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Effect of Chewing Hardness on Cognitive-Associated Brain Regions Activation

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ABSTRACT

Introduction and aims: Recent findings suggest a potential correlation between mastication and cognitive processes. However, the comprehensive investigation into the neurobiological mechanisms of masticatory control, such as the impact of chewing hardness, on cognitive function, remains incomplete. This study aims to investigate the impact of chewing hardness, as an aspect of masticatory control, on cognitive function by examining brain activation patterns during hard and soft chewing conditions.

Methods: A total of 52 healthy young adults (average age of 21.81 years; 24 men and 28 women) underwent fMRI scanning, during which 27 individuals chewed soft and 25 individual chewed hard material. The functional magnetic resonance imaging (fMRI) was employed to elucidate the overlapping and distinct patterns of activated brain regions associated with soft- and hard-chewing conditions. Subsequently, correlations between these activated brain regions and neuropsychological measures were assessed.

Results: Conjunction analysis revealed that both soft- and hard-chewing conditions stimulated brain regions directly associated with orofacial movement and spatial information processing. Two-sample t-test result indicated that the hard-chewing group had higher activation mostly in the caudate nucleus and frontal brain regions associated with cognitive function compared with the soft-chewing group. Furthermore, the activation strength of these brain regions positively correlated with neuropsychological measures.

Conclusion: The findings suggest that hard-chewing may be more effective than soft-chewing in stimulating cognition-associated brain regions, potentially enhancing cognitive processing.

Clinical relevance: Our study shows that hard-chewing activates brain regions linked to cognitive function more than soft-chewing. This suggests that harder chewing could be used as a simple, non-invasive method to enhance cognitive processing. Incorporating harder foods into the diet may offer a practical approach to support cognitive health and improve mental performance.

Introduction

Mastication is important not only for oral health and function but also for cognitive function, such as memory.[1,2] Evidences indicated the possible association between masticatory dysfunction and cognitive decline. Memory and learning are significantly impaired by masticatory dysfunction caused by

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tooth loss, periodontal diseases, or soft diet.[3-5] In addition, masticatory dysfunction due to weakened muscles of mastication or tooth loss leads to inadequate stimulation of the central nervous system.[1] Thus, healthy masticatory function is of great importance to preserve lifelong physical and mental health.[6,7]

In addition to the association between masticatory dysfunction and cognitive decline, the possible association between mastication and cognitive function in healthy masticatory function was also documented. Several studies reported that chewing soft and elastic material, such as gum, exerted an enhancing effect on cognitive performances in healthy subjects. For example, it was observed that gum chewing was beneficial to working memory, episodic long-term memory, and attention.[8-10] In these studies, the use of functional magnetic resonance imaging (fMRI) was introduced to elucidate the neural correlates for the chewing effects,[11-14] whereby it has been reported that gum chewing induced neural activation in various brain regions.[15] Some fMRI studies have focused on the orofacial motor system related to mastication, such as chewing movements, whereas others examined the influence of chewing on neuronal activities in the brain during a cognitive task using fMRI. However, the relationship between mastication features, such as hardness, and cognitive performances remains unclear.

In this study, we investigated whether differences in chewing characteristics, such as hardness, influence cognitive function in individuals with healthy chewing abilities. This question is quite important as understanding the roles of the different characteristics of mastication features (eg, hardness and texture) and their influence on cognitive function might provide new insights and preventive strategies for cognitive decline. We hypothesized that mastication of a hard material would stimulate more broad brain regions, including cognition-associated regions, than mastication of a soft material. To test the hypothesis, we employed 2 mastication paradigms with wood block and gum in our fMRI study. Finally, we aimed to identify the possible neural correlates related to chewing hardness and the possible association between these neural correlates and cognitive function by measuring the correlation between them.

Methods

Study participants

This study was approved by the Institutional Review Board of Kyungpook National University Dental Hospital (KNUDH-2021-06-09-02). A total of 52 dental students (24 (46.20%) men, and 28 (53.80%) women) in Kyungpook National University, Daegu, Korea, ranging in age from 19 to 27 years old, were recruited from August 2022 to August 2023. The total average age was 21.81 ± 1.56 years, and education period was 14.63 ± 1.14 years. The sample size was calculated using G*Power software, based on an effect size (Cohen's d) of 0.8, a significance level of 0.05, and a statistical power of 0.8. We assumed a large effect size of 0.8 with empirical justification from the literature. Geuter et al[16] reported that sample sizes of 40 are adequate to identify regions with large effect sizes (Cohen's d > 0.8). Furthermore, the voxels with the largest effects in the fMRI tasks usually achieved 95% power with sample sizes of N = 20-40. These empirical power estimates showed that with very robust tasks such as the task in the current study at least some significant results are almost guaranteed with sample sizes of N = 20.

