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# Dynamical complexity of postural control system in autism spectrum disorder: a feasibility study of linear and non-linear measures in posturographic analysis of upright posture

Fabio Pettinato[1†], Maria Stella Valle[2†], Matteo Cioni[2,3], Lara Cirnigliaro[1], Renata Rizzo[1], Rita Barone[1,4*], Gianfranco Bosco[5*] and Antonino Casabona[2]

## Abstract

**Background** Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder, characterized by impairments in social interaction and communication with restricted and repetitive behavior. Postural and motor disturbances occur more often in ASD, in comparison to typically developing subjects, affecting the quality of life. Linear and non-linear indexes derived from the trajectory of the center of pressure (COP) while subjects stand on force platforms are commonly used to assess postural stability. The aim of the present feasibility study was to investigate whether combining linear and non-linear parameters of the COP during stance in subjects with ASD, could provide insight on specific features of motor dysfunction possibly linked to ASD cognition and clinical characteristics.

**Methods** Twenty-two males, aged 10–15 years, including subjects with ASD and healthy controls ($N=11$, respectively), were studied. They all had normal cognitive level and independent walking ability. A piezoelectric force platform was used to evaluate posture over three feet positions, with eyes open, closed and during visually-guided saccades. Linear (sway path, total area and root mean square) and non-linear parameters (fractal dimension and sample entropy) of the COP were measured to determine postural stability and the complexity and regularity of the COP signals. GLMM analyses were performed to assess COP parameter changes across experimental conditions and subject groups. Finally, Spearman correlations evaluated the significance of potential relationships between linear and non-linear measures as well as between non-linear parameters and clinical data in patients with ASD.

[†]Fabio Pettinato and Maria Stella Valle contributed equally to this work.

*Correspondence:
Rita Barone
rbarone@unict.it
Gianfranco Bosco
bosco@med.uniroma2.it

Full list of author information is available at the end of the article

**Results** Compared to controls, subjects with ASD showed reduced postural stability and complexity, with higher regularity of COP trajectories, particularly in the most unstable feet positions, during visually-guided saccades and in the medial-lateral direction. Spearman correlations indicated that, in the patients' group, postural instability was associated with a decrease in the geometric complexity and an increase in the regularity of the COP trajectory. Moreover, the increase in regularity of the COP trajectory was associated to the severity of restricted and repetitive behavior.

**Conclusions** The results of this study highlight the importance of combining linear and non-linear measures in evaluating postural control in patients with ASD, also with respect to the outcome of interventions on these patients targeting postural balance.

**Keywords** Autism spectrum disorder, Postural control system, Posturographic analysis, Complexity, Postural stability, Restricted and repetitive behavior

## Background

Autism Spectrum Disorder (ASD) is a common, highly heritable neurodevelopmental disorder, characterized by impairments in reciprocal social interaction and communication and a tendency to engage in repetitive stereotyped patterns of behavior, interests, and activities [1]. Its prevalence rate is approximately 1 in 44 children aged 8 years old, with a male to female ratio close to 3 in children and of 2,57 in adults reflecting the influence of non-aetiological factors such as later diagnosis in females [2]. Clinical and molecular features of ASD are highly heterogeneous and core symptoms frequently associate with co-occurring medical conditions such as sleep and eating disturbances, epilepsy and gastrointestinal issues. Other neurodevelopmental disorders occur in almost 80% of patients with ASD, while at least 10% has an additional psychiatric diagnosis. Co-occuring conditions such as anxiety, attention deficit hyperactivity disorder, obsessive-compulsive disorder, intellectual disability, irritability and disruptive behavior greatly influence independence and well-being [3]. A large amount of evidences support also motor function impairment in patients with ASD including motor coordination disturbance, gait anomalies and impaired postural control [4–7]. Analyses of a population-based cohort that included 2,084 children with ASD aged ≤ 6 years found that almost 35% of the sample met criteria for motor difficulties [8]. A variety of motor challenges has been described at different ages, including both fine motor skills (e.g. poor manual dexterity, poor upper limb coordination, weaker fine motor precision, poor eye-hand coordination, weaker fine motor integration) and gross motor skills (slower running speed, decreased agility, poor motor coordination, reduced strength, poor balance and weaker postural control) [9]. Motor difficulties may persist beyond childhood into adulthood, as reported for gait anomalies [10] and differences in static and dynamic balance [7; 11] with relevant influence on autonomy and wellbeing.

Thus, quantitative assessments of the motor behavior in these patients have become increasingly compelling. With respect to postural stability, quantitative analyses of the trajectory of the Center of Pressure (COP) represent the elective methodology to evaluate postural control. COP measurements typically involve recording the time course of the ground reaction force while an individual stands on a force plate or balance board. Two main analysis approaches are used: linear measures stemming from the traditional biomechanical models of postural stability (such as COP trajectory area, sway path length and amplitude over the time) and measures derived from nonlinear dynamics approaches (i.e. fractal dimension, sample and approximate entropy, Lyapunov exponent). These latter have been introduced to detect the presence of subtle physiological changes, hardly detected by linear models [12], which may reflect the strong nonlinearities of neuromuscular feedback and sensory control of standing [13]. Based on the "optimal movement variability" theory [14], mature motor skills and healthy states are associated with an optimal amount of movement variability, which is reflected by the degree of complexity generated into a chaotic state. As a matter of fact, periodic and random states present lower degree of complexity and are related with too rigid (highly predictable) or too unstable (less predictable) systems, respectively. Overall, a complete assessment of the postural behavior may require quantification of the postural stability, as well as measures reflecting the potential complexity of postural control which, altogether might provide insight on the ability of adapting to different postural conditions [15]. In this regard, various nonlinear variables have been introduced to quantify postural complexity (i.e. fractal dimension – FrDim) and regularity features of COP signals (i.e. sample entropy – SampEn). Chaos in physiological systems may be characterized and quantified by calculating fractal dimension (FrDim) of the time series representing a biological signal [16]. For a simple smooth curve, the FrDim is equal 1; for a curve which nearly fills out a two-dimensional plane, FrDim is close to 2. Thus FrDim is a measure of *complexity* of the same curve by describing its shape. In line with Goldberger's

findings [17], higher FrDim (i.e., FrDim values closer to 2), are more compatible with signals showing physiological characteristics. On the other hand, the breakdown of fractal physiologic complexity, as in the case of lower FrDim values, may point to reduced complexity and less optimal postural control strategies.

An additional non-linear measure, sample entropy (SampEn), informs on the *regularity* of postural sway patterns. SampEn estimates the conditional probability that similar patterns of subseries COP will be followed by additional similar measurements without self-matches [18]. A greater SampEn indicates lower predictability for future COP data points and greater irregularity of COP [19]. In this case, intermediate values of SampEn may be associated to signals within the physiological range, as excessively high SampEn values would signify random processes (not optimal), whereas very low values may be associated to a lack of adaptability (too predictable). A healthy postural control system would allow the individual to explore more varied motor strategies, resulting in an optimal level of complexity and regularity in the COP time series [14].

The integration of vestibular, visual, and somatosensory signals is necessary for the maintenance of upright posture. In general, children with neurodevelopmental disorders, including ASD, show more difficulties in maintaining a good postural control when performing oculomotor tasks such as visually-guided saccade tasks, than typically developing (TD) children [20]. Previous studies showed that motor control system in ASD might be less adaptable to sensory information, reflecting difficulties in sensory integration [21; 22] and supporting a relation with abnormal ASD brain connectivity [23]. The use of electronic devices enabled to revealing the presence of a significant increased postural sway in ASD, under certain conditions, including visual input modification, feet position modification or changes in the platform features, thus measuring the contribute of various afferent system to postural control [24]. A pioneer study on postural control dysfunction in ASD already indicated that it occurs across developmental ages, it is not dependent on the possible co-occurrence of intellectual disability and, particularly, that it can be related to difficulties in integrating sensory information [25]. Actually, children with ASD had more difficulty maintaining an upright balance when somatosensory input was modified and especially when visual cues were omitted, showing significantly greater increase in their sway area compared with the controls [25]. Moreover, in children with ASD compared to healthy controls, the effect of removing visual cues (closing the eyes) to postural sway was found larger compared to an attentional task (word memorization) [26].

