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Research Article

Effect of Korean Red Ginseng on the motor performance and ataxia

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ABSTRACT

This study presents a preliminary exploration into the effect of Korean Red Ginseng (KRG) on the cerebellum in individuals with cerebellar atrophy. Over a three month-long period, nine subjects received a 4.5g of KRG daily, with assessments including the ARS, ADAS-Cog, and FDG-PET/CT scans. Results revealed a notable improvement in ataxia and cognitive function without a significant correlation between them. PET/CT scans and SUVR analyses supported these findings, showing an increase in cerebellar glucose uptake after KRG intake. These outcomes suggest a potential pleiotropic effect of KRG on cerebellar function.

1. Introduction

Korean Red Ginseng (KRG) is known for its multifaceted health benefits, including antioxidant, anti-inflammatory, and immune-stimulating properties [1]. While the majority of research focuses on KRG's impact on the cerebrum, its effects on the cerebellum are not well-documented [2,3]. The challenge lies in selectively assessing the cerebellum's functionality, as current tools cannot isolate it from the cerebral motor region. This limitation is evident in healthy individuals, where even advanced techniques like fMRI struggle to differentiate cerebellar activity [4]. However, in conditions where cerebellar function is compromised, symptoms like ataxia offer a more quantifiable measure of its functionality [5]. Recognizing this gap, our study aims to explore the efficacy of KRG on the cerebellum, particularly in individuals with cerebellar atrophy.

2. Materials and methods

10 individuals with cerebellar atrophy were consecutively enrolled at a neurology outpatient clinic from September 2021 to August 2022. The cohort, comprising an equal number of men and women, had an average age of 44.7 years and a near-perfect average cognitive score on the MMSE (29.4 points out of a full 30 points). One man was excluded before taking KRG due to the progression of symptoms after enrollment, resulting in 9 participants completing the study.

During the three-month study, subjects received a daily dosage of 4.5g of Korean Red Ginseng (composed of Ginsenoside Rc, Rb2, Rd, Rg3r, etc., The Korean Society of Ginseng, South Korea), split into 2 or 3 intakes. The Ataxia Rating Scale (ARS) and Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) were administered at baseline and during three monthly follow-up visits. Additionally, 18F-FDG-PET/CT scans were conducted at the start and end of the study for interested participants, with a focus on cerebellar metabolism.

The primary endpoint was the change in the total ARS scores, indicating ataxia improvement. Secondary endpoints included changes in specific ARS items reflecting motor enhancement and the correlation of total ARS scores change with cognitive function (assessed by ADAS-Cog), as well as cerebellar metabolic changes observed in PET/CT scans. Furthermore, PET/CT was quantified by the Standardized Uptake Value Ratio (SUVR) method because of the low baseline glucose uptake characteristics in cerebellar atrophy.[6,7]

Given the study's preliminary nature and the small, specialized participant group, descriptive statistics were prioritized over complex statistical methods to present the findings effectively.

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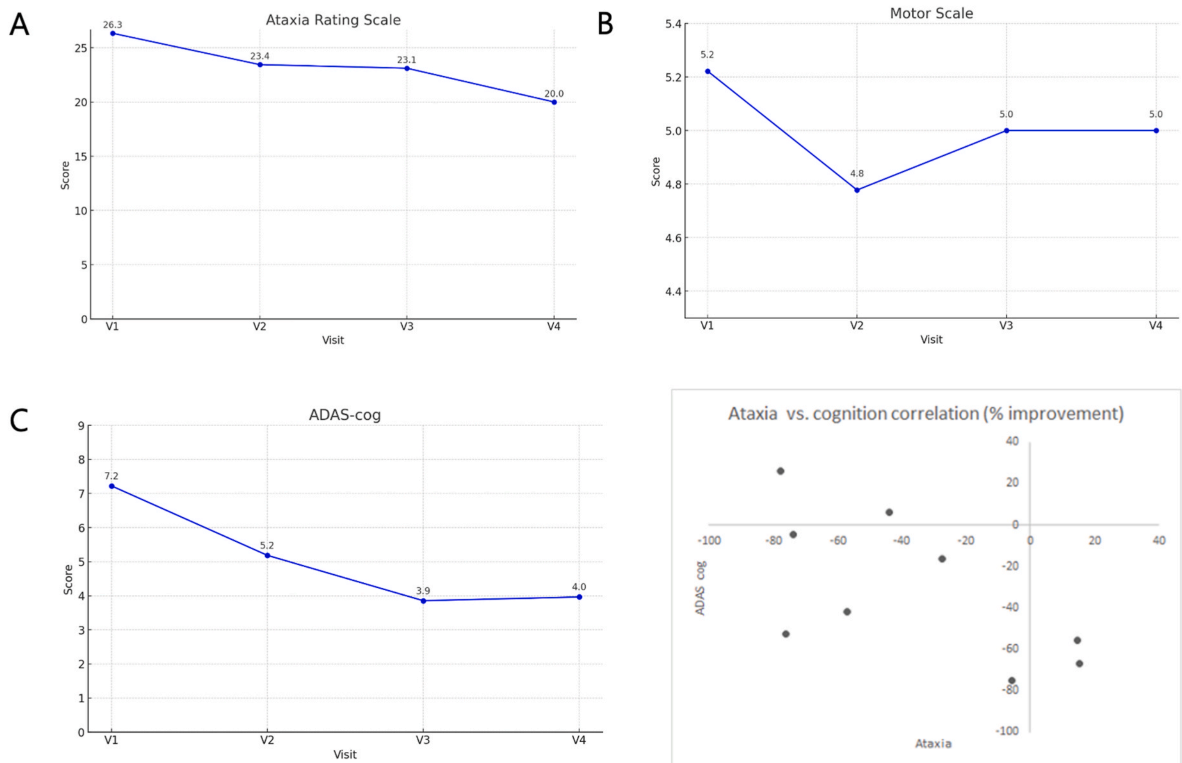