All volunteers signed the consent form after receiving a full explanation of the study purpose and methods. The exclusion criteria were as follows: 1) having neurological or psychiatric illnesses, 2) receiving orthodontic treatment, 3) having temporomandibular joint disorder, and 4) having contraindications to MRI. The subjects were divided into 2 groups based on the chewing hardness conditions: the soft-chewing group (n = 27), consisting of participants chewing gum, and the hard-chewing group (referred to as "tongue blade"), with the participants chewing on a wood stick (n = 25).

Neuropsychological measurement

Each subject completed a questionnaire on demographic characteristics, including age, sex, grade, education, and general health condition. A neuropsychological evaluation was conducted by skilled examiners using the Korean-Repeatable Battery for the Assessment of Neuropsychological State (K-RBANS).[17] K-RBANS is a Korean-adapted version of the original RBANS (Repeatable Battery for the Assessment of Neuropsychological Status), which was developed by Randolph et al[18] in the United States. Although initially designed to assess neuropsychological disorders such as dementia and stroke, K-RBANS offers several advantages, including short administration time, repeatable measurements, and comprehensive assessment, which have led to its widespread use in evaluating cognitive abilities not only in patients with neuropsychological disorders but also across various age groups and populations. The K-RBANS consists of 12 subtests and evaluates 5 cognitive abilities: immediate and delayed memory, visuospatial capacity, language ability, and attention. Immediate memory is assessed through list learning and story memory, which measure the ability to recall information immediately after it is presented. Visuospatial capacity is measured through figure copy and line orientation, which reflect the ability to accurately reproduce visual stimuli and understand the spatial relationships within images. Language ability is evaluated through picture naming and semantic fluency, which gauge the examinee's capacity to verbally recall or name objects they have learned. Attention is the ability to briefly retain and manipulate both visual and verbal information, assessed by digit span and coding tasks. Delayed memory evaluates the ability to recall information after a certain period of time following learning, consisting of list recall, list recognition, story recall, and figure recall. The total scale index (TSI), which combines scores from the 5 cognitive domains, provides an overall measure of an individual's cognitive abilities.[17]

Functional MRI data acquisition

All participants were instructed to lie in a supine position with their heads secured and chew gum or a wood stick in accordance with a 1 Hz rhythm during the fMRI scan. The material was tied with dental floss to prevent it from accidentally entering the airway during chewing. To prevent accidental aspiration during chewing, both the chewing gum and the wooden stick were tied with dental floss. The task paradigm employed a block design, with the rest and mastication procedure repeated 5 times for 30 s each. This procedure was guided to the participants via the screen. All images were acquired using a 3.0 Tesla MRI scanner (Signa Architect, GE Healthcare) with a 48-channel head coil. Functional images were acquired via gradient echo planar imaging (EPI). The EPI parameters consisted of repetition time (TR) = 2000 ms, echo time (TE) = 30 ms, flip angle (FA) = 90°, field of view (FOV) = 24 cm, and matrix size = 64 × 64. T1-weighted 3D brain volume imaging (BRAVO) was used to acquire brain structure images. The BRAVO parameters consisted of TR = 7.7 ms, TE = 3.1 ms, FA = 12°, FOV = 25.6 cm, and matrix size = 256 × 256.

Functional MRI data analysis

All functional images were pre-processed and analysed using a statistical parametric mapping toolbox (SPM12; http://www.fil.ion.ucl.ac.uk/spm/software/spm12/). The preprocessing steps included slice timing, realignment, co-registration, segmentation, normalization, and smoothing. The segmentation step was carried out using a computational anatomy toolbox (CAT12; http://neuro-jena.github.io/cat/). All functional images were normalized to a Montreal Neurological Institute standard space and smoothed using a 8-mm full-width at half maximum Gaussian kernel. Individual images were analysed based on a general linear model. In addition, motion parameters were applied as individual analysis covariates (for gum-chewing condition, X = 0.003 ± 0.239 mm, Y = 0.049 ± 0.109 mm, Z = −0.254 ± 0.347 mm, pitch = 0.006° ± 0.01, roll = −0.000° ± 0.004, and yaw = −0.000° ± 0.007; for wood-chewing condition, X = 0.066 ± 0.166 mm, Y = 0.021 ± 0.084 mm, Z = −0.063 ± 0.282 mm, pitch = 0.001° ± 0.006, roll = 0.002° ± 0.003, and yaw = 0.001° ± 0.003) Conjunction analysis was conducted to highlight the brain activation regions involved in both soft-chewing and hard-chewing groups.

Statistical analysis

To test for normality, the Shapiro−Wilk test was conducted for each variable. Variables that did not meet the assumption of normality were analysed using non-parametric tests. The general characteristics and neuropsychological results between the 2 groups were compared using the chi-squared test or Mann−Whitney U test with IBM SPSS version 26.0 for Windows (SPSS Inc., Armonk, NY, USA). The significance level was set to 0.05.