Previous studies found that children with ASD demonstrated greater COP sway displacement [27; 28], sway areas [27; 29] and velocities [30], and root mean square [31] compared to age-matched children with typical development (TD). Nonetheless, a few posturography analyses in the medical literature have included nonlinear analysis of the COP time-series in evaluating postural control in patients with ASD. Two previous studies observed that ASD patients have more repetitive patterns in their COP trajectories, demonstrated by smaller multiscale entropy during quiet stance [27; 29]. Interestingly, it was suggested [27] that such posturography features of motor behavior might represent repetitive and restricted postural control pattern linking with autism core features such as restricted and repetitive behavior. Pathological postural control might underly the involvement of cortical and subcortical structures networks implicated in the ASD primarily involving the cerebellum [32] and cerebellar connectivity with other brain regions related to multiple functions, including motor, coordination, visuospatial, learning, and balance [33]. Reduction in regional and lobular gray matter volume in distinct cerebellar subregions was consistently correlated with the severity of social interaction, communication, and repetitive behaviors in children with ASD [34; 35].

In the present study we analyzed postural control features during quiet standing in children with ASD and TD children. In addition to measuring standard linear parameters of the COP trajectories (area, sway path length and root mean square), as a main motivation, we aimed at examining two nonlinear features, namely the complexity and the regularity of COP time-series, by computing the FrDim and SampEn, respectively. To evaluate the adaptability of the postural control system in patients with ASD, a sequence of quiet stances was carried out under different feet positions and visual conditions (with eyes open, eyes closed and during visually guided saccades). We pursued to measure dynamical variations of postural control along with the level of complexity and regularity of the COP time series. Correlations were searched for relationships between COP linear and non-linear variables and pertinent clinical features.

## Methods

### Participants

The current study was part of an overall larger study aimed at identifying markers, predictors and developmental trajectories of ASD. The larger overall study was approved by the local ethics committee at Policlinico "G.Rodolico-San Marco", University Hospital of Catania, Italy. Written informed consent was obtained from the parents of all participants. Twenty-two participants were enrolled in the study. Eleven patients with a confirmed clinical diagnosis of ASD were recruited at the Neuropsychiatry section of the Clinical and Experimental Medicine Department University of Catania. All individuals

with ASD met the DSM V-TR (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision) diagnostic criteria for ASD. They were compared to eleven healthy subjects with equal age distribution recruited from a pool of voluntary students attending the hospital. All participants were males, aged 10–15 years, with normal cognitive level and independent walking ability. Demographic, anthropometric and clinical characteristics of study participants are summarized in Table 1. Gross sensory deficits, use of assistive devices or significant physical impairment and associated intellectual disability were exclusion criteria.

### Clinical assessment

Autism symptoms were measured on the Autism Diagnostic Observation Schedule 2 (ADOS-2), the gold-standard tool for ASD diagnosis [36]. All patients presented a calibrated severity score (CSS) above 4, meeting criteria for ASD diagnosis. Autism restricted and repetitive behavior was quantified through the Repetitive Behavior Scale-Revised (RBS-R) [37]. This questionnaire focuses exclusively on RRBs and includes 43 items rated on a four-point Likert scale (scores ranging between 0 and 3 for each item), with higher scores related to more severe RRBs. The RBS-R items are classified into 6 subscales, related to different presentations of RRBs: stereotyped, self-injurious, compulsive, ritualistic, sameness behavior, and restricted interests. Clinical assessment of gross-motor function and balance ability was obtained by clinical examination and measured on the Sensory Profile Measure 2 (SPM-2) [38]. The Home Form, adopted for this study, is structured on eight parallel standard subscales: social participation, vision, hearing, touch, body awareness, balance and motion (vestibular function), planning and ideas and total sensory systems. T-scores for each subscale are grouped into 3 ranges describing the subject sensory profile as typical (T-scores range 40–59), borderline (T-scores range 60–69) or atypical (T-scores range 70–80). Cognitive level (IQ) was

**Table 1** Demographic, anthropometric and clinical characteristics of study participants

| | ASD ($n=11$) | | TD ($n=11$) | | stat | |
|---|---|---|---|---|---|---|
| | Mean | (SD) | Mean | SD | | p |
| **Demographic and anthropometric data** | | | | | | |
| Age (years) | 12 | (1.7) | 12.8 | (1.4) | 1.218 | 0.237 |
| Height (cm) | 159.4 | (6.7) | 161.7 | (8.9) | 0.678 | 0.506 |
| Weight (Kg) | 57.2 | (9.5) | 55.9 | (10.2) | -0.295 | 0.771 |
| **Autism Diagnostic Observation Schedule 2** | | | | | | |
| Social Affect domain | 8.3 | (3.5) | 0.2 | (0.4) | -66 | < 0.001 |
| Restricted and Repetitive Behaviors score | 2.3 | (0.9) | 0.4 | (0.7) | -9.5 | < 0.001 |
| Total score | 10.6 | (4.1) | 0.4 | (0.7) | -50 | < 0.001 |
| Comparison Score | 6 | (2.2) | 1 | (0) | -50 | < 0.001 |
| Calibrated Severity Score (CSS) | 6.1 | (2.2) | 1 | (0) | 0 | < 0.001 |
| **Wechsler Intelligence Scale for Children IV** | | | | | | |
| Intelligent Quotient | 90.4 | (17.7) | 96.5 | (10.8) | 1.125 | 0.343 |
| Verbal Comprehension | 96.5 | (20) | 93 | (11.9) | -0.586 | 0.599 |
| Perceptual Reasoning | 101.6 | (16.7) | 98.7 | (13.9) | -0.411 | 0.709 |
| Working Memory | 83.7 | (15.7) | 101.5 | (17.7) | 2.006 | 0.139 |
| Processing Speed | 84.4 | (16.8) | 95.2 | (9.5) | 2.284 | 0.107 |
| **Restricted Behavior Scale Revised** | | | | | | |
| Stereotyped Behavior | 4.9 | (4.7) | 0.45 | (0.9) | 23 | 0.016 |
| Self-injurious Behavior | 1.3 | (2.3) | 0 | (0) | 33 | 0.027 |
| Compulsive Behavior | 6.2 | (4.3) | 0.54 | (0.9) | 6 | < 0.001 |
| Ritualistic Behavior | 6.6 | (4.5) | 1 | (1.3) | 12 | 0.002 |
| Sameness Behavior | 11.2 | (7.5) | 0.82 | (1.3) | 4 | < 0.001 |
| Restricted Behavior | 3.7 | (3.4) | 0.27 | (0.6) | 11.5 | 0.001 |
| Total Raw Score | 33.9 | (22.5) | 3.73 | (4.2) | 4 | < 0.001 |
| **Sensory Profile Measure 2 - Equilibrium Subscale** | | | | | | |
| Total T-Score | 74.1 | (7.9) | 45.5 | (3.3) | < 0.001 | 0 |

ASD: subjects with autism spectrum disorder; TD: subjects with typical development. Repetitive Behavior Scale-Revised: higher scores relate to more severe RRBs. Sensory Profile Measure-2 T-scores ranges: typical (40–59), borderline (60–69) or atypical (70–80)

measured by using the Wechsler Intelligence Scale for Children IV (WISC IV) [39].

### Apparatus and procedures

To assess postural stability, ground reactive forces were recorded by a force platform (Kistler 9286 B, Winterthur, Switzerland; 100 Hz sampling frequency) and the signals were sent to the SMART-D system (BTS, Garbagnate Milanese, MI, IT) for offline processing. Prior to participation, each participant received extensive verbal explanations and a demonstration of exercise, verifying that all participants had a clear comprehension of the task-based instruction.

The study protocol consisted in performing a sequence of quiet stances with the feet positioned as follow (Fig. 1A-B):

1. parallel feet with the heels spaced 20 cm (FP20);
2. parallel feet with the heels spaced 10 cm (FP10);
3. feet extra-rotated with the heels together and opening angle of 30° (FP30).