Fig. 1. Effect of KRG on the average score of (A) total ARS (B) ARS items 2,3 and 18, and (C) ADAS-Cog and its correlation with Ataxia Visit 1 refers to the baseline visit, while visits 2, 3, and 4 represent the visits after 4, 8, and 12 weeks of taking red ginseng, respectively. V; visit, KRG; Korean Red Ginseng, ARS; Ataxia Rating Scale, KFDA; Korean Food and Drug Administration, ADAS-cog; The Alzheimer's Disease Assessment Scale–Cognitive Subscale.

3. Results

Among the nine subjects, seven exhibited improvement, with the overall average total ARS scores showing a 24% enhancement, decreasing from 26.3 at Visit 1 to 20 at Visit 4 ($P = 0.022$, Fig. 1A). Several items within the ARS (item 2, 3 and 18), which are reflective of KFDA 'motor enhancement' criteria displayed an upward trend in improvement ($P = 0.25$, Fig. 1B). Among the nine subjects, seven showed improvement with an overall average decrease in the ADAS-Cog score by 45%, from 7.22 at Visit 1 to 3.96 at Visit 4, highlighting KRG's cognitive enhancement effects (3.26 points; $p = 0.0048$, Fig. 1C). Despite the observed improvements in both cognitive function and ataxia, as indicated by negative percentage changes in ADAS and ARS scores respectively, no significant correlation was found between these improvements (correlation coefficient $= -0.64$, Fig. 1C).

Both subjects, exhibiting cerebellar atrophy as indicated by decreased baseline cerebellar glucose uptake in the original PET/CT scan images, showed an increase in FDG uptake in the cerebellum after taking KRG (Fig. 2A). Visual analysis highlighting the absolute amount of change indicates cerebral uptake increased more than cerebellar uptake; however, SUVR analysis of PET/CT scans revealed a proportionally greater increase in the cerebellum, as evidenced by elevated cerebellum-to-whole brain and cerebellum-to-pons ratios following KRG intake (Fig. 2B).

Throughout the study, no adverse events were reported.

4. Discussion

This preliminary study noted a statistically significant decrease in total ARS scores, indicating an overall improvement in ataxia with KRG intake. However, specific 'motor enhancement' related items did not show statistical significance, suggesting a possible independent enhancement of cerebellar function by KRG, rather than through general motor function improvement. Interestingly, there was a weak negative correlation between cognitive function improvement and ataxia, pointing towards independent mechanisms for these enhancements. SUVR analysis of PET/CT imaging supported these suggestions, revealing a proportionally greater increase in the cerebellum than other brain regions. This might suggest KRG directly enhances the cellular activity of cerebellar Purkinje cells.

The study's limitations include the small sample size due to the rarity of cerebellar atrophy. Thus, more extensive studies may be necessary to validate the pleiotropic effect of KRG on the cerebellum.

Credit author statement

SHL contributed to data analysis, data interpretation, drafting of the manuscript, manuscript revision and approval of the final version.

YRW contributed to project concept, protocol design and approval, sharing data collection and interpretation, and approval of the final version.