Two sample t-test was conducted to compare differences in brain activation between the soft-chewing group and the hard-chewing group. The significant difference among the groups was determined by the false discovery rate (FDR) corrected for multiple comparison threshold $P < .05$. Regions of interest (ROI) were acquired by forming a sphere with a 5-mm radius based on the location of the maximum *t*-value of each activated brain region. The beta values of ROIs were extracted using the REX toolbox (https://www.nitrc.org/projects/rex/).

Correlation analysis was conducted to evaluate the relationship between neuropsychological scores and beta values using Jamovi software (http://www.jamovi.org). The normality of the data was assessed using the Shapiro−Wilk test. Pearson's correlation was applied to normally distributed data because Pearson's correlation is appropriate when both variables follow a bivariate normal distribution.[19] Spearman's correlation was used for non-normally distributed data because Spearman's correlation ranks the values of each variable and calculates the correlation based on these ranks, making it more robust to violations of normality and suitable for non-normally distributed data.[19]

Results

Demographic characteristics and neuropsychological analysis

No significant difference was observed in demographic characteristics between the groups ($P > .05$). Neuropsychological evaluation using K-RBANS also showed no significant difference between the groups ($P > .05$).

Functional MRI − conjunction analysis

Conjunction analysis revealed the common brain regions involved in orofacial movement in both the hard- and soft-chewing conditions (Figure 1 and Table 1). The activated brain regions from the conjunction analysis were bilateral clusters of the pre- and post-central gyrus, supplemental motor area, and medial cingulate cortex (MCC). Activations were also observed in the bilateral insula, superior temporal gyrus (STG), and bilateral superior cerebellar hemispheres. In addition, the bilateral thalamus, putamen, and bilateral amygdala were the common brain regions that showed activation in the hard- and soft-chewing conditions.

Functional MRI − 2-sample analysis

The 2-sample analysis revealed brain regions that were different between the 2 tasks (Figure 2 and Table 1). Compared with the soft-chewing task, the hard-chewing task induced higher activation in the bilateral anterior cingulate cortex (ACC) and bilateral caudate nucleus. In addition, the bilateral superior frontal gyrus showed high activation in the hard-chewing condition.

Functional MRI − correlation analysis

Some of the activated brain regions from the conjunction and 2-sample analyses exhibited correlation with the neuropsychological measures. For the conjunction analysis (Figure 3), the beta values of right hippocampus, left MCC, activations in the hard-chewing and soft-chewing groups were positively correlated with line orientation.

For the 2-sample analysis (Figure 4), the beta values of left caudate nucleus activation in the wood group were positively correlated with, list learning, and coding. On the other hand,