The decision of evaluating different feet configurations, stems from the consideration that foot positioning affects the kinematics of standing body sway, where FP20 represents the most stable postural condition, and a decrease in the base of support in FP10 and FP30 implies a reduction of the postural stability [40].

For each feet position, the test was performed with eyes open gazing a target (FP20EO, FP10EO, FP30EO), eyes closed (FP20EC, FP10EC, FP30EC) and during visually-guided saccades (FP20Sac, FP10Sac, FP30Sac). For the visually-guided saccades conditions, participants were asked to perform voluntary horizontal eye saccadic movements between two visual targets. The order of presentation of feet positions and vision conditions was randomized across the participants. Subjects stood barefoot with their arms placed downward at their sides of the body, and visual targets were located at a distance of 3 m,

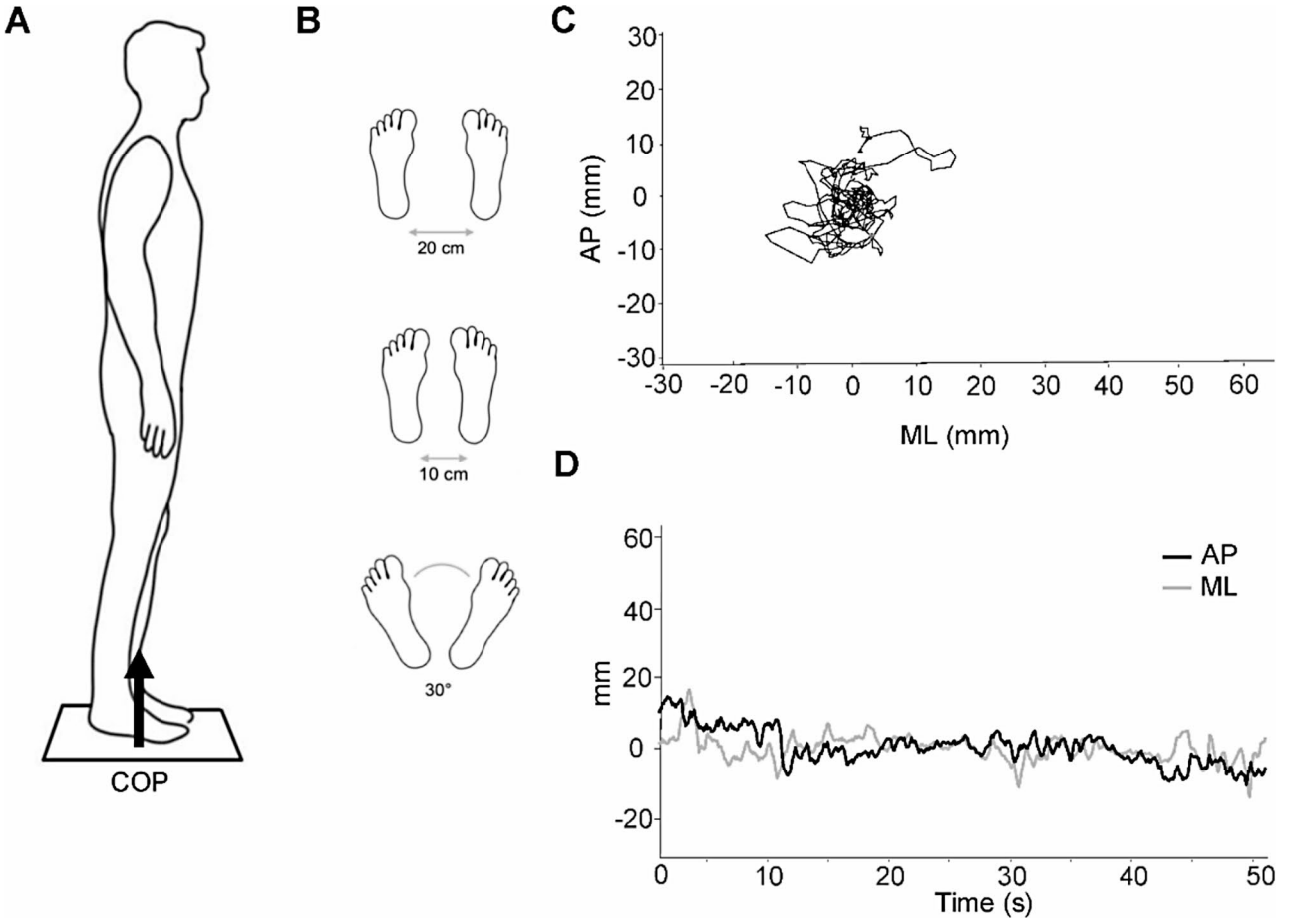


**Fig. 1** Representation of the experimental conditions of the study and of COP measures. A force platform (**A**) was used to measure ground reaction forces and to obtain the trajectory and time related data of the center of pressure (COP). Schematic representation of the three feet positions used for the postural tests are depicted in panel (**B**). For each foot position, the postural tests were performed with eyes open, closed and during visually-guided saccades. The COP sway path is represented as temporal oscillations along AP and ML directions (**C**) and as the COP spatial trajectory (**D**)

with the center point of each target adjusted at the participants' eye level. The feet were placed inside an outline border to guarantee constant feet positioning across the tests. The participants were asked to stand as still as possible during the trials, which lasted 50 s each. The participants were frequently asked about their fatigue level and instructed to alert the examiners when they were feeling fatigued. The room where the sessions were held, had a comfortable temperature, diffused light and no external noises.

#### Data processing and measurements

Data for each trial were collected for 50 s and downsampled at 10 Hz. The 3D raw signals of forces and moments, acquired by the force platform, were first filtered (second-order low-pass Butterworth filter, cutoff frequency 5 Hz) and then used to calculate COP-based measures in anterior-posterior (AP) and medial-lateral (ML) displacements. From AP and ML time series, the two-dimensional trajectory of the COP was reconstructed, and two subsets of linear and non-linear parameters were determined. Along with linear measures to assess postural stability, non-linear parameters were used to investigate complexity and adaptability of the postural control system.

The first set of linear measurements comprised the following parameters:

*Sway path (SP): total length of the COP trajectory, expressed in mm, computed as the sum of the distances between two consecutive points in the two-dimensional space;*
*SP AP and SP ML: the length of the COP displacement computed as SP, however measured along the AP and ML directions;*
*Area SP: total area ($mm^2$) covered by the COP trajectory computed as the 95% confidence ellipse;*
*Root Mean Square (RMS): variability of amplitude oscillations along AP and ML directions computed as standard deviation from the mean of each time series.*

The second set of parameters were derived from non-linear dynamics analyses applied to the ML and AP time series components of the COP. Before computing these parameters, time series were reconstructed in state space using the method of delayed embedding implemented for MATLAB by Wallot and Mønster (2018) [41]. The embedding time delays and dimensions were computed for each time series by using the Average Mutual Information and False Nearest Neighbor algorithms, respectively, and their mean values across subjects and trials, rounded to nearest integers (time delay=6 and embedding dimension=4), were, then, applied to the estimation of the following non-linear measurements:

*Fractal Dimension (FrDim), which represents a non-linear measure of the COP trajectory geometrical complexity. The FrDim was computed separately for AP and ML time series according to the Higuchi method implemented by the Matlab function "Higuchi_FD.m" and using the default Kmax value of 10. Changes in FrDim indicate a change in control strategies for maintaining quite stance [42; 43].*
*Sample Entropy (SampEn): non-linear parameter to estimate the level of complexity or regularity of the time series oscillations, considering the non-stationarity of the postural signal. SamEn was computed separately for the AP and ML components according the Richman & Moorman algorithm (2000) [18] implemented by the matlab function "SampEn.m". For the computation of the SampEn we adopted a tolerance value equal to 0.2 the standard deviation of the time series, and the aforementioned embedding dimension value of 4.*
*The SampEn ranges between 0 and 2 with 0 indicating a phenomenon with high regularity, and 2 indicating a completely random data behavior, while intermediate values are typical of more or less complex deterministic systems.*

Signal processing was implemented by using Matlab version R2022a (Mathworks Inc, Natick, MA, USA).

