and to identify nonlinear metrics that predict ankle instability. Finally, future research should consider measuring the effects of SRS on the dynamics of functional movement in addition to static postural control.
Implications for Clinical Practice

Decreased SampEn in individuals with CAI likely relates to the sensorimotor deficits associated with the pathology. The group differences observed in baseline single-leg MLCOPV and RCOPV SampEn were not present in the SRS_{on} condition. Although we acknowledge that the associated within-treatment effects were not statistically significant, the direction and magnitude of the observed changes could hold promise for future studies involving more participants. Therapies such as stochastic resonance, which target peripheral nervous system function, may mitigate the sensory deficits associated with CAI, thereby restoring complex, adaptive motor function related to postural control dynamics. SRS is noninvasive and can be used in conjunction with exercise-based interventions.

The inability to quantify functional deficits limits not only our ability to assess and treat CAI in individual cases but also our ability to conduct well-controlled research. SampEn may provide valuable information that is not captured with more conventional summary measures. Our results support the conclusion that single-leg ML COP velocity SampEn effectively distinguishes between CAI and healthy populations. The findings of this investigation therefore have clinical implications relating to both assessment and intervention. Further research is warranted on the use of stochastic resonance and SampEn in CAI populations.

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