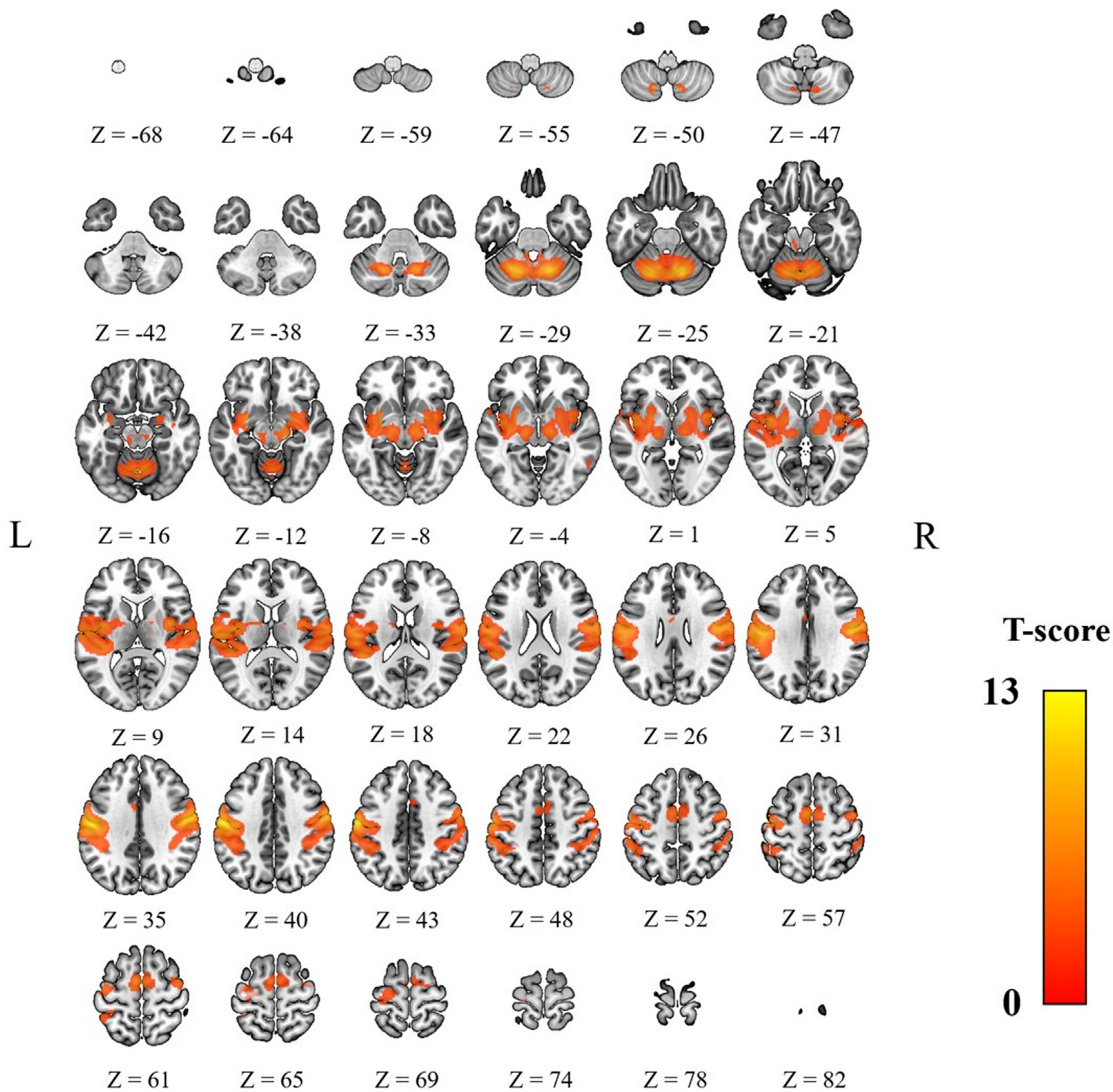

Fig. 1 – fMRI results of the conjunction analysis. The SPM{t}s had a threshold of $P < .05$, with FDR correction for multiple comparisons at the whole brain level. The conjunction analysis revealed the common brain regions involved in orofacial movement in the wood- and gum-chewing conditions.

the beta values of right caudate nucleus activation in the hard-chewing group were positively correlated with list learning (Figure 5). The beta values of right ACC activation in the hard-chewing group were positively correlated with list learning, coding, and sum of index scores. Conversely, the beta values of left ACC activation in the hard-chewing group were positively correlated with immediate memory, list learning, and coding (Figure 6). In addition, the beta values of left superior frontal gyrus activation in the hard-chewing group were positively correlated with story memory.

Discussion

Conjunction analysis showed that the common activated brain regions between the soft- and hard-chewing conditions are mostly involved in orofacial movement, such as jaw movement, and are in good agreement with the previous fMRI studies for orofacial movement.[20-22] In addition to brain regions associated with orofacial movement, the hippocampus, MCC showed common activation between the gum- and wood-chewing conditions. Correlation analysis between the activated brain regions from the conjunction analysis and neuropsychological cognitive measures indicated that some of the neuropsychological measures were positively correlated with the brain regions not associated with orofacial movement.

Among the brain regions showing correlation with the neuropsychological measures in the conjunction analysis, evidences indicated that the hippocampus played an important role in cognition.[23,24] Memory seems to be the first cognitive function associated with the hippocampus. In addition, the hippocampus is capable of encoding a great deal of spatial information, such as line orientation.[25] Furthermore, a previous study demonstrated that the right hippocampus plays a central role in spatial memory processing whereas the left

Table 1 – Conjunction analysis and 2-sample analysis result (FDR corrected for multiple comparison, $P < .05$).

Brain region	Side	Cluster size	MNI-coordinates			Peak T
			x	y	z	
Conjunction analysis						
Amygdala	R	79	22	−2	−12	5.61
Thalamus	L	80	−18	−22	2	4.87
Thalamus	R	107	14	−4	12	2.7
Insula	L	592	−40	−10	−4	4.73
Insula	R	429	40	0	2	6.25
Putamen	L	492	−24	−2	2	5.6
Putamen	R	387	28	2	−4	4.04
Hippocampus	L	31	−30	−14	−12	3.6
Hippocampus	R	70	34	−20	−8	3.13
Superior temporal gyrus	L	1249	−48	−38	16	6.02
Superior temporal gyrus	R	725	50	−32	16	5.61
Supramarginal	L	779	−50	−40	28	4.39
Rolandic operculum	L	716	−54	−4	8	3.66
Inferior parietal lobule	L	931	−44	−42	42	5.37
Inferior parietal lobule	R	239	48	−38	48	4
Precentral	L	1251	58	4	36	5.66
Precentral	R	804	−38	−16	56	4.91
Postcentral	L	1963	−58	−14	42	13.19
Postcentral	R	1251	52	−10	34	10.37
Supplementary motor area	L	538	−6	−6	58	6.96
Supplementary motor area	R	512	4	−6	58	4.56
Two sample analysis Wood > Gum						
Caudate	L	126	−16	18	10	4.25
Caudate	R	154	16	14	12	3.84
rostral anterior cingulate cortex	L	182	−10	38	20	4.5
rostral anterior cingulate cortex	R	155	16	46	20	4.09
Superior medial frontal gyrus	L	22	−8	60	22	3.54
Superior medial frontal gyrus	R	321	4	62	22	3.87
Superior frontal gyrus	L	257	−22	50	18	3.41
Superior frontal gyrus	R	235	14	58	20	3.62
Inferior frontal gyrus	L	122	−44	26	4	4.23
Inferior parietal lobule	R	142	58	−48	50	4.52
Precentral	R	18	50	8	50	3.79