#### Statistical analyses

Preliminary tests for normality were performed by using Shapiro-Wilk tests on the distributions of all the COP-derived indexes, providing the basis for the type of statistical analyses used further. The assumption of normality was not met by all distributions except for that of the AP component of the SampEn in the patients group. Accordingly, the descriptive statistics of the distribution of these parameters for each group will be reported as median, interquartile range and minimum and maximum values.

To assess potential differences in the postural indexes between patients and controls during the different postural conditions set experimentally, we applied Generalized Linear Mixed Models on the distribution of each COP-derived parameter with Postural Condition (9 levels: FP20EO | FP10EO | FP30EO | FP20EC | FP10EC | FP30EC | FP20Sac | FP10Sac | FP30Sac) as "within subject" fixed effect predictor, Subject Group (2 levels: Patients | Controls) as "between subject" fixed effect predictor and their interaction. We also modeled as random effect the intercept of the data of each subject to account for interindividual variability. Since COP-derived parameters were generally not normally distributed and

comprised only positive values, we determined, by applying one-sample Kolmogorov-Smirnov tests, that they conformed to the Gamma distribution. Accordingly, we modeled the response function of each GLMM by assuming a Gamma distribution. For the statistically significant main effects of Postural Condition and interaction effects of Group*Postural Condition we examined also the statistical significance (LSD adjusted) of the pairwise comparisons between the estimated marginal means of the predictors' levels.

Finally, Spearman correlation coefficients were computed to determine the degree of correlation between linear and non-linear measures as well as the correlations between non-linear parameters and clinical data in patients with ASD and control subjects. The statistical significance cut-off was set to $p<0.05$ for all analyses.

SPSS version 27 (SPSS, Inc., Chicago, IL, USA, IBM, Somers, NY, USA) was used for the statistical analyses.

## Results

Participant's demographic, anthropometric and psychometric features are reported in Table 1. Since height and weight have been shown to affect the reliability of COP measures, we assured that no significant differences in anthropometric parameters were recorded between groups. Individuals with ASD (11 males, mean age 12 years, SD 1.7), had normal cognitive levels (mean IQ 90.4, SD 17.7) and mild to moderate autism severity levels (ADOS CSS: mean 6.1, SD 2.2). Repetitive and restricted behaviors had variable severity, with a total score ranging from a minimum of 6 to a maximum of 74, out of a maximum severity score of 129. Insistence on sameness, ritualistic and compulsive behaviors were the most frequent RRBs, followed by stereotyped and restricted behaviors. Balance and motion sensory profile (vestibular function) was clinically abnormal in all ASD participants, with a mean T-score of 74.1 (SD 7.9) falling within the range of definite dysfunction. Participants with typical neurodevelopment (control group) included age- and gender-matched healthy individuals ($N=11$, mean age 12.8 years, SD 1.4), with normal cognitive levels (mean IQ 96.5, SD 10.8, p 0.343). Control individuals scored in the normal range on the ADOS 2 (no evidence on autism symptoms), the RBSR and SPM2 equilibrium subscale showing no pathological repetitive behaviors or disequilibrium, respectively (Table 1).

### Results of GLMM analyses on COP linear and non-linear parameters

We quantified potential differences between the postural behavior of patients and control subjects and assessed whether these differences may depend on the difficulty of the postural condition and on the continuous availability of visual information by applying GLLMs to each of the linear and non-linear parameters derived from the COP trajectory.

#### Linear parameters

GLMM analyses of the total sway path and of its AP and ML components indicated that in both subject groups the SP length varied significantly in relation to the experimental condition (main effect of condition in Table 2A, see also Fig. 2A-C). The degree to which the length of the SP was modulated across experimental conditions was, however, significantly different between patients and control subjects, as exemplified by the significant Group*Condition interaction effect. Pairwise comparisons showed that this interaction effect was, for most part, accounted by the larger differences among experimental conditions observed in the control compared to patients' group. Indeed, we found for all three measures of SP a consistently higher number of statistically significant pairwise comparisons in the control group (24 vs. 19 for SP; 26 vs. 16 for SP AP and 19 vs. 14 for SP ML). This result may suggest that patients were not as flexible as control subjects in adapting their postural strategy to the different conditions.

As illustrated by Fig. 2D, the area covered by the COP displacement was significantly greater in patients than in control subjects (main effect of Group, see Table 2 A) and, in both subject groups, it was significantly modulated by the experimental condition (main effect of Condition). The significant interaction effect of Group*Condition indicated that control subjects varied the COP area among experimental conditions more than patients, since a larger number of statistically significant pairwise comparisons between conditions was found in the control compared to the patients' group (20 vs. 12). In addition, significant pairwise differences between patients and controls were evident in the FP10SAC, FP30SAC, FP30CE and FP20OE conditions, suggesting further that postural differences between patients and control subjects were exacerbated by reduced visual inputs.

The variability of COP oscillations measured by the RMS along the AP and ML components was significantly higher in patients compared to control subjects, and it varied significantly in both groups depending on the experimental condition (significant main effects of Group and Condition, see also Fig. 3). For both AP and ML components, we found also highly significant interaction effects of Group*Condition. This interaction effect was explained for the AP component by the larger changes among experimental conditions in patients compared to control subjects (5 vs. 1 statistically significant pairwise comparisons) and by significant differences between patients and control subjects in the FP30EC condition. Unlike the AP component, for the ML component, RMS values varied more among postural

**Table 2** Results of GLMM analyses on the COP linear (A) and non linear (B) parameters

**A**

| | | SP | | SP AP | | SP ML | | AREA | | RMS AP | | RMS ML | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **df** | **F** | ***p*-val** | **F** | ***p*-val** | **F** | ***p*-val** | **F** | ***p*-val** | **F** | ***p*-val** | **F** | ***p*-val** |
| ***Condition*** | 8,180 | 22.5 | < 0.001 | 24.1 | < 0.001 | 22.1 | < 0.001 | 12.4 | < 0.001 | 3.04 | 0.003 | 23.8 | < 0.001 |
| ***Group*** | 1,180 | 1.6 | 0.2 | 2.02 | 0.15 | 1.02 | 0.31 | 8.07 | 0.005 | 4.05 | 0.046 | 8.21 | 0.005 |
| ***Group* Condition*** | 8,180 | 3.6 | < 0.001 | 3. | < 0.001 | 2.64 | 0.009 | 8.55 | < 0.001 | 3.25 | 0.002 | 3.43 | 0.001 |

**B**

| | | FrDim AP | | FrDim ML | | SampEn AP | | SampEn ML | |
|---|---|---|---|---|---|---|---|---|---|
| | ***df*** | ***F*** | ***p-val*** | ***F*** | ***p-val*** | ***F*** | ***p-val*** | ***F*** | ***p-val*** |
| ***Condition*** | 8,180 | 0.57 | 0.795 | 27.2 | < 0.001 | 3.87 | < 0.001 | 9.27 | < 0.001 |
| ***Group*** | 1,180 | 10.7 | 0.001 | 10.5 | 0.001 | 4.35 | 0.038 | 12.9 | < 0.001 |
| ***Group* Condition*** | 8,180 | 1.38 | 0.208 | 1.0 | 0.434 | 2.71 | 0.008 | 2.54 | 0.012 |

SP: sway path length; AP: anterior-posterior; ML: medial-lateral; RMS: root mean square; FrDim: fractal dimension; SampEn: Sample entropy

conditions in the control compared to the patients' group (23 vs. 15 statistically significant pairwise comparisons) and significant differences between control subjects and patients were evident in a larger number of conditions (FP10SAC, FP30SAC, FP30CE and FP20OE). Therefore, also the differences in the variability of the COP trajectories between control subjects and patients tended to be accentuated by reduced visual inputs.