MHK contributed to study concept and design, obtaining funding, data interpretation, editing the manuscript, and approval of the final version.

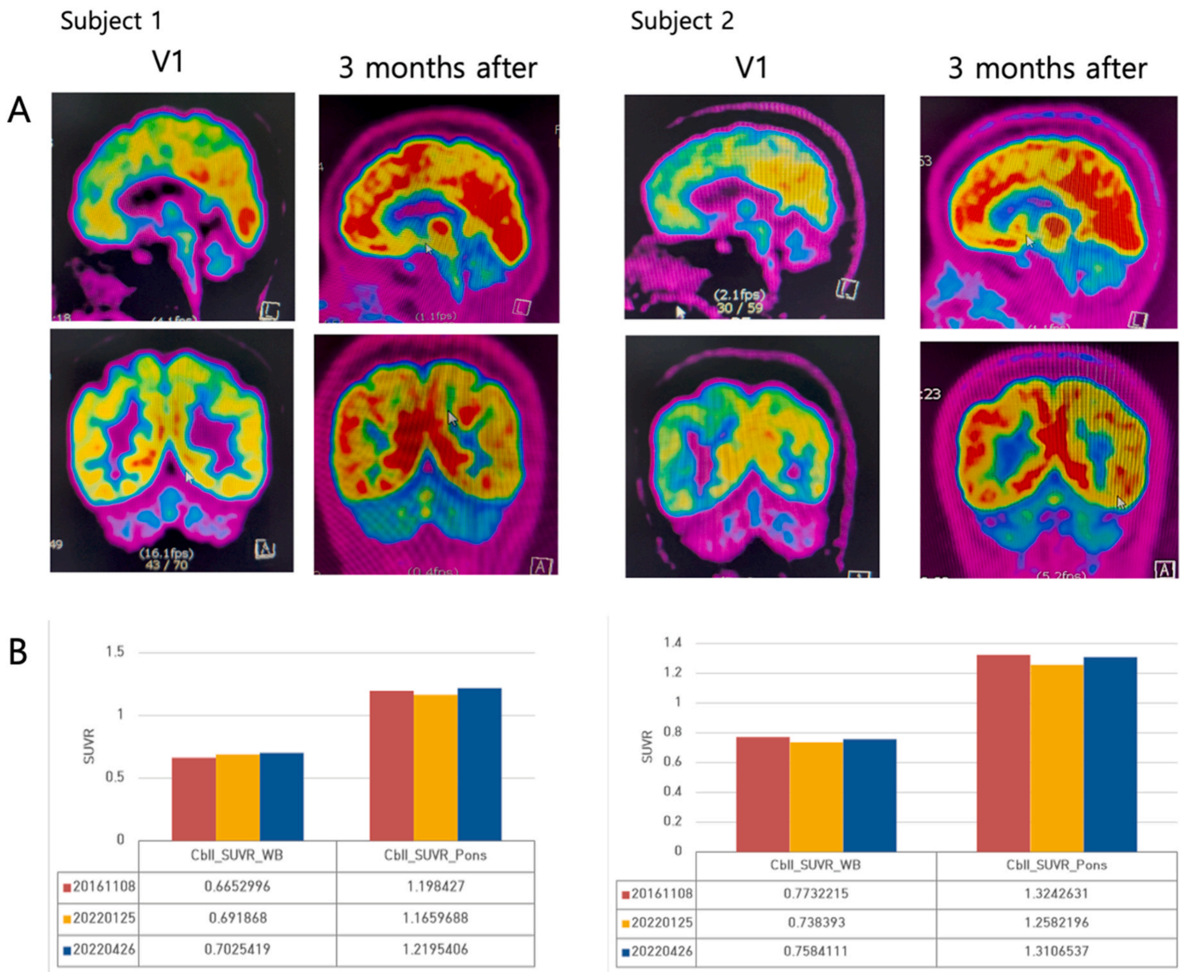

Fig. 2. Changes in the (A) original FDG PET/CT and (B) FDG PET/CT SUVR quantification before and after taking KRG in two subjects Coincidentally, both participants had taken FDG PET/CT scans in 2016, which were also compared (indicated in red). Each graph on the left and right shows the cerebellar glucose uptake ratio to the whole brain (WB) and Pons, respectively. The pons, with its stable and uniform tracer uptake, and the whole brain are often used as reference regions to compare changes in cerebellar metabolic activity. FDG PET/CT; fluorodeoxyglucose positron emission tomography-computed tomography, SUVR; Standardized Uptake Value Ratio, KRG; Korean Red Ginseng.

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