L = left side brain; R = right side brain.

hippocampus might be more important for verbal memory.[26] The left STG is also often considered to be responsible for coding object information and processing the shape of an object.[27] Therefore, the findings from the conjunction and correlation analyses suggest that both the soft- and hard-chewing conditions can induce activation not only in brain regions directly associated with orofacial movement but also in those associated with cognitive function. Specifically, our findings suggest that these conditions can stimulate brain regions associated with spatial information processing.

An important finding from the 2-sample t-test analysis was that the hard-chewing group exhibited higher activation than the soft-chewing group mostly in the caudate nucleus and frontal brain regions. Furthermore, the beta values showing the activation strength of these brain regions exhibited a positive correlation with neuropsychological measures. Importantly, among the neuropsychological measures, memory function was strongly associated with these brain regions. ACC, superior frontal cortex, and caudate nucleus exhibited a positive correlation with memory-associated items. These brain regions are thought to form neural circuit responsible for the aspects of memory, executive function, and attention. The ACC is implicated in cognitive control during associative memory.[28-30] Cognitive control includes processes that facilitate the execution of effortful cognitive tasks, including associative memory.[31] Our correlation analysis therefore revealed that the activation strength in these brain regions is associated with performance in memory functioning. That is, a stronger activation in these brain regions indicates better performance in memory function. Therefore, the results suggest that the hard-chewing condition can effectively stimulate these brain regions and may increase the performance in cognitive function.

The 2-sample analysis also revealed that the hard-chewing group exhibited higher activation than the soft-chewing group in the head of the bilateral caudate nucleus. The strong activation of the head of the caudate nucleus seems to implicate multiple roles of the head of the caudate nucleus in the hard-chewing condition. First, a previous meta-analysis study has revealed that the head of the caudate nucleus plays a role in the evaluation of value of different actions and thus in cognition and emotional function.[32,33] A previous functional imaging study has also reported that activity in the head of the caudate was related to feedback processing.[30] Based on the results of these studies, we postulated that the hard-chewing condition needs brain resources, such as the