### Non-linear parameters

GLMM analysis applied on the Higuchi fractal dimension of the AP and ML components of the COP trajectory (Fig. 4 A-B and Table 2B) showed statistically significant main effects of Group, due to the smaller fractal dimension values observed in patients compared to control subjects. The Higuchi fractal dimension of the ML component varied significantly also with the experimental condition (main effect of Condition in Table 2B). Pairwise comparisons between the levels of the experimental condition, indicated that this effect was mostly accounted for by the smaller FrDim values when feet were extra-rotated at an opening angle of 30 degrees.

SampEn values for both the AP and ML components of the COP trajectory were also significantly smaller in patients compared to control subjects (significant main effects of Group, see Fig. 4C-D and Table 2B). For both components, we found also significant main effects of the experimental condition, which were mostly related to the smaller SampEn values observed in experimental conditions with feet extra-rotated at an opening angle of 30 degrees. These changes were more pronounced in control subjects, explaining the significant interaction effect of Group* Condition. Indeed, a larger number of significant pairwise comparisons were observed in the control compared to the patients' group (9 vs. 0 and 23 vs. 15, for the AP and ML components, respectively). These interaction effects were also driven by significant differences between the SampEn values of the two groups. For the AP component significant differences between groups occurred during the FP30CE condition, while for the ML component they occurred during the FP10CE, FP20CE, FP30CE, FP10SAC, FP30SAC and FP30OE conditions. Notably, the experimental conditions that produced larger differences between patients and controls were those that involved either absence or reduction of visual information (eyes closed or saccades) and more unstable posture conditions (feet diverging at 30 degrees angle), much alike the pattern emerging from the analysis of the linear parameters (Table 2 A-B).

### Correlations between linear and non-linear postural parameters in patients with ASD

We performed Spearman correlations between linear and nonlinear parameters for each experimental condition

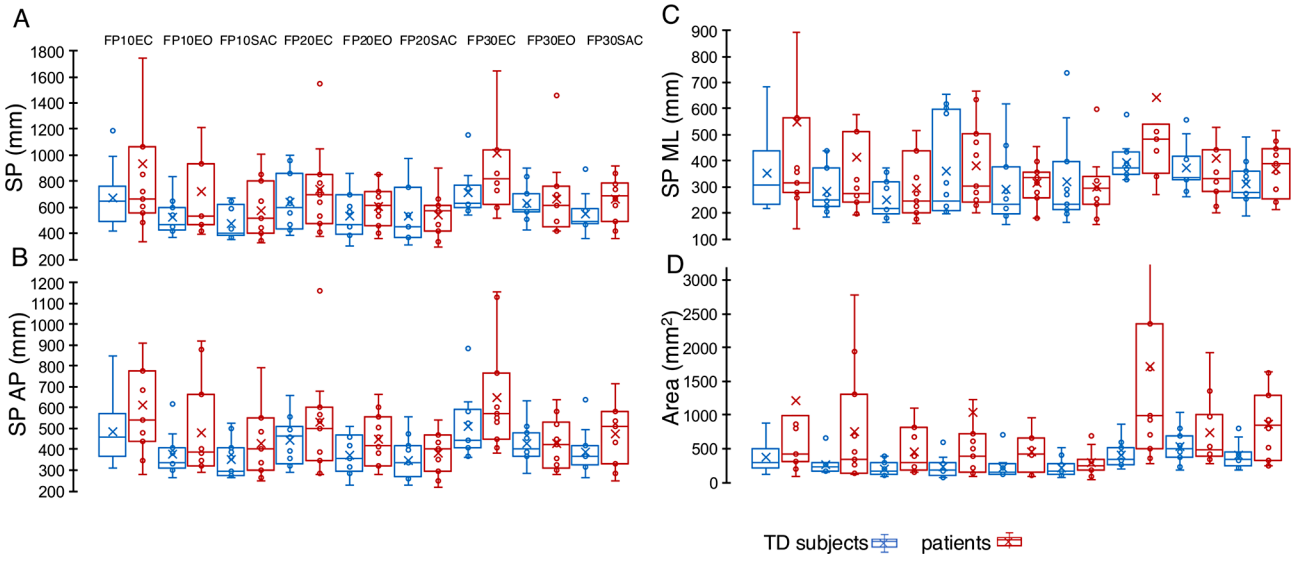


**Fig. 2** Distributions of COP Sway Path and Area values across experimental conditions and subject groups. Box and whisker plots report the median value (horizontal line within the box) and the variability represented as interquartile range (vertical length of the box), as well as the highest and the lowest value (lines above and below the box), of the total SP (**A**), AP and ML components of the SP (**B** and **C**, respectively) and Area, computed separately for ASD patients (red) and controls (blue). *Abbreviations* FP, foot position; ASD, Autism Spectrum Disorder; SP, sway path; AP, anterior-posterior; ML, medial-lateral; EC, eyes closed; EO, eyes open; Sac, visually-guided saccades

and in both subject groups. Although a similar number of statistically significant Spearman correlations were found in both groups (20/108 and 24/108 in the control and patients' group, respectively), the distribution of statistically significant correlations across parameters and conditions, as well as their sign of the correlations, were remarkably different between controls and patients. In the patients' group, all statistically significant correlations were negative, and they were found primarily between SampEn and area ($n$=5), SampEn and RMS ($n$=11) SampEn and SP (1) values. Other significant correlations were found between the Higuchi FrDim and either the area or the RMS values (3 and 4 significant correlations, respectively). Examples of significant negative correlations between linear and nonlinear parameters in the patients' group are illustrated in Fig. 5A-B. Conversely, with the control group, we found that 12 of the significant correlations were positive and 8 were negative. Positive correlations were found between FrDim and SP ($n$=9), RMS ($n$=1) and area ($n$=1) values, as well as between SampEn and RMS values ($n$=1). Negative correlations were found between SampEn and RMS values ($n$=7), as well as between FrDim and RMS values ($n$=1). Thus, there was very little overlap between the distributions of the significant correlations in the control and the patients' groups. This is also evident from the examples in Fig. 5A-B, where significant negative correlations in the patients' group were not accompanied by significant correlations in the control group. Overall, we did find only three experimental conditions where SampEn and RMS values were significantly, negatively correlated in both groups namely 20CE, 30CE and 10OE, all in the ML dimension. Finally, it is also worthwhile noting that, while in the control group the positive correlations between the values of the linear parameters of postural stability (area, SP) and those of the FrDim might indicate that decrease in the postural stability was associated to increased complexity of the COP trajectory, the negative correlations found in the patients' group between nonlinear parameters FrDim and SampEn and linear parameters area and SP might denote that decreased postural stability was associated with less complex and more regular COP trajectory.

### Correlation between non-linear postural parameters and clinical data

We evaluated possible associations among non-linear parameters and clinical severity of ASD, measured by using the SPM and RBS-R total scores. We considered all the studied conditions in the two groups. We found that in conditions of visual input modification, with feet positioned at 20 cm, in patients with ASD SampEn of the ML component was inversely correlated to the total score of the SPM-2 Equilibrium subscale (Fig. 5C: $r$ = -0.83, $p$=0.001). In the same condition, patients with ASD also exhibited an inverse correlation between SampEn of the ML component and the total RBS-R score, measuring the severity of repetitive behavior (Fig. 5D: $r$ = -0.68, $p$=0.028). Moreover, we found that in the condition of absent visual information (FP30EC) and/or less stable feet position (FP10EO, FP30EC), SampEn decrease was significantly associated with increased RBS-R clinical score in the patient group (Fig. 5E: $r$= -0.71; $p$=0.013;

