News Release

Title

Quantitative evaluation of upper limb ataxia in spinocerebellar ataxias

Key Points

- Spinocerebellar ataxias (SCAs) are incurable hereditary progressive neurodegenerative disorders showing a slow progression.
- Semiquantitative scales for evaluating disease severity of SCA have been used widely but their sensitivities to disease progression are limited.
- In this study, a distortion index, which is a quantitative evaluation method for ataxia using a novel pen-like sensor device, has been developed.
- Our findings indicate that the distortion index is a reliable functional marker that is sensitive to disease progression in SCA, and distortion index can be a useful outcome measure for clinical trials.

Summary

A group of researchers, headed by Prof. Masahisa Katsuno, Department of Neurology, Nagoya University Graduate School of Medicine have developed a quantitative evaluation method for upper limb ataxia using a novel pen-like sensor device and revealed that the distortion index could be a marker of the severity of upper limb ataxia in patients with SCA. This work was published online in *Annals of Clinical and Translational Neurology* on March 2022.

Spinocerebellar ataxia (SCA) is a subset of hereditary progressive neurodegenerative disorders with ataxia, and the onset of SCA is usually in adult life and the progression is usually slow. There is currently no effective treatment to slow the progression of SCA, although several clinical trials for disease-modifying treatments are now underway. The reliable and sensitive biomarkers are essential to conduct clinical research, but there is no sensitive biomarker that reflect the disease severity of SCA.

In this study, the distortion index, which is a quantitative evaluation method for upper limb ataxia using a novel pen-like sensor device, has been developed. Compared with healthy controls (HC), patients with SCA showed significantly high score of the distortion index, which strongly correlated with the Scale for the Assessment and Rating of Ataxia (SARA) and the International Cooperative Ataxia Rating Scale (ICARS) upper limb scores. Test-retest reliability was excellent for the distortion index. Furthermore, in the longitudinal analysis the distortion index showed longitudinal deterioration, whereas other scores failed to demonstrate such changes.

Our findings indicate that the distortion index is a reliable and sensitive biomarker of the severity of upper limb ataxia, and it could be a useful outcome measure for clinical trials for SCA.

Research Background

Spinocerebellar ataxia (SCA) is a subset of hereditary progressive neurodegenerative disorders with ataxia showing a slow progression. There is currently no effective treatment to slow the progression of SCA, which

could be attributed to a lack of reliable and sensitive biomarker that reflect the disease severity of SCA. For SCA, semiquantitative scales such as SARA and ICARS have been used widely to evaluate the disease severity, although these rating scales are not sensitive enough to quantify subtle changes in ataxia with disease progression and tend to vary among raters.

Therefore, reliable and sensitive biomarker to disease progression of SCA are warranted to conduct clinical research successfully.

Research Results

In this study, an ataxia measurement device that consisted of a commercially available device (Geomagic Touch™, 3D Systems, Inc., SC, USA), which accurately measures a three-dimensional position of the top of pen, and four buttons (Figure 1A) was developed. Participants were instructed to move a pen between the two buttons 9.5 times as quickly as possible, and by the obtained data of three-dimensional position of the top of pen (Figure 1B) approximated trajectories were calculated and then the deviation of the observed trajectory from the approximate curve was calculated using the mean squared error and defined as the distortion index.

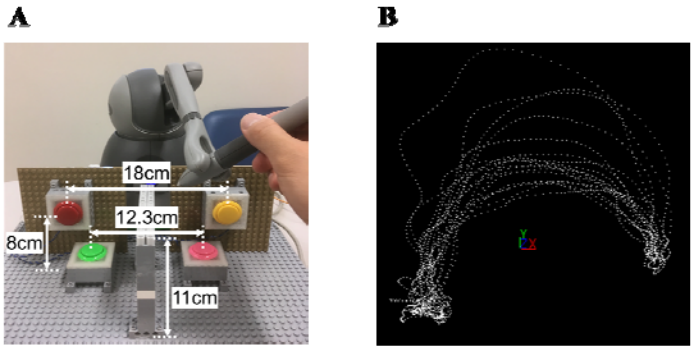

Figure 1. Experimental setup of the device and plot of the trajectories

Compared with healthy controls (HC), patients with SCA showed a significantly high score of the distortion index (Figure 2A). To examine the validity of the distortion index as a biomarker that reflects upper limb ataxia severity, we investigated the association of the distortion index with the SARA upper limb score in the patients with SCA. The distortion index was strongly correlated with the SARA upper limb score (Figure 2B).

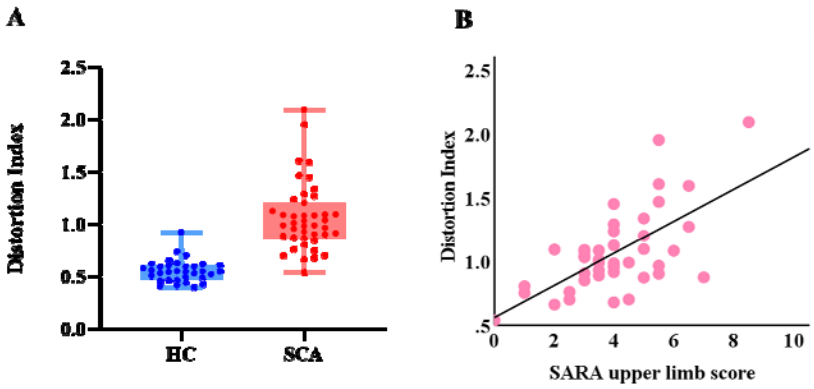

Figure 2. The distortion index and its relation to SARA upper limb score

Subsequently, to estimate the reliability of the distortion index, participants were examined twice within about 2 weeks. The intra-class correlation coefficient (ICC) of the distortion index was 0.984, which means the reliability of the distortion index was excellent.

Next, to evaluate the sensitivity of the distortion index, we prospectively analyzed the longitudinal changes in the distortion index, SARA and ICARS in the patients with SCA over 12 months. The distortion index showed a significant deterioration and the sample size estimation based on the longitudinal analysis showed that the distortion index would require the smallest sample size (Figure 3).

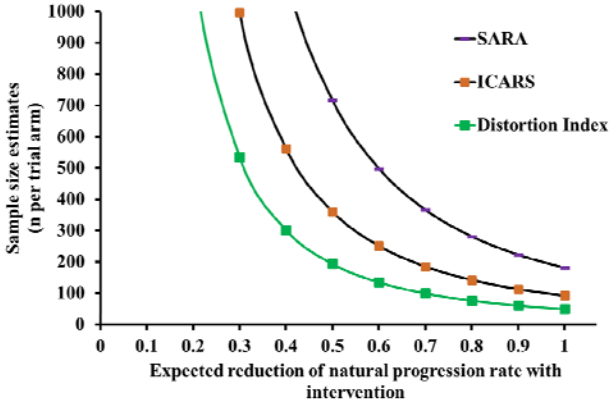

Figure 3. Sample size estimation

Research Summary and Future Perspective

Our findings indicate that the distortion index is a reliable and sensitive biomarker of the severity of upper limb ataxia for SCA. Future prospective, multicenter studies are warranted to confirm our findings and to examine whether the distortion index can be a useful outcome measure for clinical trials for SCA.

Publication

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