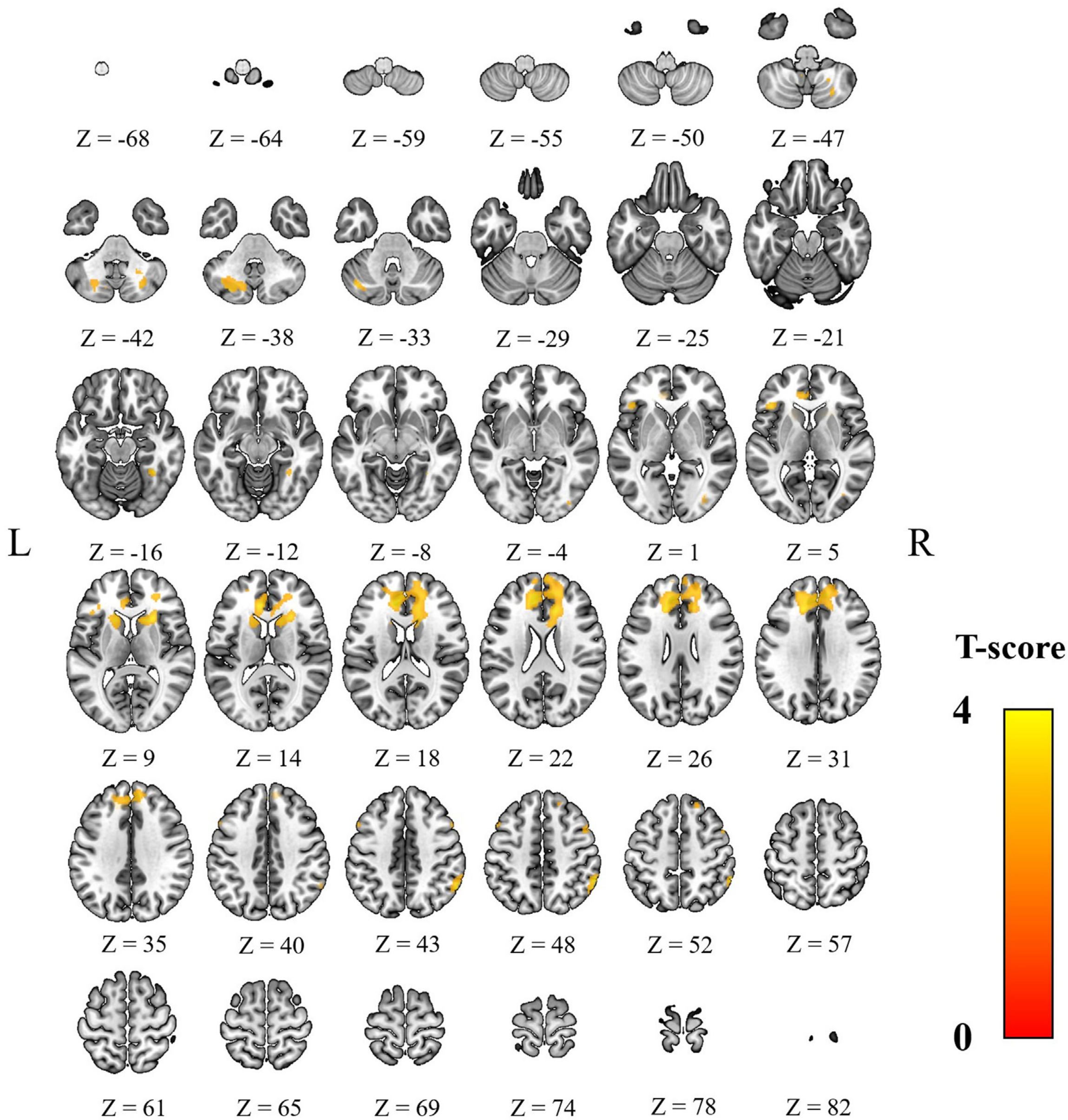

Fig. 2 – fMRI results of the 2-sample analysis (wood chewing > gum chewing). The SPM{t}s had a threshold of P < .05, with FDR correction for multiple comparisons at the whole brain level. The 2-sample analysis revealed the brain regions on which the wood-chewing condition induced a higher activation than the gum-chewing condition.

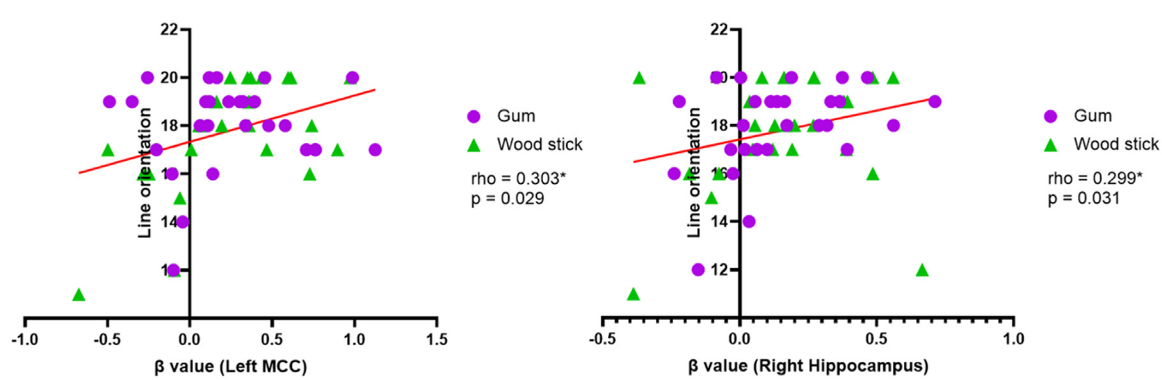

Fig. 3 – Correlation analysis between the neuropsychological measures and the mean beta values of brain activations from the conjunction analysis. The mean beta values of the right hippocampus, left MCC activations in the wood and gum groups were positively correlated with line orientation (*P < .05, **P < .01). MCC = middle cingulate cortex.