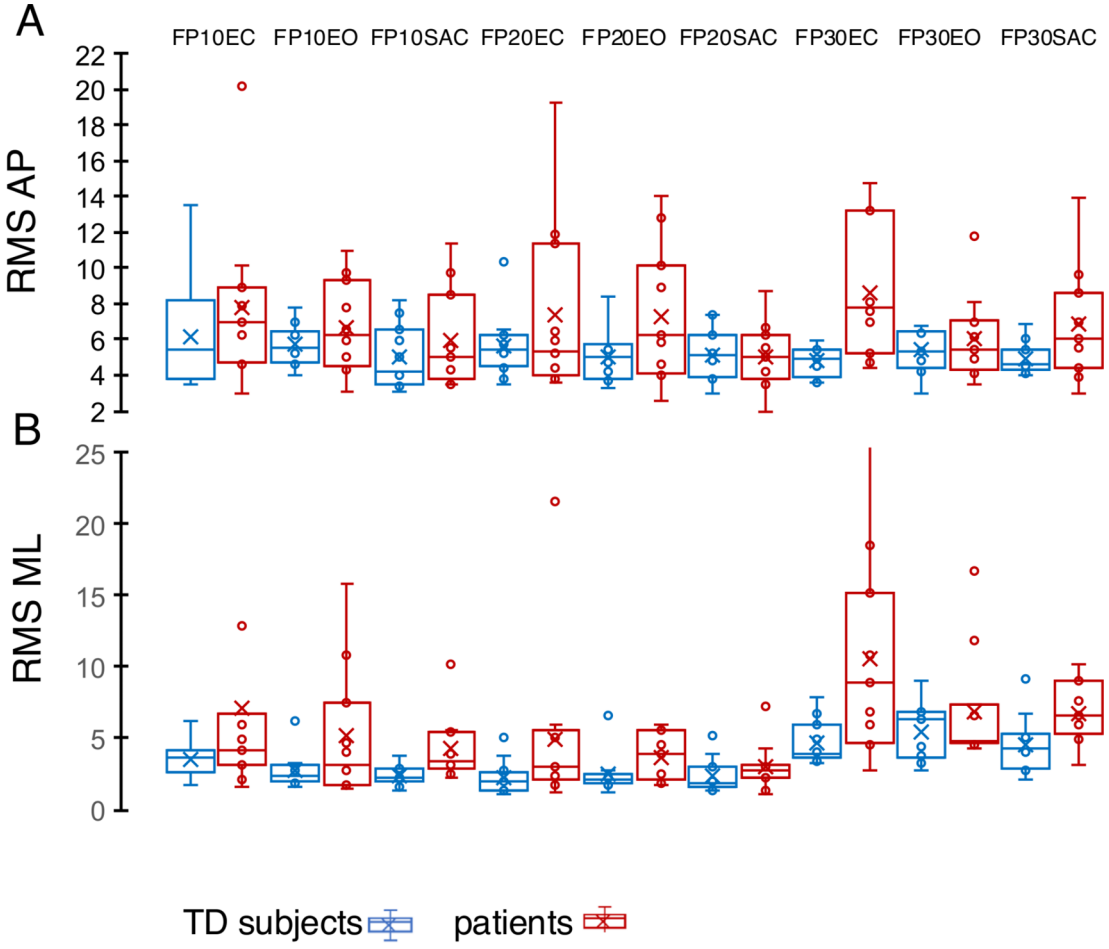


**Fig. 3** Distributions of COP RMS values across experimental conditions and subject groups. Same layout as Fig. 2, for the RMS of the AP and ML components (**A** and **B**, respectively). *Abbreviations* FP, foot position; ASD, Autism Spectrum Disorder; RMS, Root Mean Square; AP, anterior-posterior; ML, medial-lateral

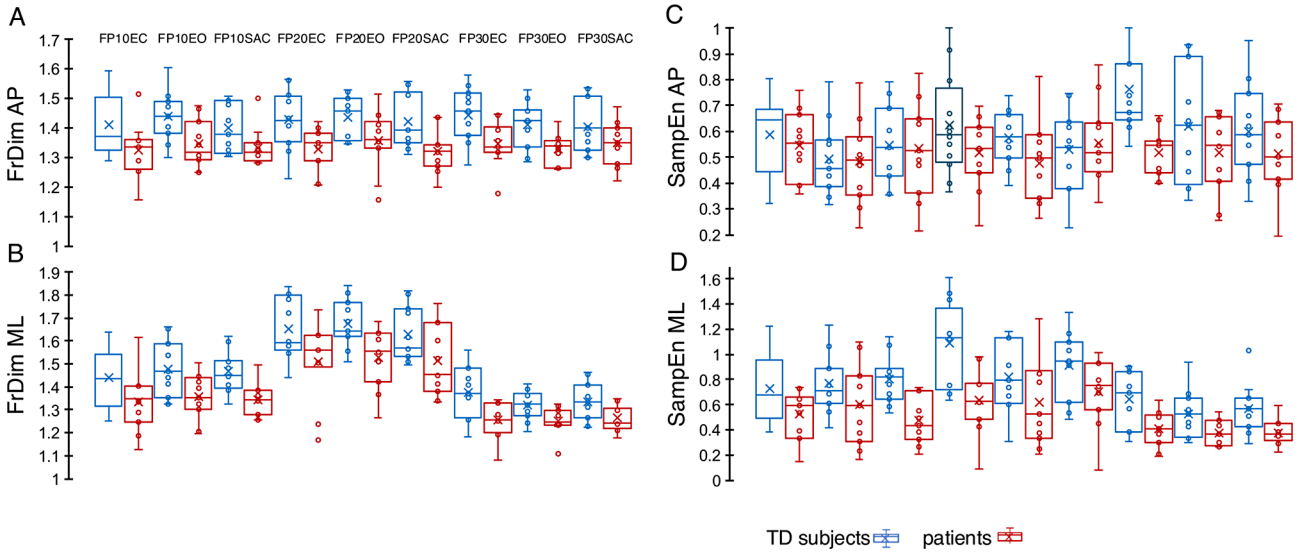


**Fig. 4** Distributions of COP nonlinear parameters across experimental conditions and subject groups. Same layout as Fig. 2, for the FrDim of the AP and ML components (**A** and **B**, respectively), and for the SampEn of the AP and ML components (**C** and **D**, respectively). *Abbreviations* FP, foot position; ASD, Autism Spectrum Disorder; FrDim, Fractal Dimension; SampEn, Sample Entropy; AP, anterior-posterior; ML, medial-lateral

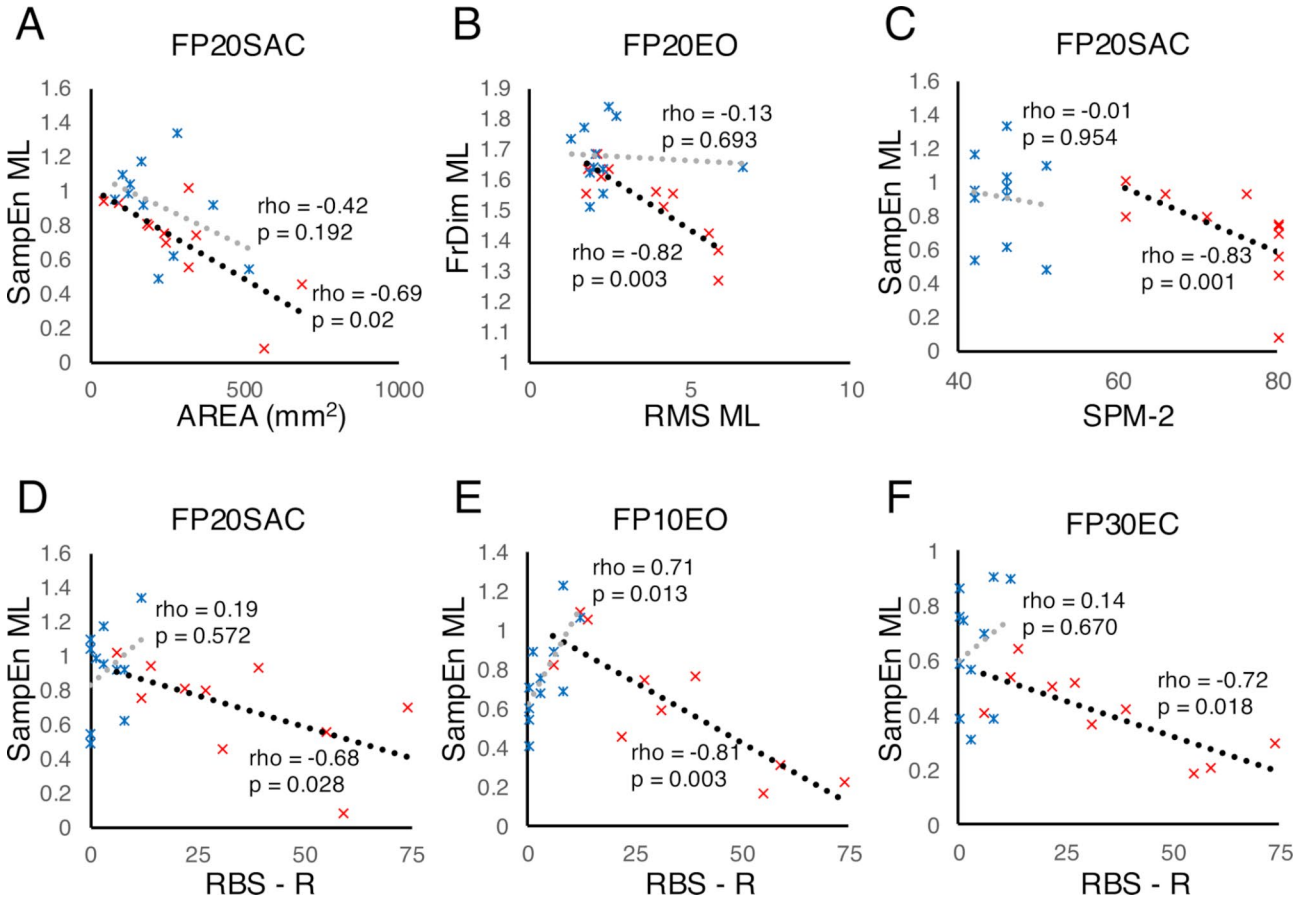


**Fig. 5** Correlations between COP nonlinear parameters and COP linear parameters and between COP nonlinear parameters and clinical scales. Correlations between nonlinear (SampEn in **A**, FrDim in **B**) and linear postural parameters (Area in **A**, RMS in **B**), and between nonlinear parameters (SampEn) and clinical scales (SPM-2 in C, RBS-R in D-F) in subjects with ASD (red circles) and controls (blue circles). *Abbreviations* ASD, Autism Spectrum Disorder; SampEn, Sample Entropy; RMS, Root Mean Square; SPM-2, sensory profile measure 2; RBS-R, repetitive behavior scale revised; ML, medial-lateral

Fig. 5F: $r$= -0.72; $p$=0.018;). We then assume that in the ASD group only, patients with more severe sensory dysfunction (SPM score) and behavioral repetitiveness (RBS-R score) manifested more regular COP trajectory measured by SampEn, particularly in the ML dimension, and especially in conditions of visual control modification or with more unstable feet position.

## Discussion

In this study, we used quantitative posturography analyses to characterize the postural behavior of school-aged patients with ASD in comparison with neurotypical, age-matched controls. The two cohorts were submitted to nine different experimental conditions by which we manipulated the availability of visual information (gaze on target, closed eyes and visually guided saccades), as well as the stance support base, with subjects standing up in three different feet position configurations, to determine their ability to adapt postural control to different environment conditions. The main motivation of the study was to combine linear (area, SP lenght, RMS) and nonlinear parameters (SampEn, FrDim) derived from the COP trajectory, to get insight on the nature of the potential differences emerging between ASD patients and controls and further validate the use of nonlinear parameters of the COP trajectory as means to potentially inform the diagnostic and rehabilitation processes in these patients. Thus, we characterized postural stability with standard linear parameters, such as the area of the COP trajectory, the length and the variability of the sway path, while extracting information about the complexity and regularity of the postural control by way of two nonlinear measures, namely the FrDim and the SampEn. Lower FrDim values may inform about the loss of physiological complexity suggesting reduced adaptability [17]. Additionally, too low SampEn values may point to excessive regularity and predictability of COP signal, also implicating reduced adaptability and inefficient postural control strategies [18].

Potential differences in the postural behavior between patients and control subjects and the effects of the different postural conditions were evaluated statistically

by applying GLLMs to each COP-derived parameter with subject group, the type of experimental condition, and their interaction as predictors. GLMM analyses did show significant differences in both linear and nonlinear parameters between ASD patients and controls, which, in most cases, depended on the availability of visual information. For example, in agreement with previous studies [25; 29; 44; 45], we found that the COP sway area was significantly greater in the ASD group compared with controls, especially in those conditions where visual information was either not available or restricted by the saccadic task. Notably, Molloy et al. (2003) [25] identified a comparable group * condition interaction effect, showing that under conditions in which vision was occluded, children with ASD increased the sway area significantly more than controls, regardless of whether the somatosensory input was also manipulated. With respect to the SP length, although it did not vary significantly, on average, between subject groups, larger differences among different experimental conditions were evident in the control group compared to ASD patients, suggesting that ASD patients did not adapt flexibly to different postural conditions as neurotypical controls. The variability of COP oscillations along the AP and ML components, measured by the RMS, was significantly increased in ASD patients compared to control subjects. Although RMS values were significantly influenced in both groups also by the experimental conditions, particularly for the ML component, differences of the COP trajectories among experimental conditions were larger, again, in control subjects. Moreover, differences between patients and controls tended to be accentuated by conditions with reduced visual input. Chen and Tsai (2016) [46] compared ASD patients and controls with similar ages as in the present study (9–12 years) and they also found that the standard deviation of sway oscillations in the ML direction was significantly larger in ASD group for eyes closed than eyes open conditions. Taken together, the previous studies [31; 46; 47] and our present results indicate that children with ASD had a markedly greater amount of postural sway in the ML direction, which could be related to a limited ability using the "hip strategy" to maintain balance [46]. Moreover, these findings support the notion that ASD children may rely on visual information to regulate body movements to compensate for difficulties in proprioceptive processing [48] and, more generally, in integrating different sensory modalities for postural control. Indeed, sensory processing difficulty is a cardinal feature included in diagnostic criteria of ASD (APA, 2021) [1]. Furthermore, it has been associated with autism severity, poorer functional outcomes, and behavioral difficulties across the lifespan [49], impacting on higher-order cognitive function such as movement ideation and motor planning [50].

Only few studies, thus far, have investigated COP nonlinear measures in subjects with ASD, focusing on multiscale entropy [27; 28; 29] analyses. Notably, Fournier (2014) reported that children with ASD exhibited decreased complexity of the postural control dynamics, measured by multiscale entropy complexity index. This result has been interpreted as a more regular or restricted control of posture linking postural instability to stereotypic behavior and the neurobiology of ASD [27]. More recently, Li et al. (2019) [29] found that the ASD group exhibited lower complexity in the mediolateral sway compared with typical developing group and concluded that postural control complexity was partially compromised, potentially increasing the risk of fall in children with ASD. Following this line of evidence, the present study aimed at evaluating further and more systematically ASD patients' postural behavior across a variety of postural conditions known to influence postural stability in healthy controls and in disease populations [7; 40], by analyzing also two non-linear parameters, namely FrDim and SampEn, commonly used in the field of postural control. GLMM analyses revealed that patients exhibited reduced SampEn and FrDim values compared to the control group both for the AP and ML components, indicating excessive regularity and predictability of COP signal and loss of physiological complexity resulting in reduced adaptability and inefficient postural control strategies. Remarkably, SampEn values, particularly for the ML component, were reduced in ASD patients compared to controls for conditions with reduced visual information (eyes closed or saccades) and/or less stable support base (i.e. FP30 condition), resembling closely the pattern observed for linear parameters.

Correlations between linear and nonlinear measures of postural behavior pointed out further interesting differences between ASD patients and controls. In ASD patients only negative correlations were found between linear parameters associated to postural stability and non-linear parameters related to the complexity and regularity of the COP trajectory, indicating that postural instability in the ASD group was associated with reduced geometrical complexity and increased regularity of the repetitive patterns of the COP oscillations. Conversely in the control group, postural stability parameters (area, SP) were positively related to increased complexity of the COP trajectory (FrDim).