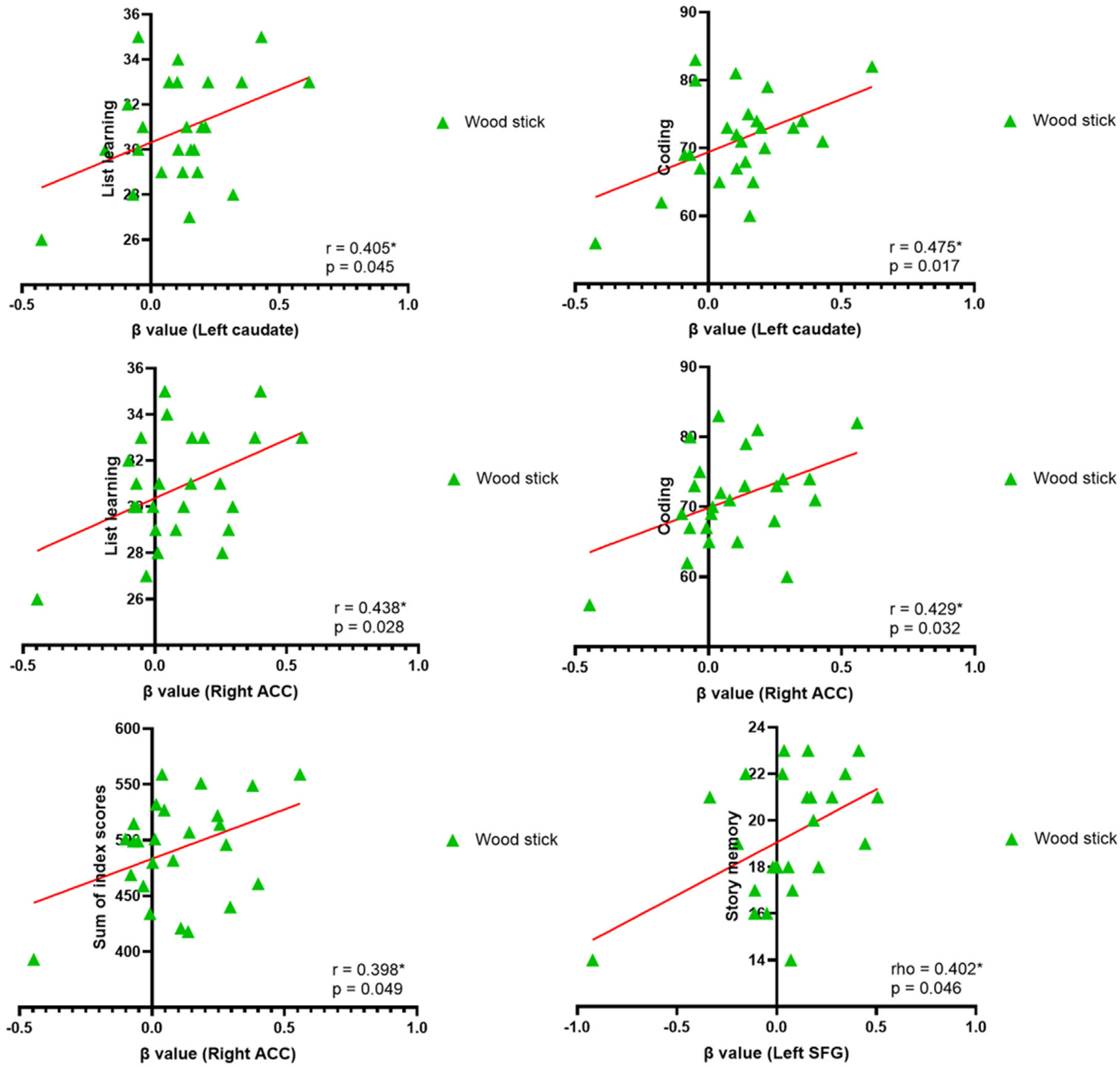

Fig. 4 – Correlation analysis between the neuropsychological measures and the mean beta values of brain activations from the 2-sample analysis. The mean beta values of the left caudate nucleus activation in the wood group were positively correlated with list learning and coding. On the other hand, the beta values of right ACC activation in the wood group were positively correlated with list learning, coding, and sum of index scores. Also, the beta values of left superior frontal gyrus activation in the wood group were positively correlated with story memory (*P < .05). Caudate = caudate nucleus; ACC = anterior cingulate cortex; SFG = superior frontal gyrus.

head of the caudate, to evaluate the different textures and hardness of chewing materials and that the right and left heads of the caudate nucleus were more active in the hard-chewing condition to process the elaborated feedback during orofacial movement. Second, the head of the caudate nucleus is strongly connected with medial frontal cortices and is involved in working memory and executive functioning.[34,35] The head of the caudate nucleus, which is situated between the frontal cortex and hippocampus, modulates cognitive functioning through the hippocampal–superior frontal cortex circuits. A clinical study demonstrated that caudate nucleus lesions lead to chronic frontal cortex dysfunction, which in turn leads to dysfunction in connected brain regions and then to cognitive decline.[36] Therefore, the head of the caudate nucleus plays an important role as relay centre from the basal ganglia to the superior frontal cortex for cognitive functioning, such as memory function.

One of the possible interpretations of the findings from the 2-sample *t*-test analysis is the difference in chewing hardness. Previous fMRI studies focused on neuronal activity in specified brain regions involved in the motor control of mastication during changes in chewing hardness.[13,14] Takahashi et al[13] observed a significant activation in the dorsolateral prefrontal cortex (DLPFC) of the left hemisphere when the chewing hardness was changed. They interpreted that DLPFC was responsible for holding the working memory component needed to continuously modulate motor control for the biting force and masticatory movements according to a precise feedback control. In the present study, we introduced gum and wood as 2 chewing materials with different hardness,

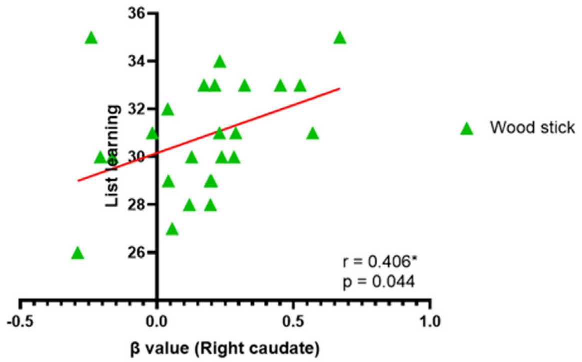

Fig. 5 – Correlation analysis between neuropsychological measures and the mean beta values of brain activation from 2-sample analysis. The mean beta values of right caudate nucleus activation in wood-chewing group were positively correlated with list learning (*$P < .05$). Caudate = caudate nucleus.

representing the soft- and hard-chewing conditions, respectively. The perception of hardness of the chewing material is known to be affected by both sensory inputs and cognitive factors.[37] Compared with the study by Takahashi et al,[13] our 2-sample analysis revealed that the hard-chewing condition involved significant activations in more brain regions of the frontal lobe. Therefore, the hard-chewing condition may need more elaborated efforts for masticatory movements than the soft-chewing condition to incorporate chewing hardness and thus stimulate several frontal brain regions to hold the elaborated efforts. Our results suggest that chewing hard materials is effective in stimulating cognition-associated frontal brain regions and may play an active role in increasing cognitive processing.

This study has some limitations that warrant acknowledgement. Firstly, while all functional imaging analyses satisfied the multiple comparison criteria to correct type 1 error statistically, the study's sample is limited. Thus, it would be necessary to generalize the findings with a larger population. Secondly, in the present study, the age rage of the subjects in our study was 20 to 30 years, using convenience sampling. Given this narrow age range, the findings of the present study need to be validated across wider age groups, encompassing both younger and older individuals. Thirdly, participants chewed materials such as gum and wood sticks with a small jaw opening, rather than actual food. This may not entirely replicate the real chewing dynamics, as natural mastication with food involves balanced lateral and vertical forces, while mastication in this experimental setting primarily utilized vertical force, as the participant were instructed to perform the chewing without head shaking. In addition, the mastication time may have been shorter than in real mastication scenarios. Lastly, it is important to mention a limitation of this study: the heightened brain activation observed may not necessarily reflect enhanced cognitive processing. Instead, this increase could be attributed to the atypical and potentially uncomfortable experience of chewing wood, a material not representative of typical chewing behaviour. These factors may confound the interpretation of the results, making it unclear whether the activation genuinely represents cognitive enhancement or is simply a reaction to the unnatural chewing task. Therefore, future studies with refined designs are warranted. Such refinements—for example, using ecologically valid materials that closely replicate natural chewing conditions and minimizing participant discomfort during tasks—would significantly enhance the study's contribution to understanding the relationship between chewing and cognitive processing.

Conclusion

In summary, 2 important findings were obtained from this study. Firstly, both the soft- and hard-chewing groups demonstrated the ability to stimulate brain regions associated with motor function and spatial information processing. Secondly, the hard-chewing group exhibited higher activation than the soft-chewing group in the caudate nucleus and frontal brain regions, which are closely linked to cognitive functioning. Furthermore, the correlation analysis between activation beta values and neuropsychological measures revealed that the subjects with higher cognitive scores exhibited stronger activation in these brain regions. These findings suggest that hard-chewing is more effective than soft-chewing in stimulating cognition-associated brain regions and enhancing cognitive processing. Based on these findings, it can be inferred that consuming harder foods might be more beneficial in activating cognitive functions in the human brain.

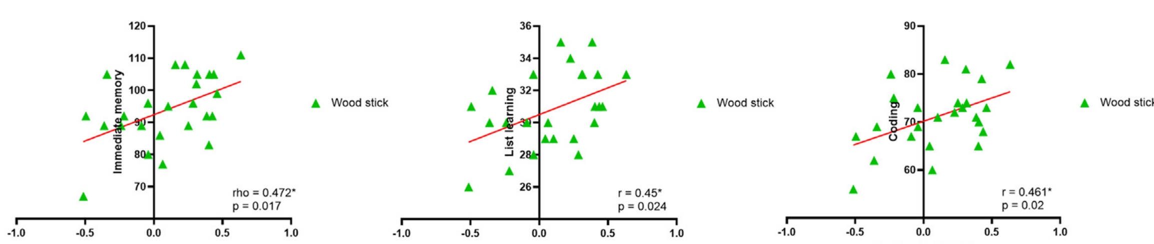

Fig. 6 – Correlation analysis between neuropsychological measures and the mean beta values of brain activation from 2-sample analysis. The mean beta values of left ACC activation in wood-chewing group were positively correlated with immediate memory, list learning and coding. (*$P < .05$). ACC = anterior cingulate cortex.

Conflict of interest

None disclosed.

CRediT authorship contribution statement

Hansol Lee: Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Ji-Hye Kim:** Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Seungho Kim:** Data curation, Writing – original draft. **Sung Ho Jang:** Methodology, Investigation. **Yongmin Chang:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing. **Youn-Hee Choi:** Conceptualization, Methodology, Resources, Investigation, Writing – original draft, Writing – review & editing.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Kyungpook National University Dental Hospital (KNUDH-2021-06-09-02).

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