In this regard, dynamic non-linear measures have been demonstrated to be rather sensitive for the evaluation of postural instability in healthy subjects [51] and in pathological conditions as in Parkinson's Disease and Spinocerebellar Ataxia [52], and to be informative in explaining postural deficit in Prader-Willi Syndrome [53], Down Syndrome [54] and Pompe Disease [40].

It appears that nonlinear indices may also capture subtle features of physiological time series that are also associated with clinical scale measurements. In this context, patients with Parkinson's disease display changes in the temporal organization of gait variability during the course of the disease which are captured by the reduction of the Hurst exponent, indicative of a more random (less structured) walking pattern, from earlier to later stages of the disease. Greater disease severity, reflected by higher scores on the Hoehn & Yahr scale demonstrated a significant negative correlation with the Hurst exponent, so that patients with higher clinical scores exhibited a more erratic and unstable gait, indicated by the lower Hurst exponent [55].

In the present study we show reduced geometrical complexity of the COP trajectory (FrDim) and greater regularity of the COP time series (SampEn) in subjects with ASD, which correlate with the degree of clinical manifestation of ASD, as measured by the SPM-2 and RBS-R scales. Our data suggest a less flexible postural control, characterized by higher levels of rigidity and reduced adaptability to environmental triggers. This diminished level of complexity might be explained by poor access to alternative strategies in postural control, ineffective ability of self-organization and lower number of sources responsible for the motor variability control [56; 57].

This scenario supports the idea that ASD individuals may have difficulties in performing anticipatory postural adjustments (APA). APA represent corrective actions that occurs prior to the forthcoming perturbation, based on predictions of the effects of the perturbation. For example, when passing from standing posture to walking, the possible posture perturbations caused by the first step are anticipated by short body oscillations to implement the adequate force for a stable gait initiation [58]. Some authors report deficits of APA in children with ASD during a bimanual load-lifting task [59] or during body oscillations [60]. The data from the study of Beker et al. [60], strongly support the presence of deficits in predicting postural perturbations associated with rhythmic body movements. That is, failure to predict excessive body sway leads to a deficit in anticipating postural control, increasing the risk of fall. Our data indicate also that the impaired postural control in ASD is especially noticeable when the contribution of specific sensory systems is compromised. We showed that reducing visual information available to subjects with ASD, significantly affects postural stability, particularly in the more challenging feet positions. Thus, it is plausible that, in ASD, sensory integration impairment may limit the ability to detect perturbations and potentially affect the ability to generate APA. Recently it has been suggested that children with autism may have altered feedback signals from higher-order brain areas to the primary sensory regions. Since these feedback signals are thought to be important in filtering sensory information based on attentive and predictive processes, individuals with autism might be disadvantaged in using prior experience or putting together parts of the sensory experience into a contextual framework to help make sense of the incoming visual information [61]. This evidence may support the view that disrupted sensory processing in autism may also account for potential altered APA mechanisms and postural stability in ASD. It has been suggested that patients with ASD might have a tighter coupling between visual channels that register changes in optic flow (as a result of postural sway) and the motor system responsible for maintaining balance [25]. Further, standing with eyes closed requires a shift from a reactive control strategy based on vision to a feedforward strategy based on anticipation. If this latter type of control is poorly developed in ASD, as these studies suggest [59; 60; 61], this would provide an explanation for the destabilizing effects observed when standing with eyes closed.

The alterations in linear parameters in subjects with ASD (larger COP Area and increased RMS) affect the projection of the center of mass beyond the stability limits of the support base and this has been linked to an enhanced risk of falls [29]. The answers provided by caregivers of individuals with ASD to the equilibrium subscale of SPM-2, seem to support this assumption. Almost all ASD participants were reported to have poor coordination and overall bad balance abilities, almost 70% of study subjects had the tendency to avoid activities requiring postural skills and the inability to regain balance while falling, whilst half of the participants showed fear of getting on elevators or escalators. Rigidity, invariance and inflexibility are also typical attributes of repetitive and restricted behavior (RRB), a core feature of ASD. Previous studies in ASD samples reported a relation between RRBs and postural asymmetry [62], correlations linking the sway area and the severity of RRBs [45] and suggested a possible link between stereotypic behavior and the mean SampEn [27]. We found a negative correlation between SampEn, as a measure of complexity in temporal sway of the COP trajectory and the severity of RRBs. The reduced complexity and higher regularity of COP time series in ASD may unravel underlying ASD cognition processes, including decreased cognitive flexibility linked to autistic children's increased susceptibility to perseverative thought and behavior.

## Conclusions

We report on the feasibility of combining linear and non-linear posturographic analyses to investigate standing postural ability in patients with ASD. We demonstrated reduced postural stability and reduced geometric

complexity of the COP sway path in patients with ASD, associated with higher levels of pattern regularity, which correlated with clinical data on balance performance and repetitive and restricted behaviour. In interpreting the results we should, however, consider that the small sample size, associated to the lack of clinical stratification, has not made possible to assess the effects of gender as well as the influences of comorbidities and the impact of age on postural control system. Notwithstanding the current limitations, present data show and support the importance of combining linear and non-linear measures in evaluating postural control in patients with ASD. Non-linear measures might represent a more functional method to unravel those changes closely related to ASD that may be further explored as possible instruments in the outcome evaluation of interventions targeting postural balance in patients with ASD.

**Abbreviations**

| | |
|---|---|
| ASD | Autism Spectrum Disorder |
| COP | Center of Pressure |
| TD | Typically Developing |
| DSM V-TR | Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision |
| ADOS-2 | Autism Diagnostic Observation Schedule 2 |
| CSS | Calibrated Severity Score |
| RBS-R | Repetitive Behavior Scale-Revised |
| RRB | Repetitive and Restricted Behavior |
| SPM-2 | Sensory Profile Measure 2 |
| IQ | Intelligent quotient |
| WISC IV | Wechsler Intelligence Scale for Children IV |
| FP20 | Parallel feet with the heels spaced 20 cm |
| FP10 | Parallel feet with the heels spaced 10 cm |
| FP30 | Feet extra-rotated with the heels together and opening angle of 30° |
| EO | Eyes Open |
| EC | Eyes Closed |
| Sac | Visually guided saccades |
| AP | Anterior-Posterior |
| ML | Medial-Lateral |
| SP | Sway Path |
| FrDim | Fractal Dimension |
| RMS | Root Mean Square |
| SamEn | Sample Entropy |

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**Author contributions**
RB, FP, and MSV conceived and designed the study. FP and LC performed clinical assessment. MSV, MC and AC conducted the posturographic analyses. AC, GB carried out data analysis. RB, FP, MSV, AC, GB performed interpretation of results and prepared the original draft. Manuscript editing was completed by RB, FP, MSV, AC, RR, GB. All authors read and approved the final manuscript.

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**Data availability**
All data generated or analyzed during this study are included in this published article.

## Declarations

**Ethics approval and consent to participate**
The current study was part of an overall larger study aimed at identifying markers, predictors and developmental trajectories of ASD. The larger overall study was approved by the local ethics committee at Policlinico "G. Rodolico-San Marco", University Hospital of Catania. Written informed consent was obtained from the parents of all participants.

**Consent for publication**
Consent for publication of individual data has been obtained from all the participants of the study.

**Competing interests**
The authors declare no competing interests.

**Author details**
[1]Child and Adolescent Neurology and Psychiatric Section, Department of Clinical and Experimental Medicine, Catania University, 95124 Catania, Italy
[2]Section of Physiology, Laboratory of Neuro-Biomechanics, Department of Biomedical and Biotechnological Sciences, School of Medicine, University of Catania, 95123 Catania, Italy
[3]Gait and Posture Analysis Laboratory, Policlinico "G.Rodolico-San Marco", University Hospital, Catania, Italy
[4]Research Unit of Rare Diseases and Neurodevelopmental Disorders, Oasi Research Institute, IRCCS, 94018 Troina, Italy
[5]Department of Systems Medicine, Center for Space Biomedicine, University of Rome Tor Vergata, 00133 Rome, Italy

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