Research report

Decaffeinated coffee prevents scopolamine-induced memory impairment in rats

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HIGHLIGHTS

▶ Decaffeinated coffee (DC) attenuated scopolamine-induced memory impairment.
▶ DC suppressed scopolamine-mediated increase in hippocampal TNF-α.
▶ DC decreased scopolamine-induced level of p-p65 and p-IκBα in hippocampus.

ARTICLE INFO

ABSTRACT

Introduction: Several human studies have reported that coffee consumption improves cognitive performance. In the present study, we investigated whether instant decaffeinated coffee also ameliorates cognitive performance and attenuates the detrimental effects of scopolamine on memory.
Methods: Memory performance was evaluated in Morris water maze test and passive avoidance test. Instant decaffeinated coffee (p.o.) at 120 or 240 mg/kg in Sprague-Dawley rats, which is equivalent to approximately three or six cups of coffee, respectively, in a 60 kg human, was administered for two weeks.
Results: Oral gavage administration of instant decaffeinated coffee inhibited scopolamine-induced memory impairment, which was measured by Morris water maze test and passive avoidance test. Instant decaffeinated coffee suppressed scopolamine-mediated elevation of tumor necrosis factor-α (TNF-α) and stimulation of nuclear factor-κB (NF-κB) pathway (i.e., phosphorylation of IκBα and p65) in the rat hippocampus.
Discussion: These findings suggest that caffeine-free decaffeinated coffee may prevent memory impairment in human through the inhibition of NF-κB activation and subsequent TNF-α production.

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1. Introduction

Several seminal studies have reported that coffee consumption is associated with better cognitive performance and is inversely associated with neurodegenerative diseases such as Alzheimer's disease [1,2]. Along the same lines, there are epidemiological, pharmacological and genetic evidences showing an inverse relation between coffee intake and parkinson's disease [3–5]. Caffeine, an adenosine A2A receptor antagonist, is considered to be primarily responsible for the neuropharmacological effects of coffee on memory performance, together with its well-known psycho-stimulating effects and the ability to cross the blood-brain barrier [6–8]. On the other hand, the effect of caffeine-free decaffeinated coffee on memory performance has not been elucidated.

Coffee is a complex chemical mixture consisting of a number of bioactive compounds called phytochemicals. Although climatic conditions, agricultural practices, processing, and storage vary its composition, coffee contains approximately 7–9% phenolic phytochemicals, and only 1% caffeine in general [9,10]. Chlorogenic acid, 5-feruloylquinic acid, 4-caffeoylquinic acid, and caffeic acid have been noted as major phytochemicals found in coffee [11], and these phytochemicals themselves have been reported to have neuroprotective activities. For example, chlorogenic acid significantly improved the scopolamine-induced impairment of short-term or working memory [12]. Caffeic acid was also found to be neuronprotective in vivo under pathological conditions of focal cerebral ischemia [13]. Kahweol and cafestol were suggested as antioxidative and neuroprotective components in coffee as well [14,15]. Taken together, combination of these phytochemicals in coffee might contribute to prevent memory impairment.

Scopolamine is a non-selective muscarinic receptor antagonist that is well known to pharmacologically interfere with memory performance in a transient manner [16]. Animals with scopolamine-induced memory impairment have been widely used to probe drugs attenuating cognitive deficits. We investigated whether instant decaffeinated coffee (IDC) attenuates learning and memory impairment induced by scopolamine in Sprague-Dawley rats. Oral gavage administration of IDC at 120 or 240 mg/kg in rats, which is equivalent to approximately three or six cups of coffee, respectively, in a 60 kg human, was used to test the preventive effects of IDC on learning and memory impairment.

2. Materials and methods

2.1. Reagents

IDC (Maxim Decaffeinated) was purchased from Dongsuh Food (Seoul, South Korea). Scopolamine hydrochloride was purchased from Sigma–Aldrich (St. Louis, MO, USA). The antibody against TNF-α was obtained from R&D Systems (Minneapolis, MN, USA). Antibodies against phosphorylated p65 and phosphorylated IκBα were purchased from Cell Signaling Technology (Danvers, MA, USA).

2.2. Animals

Male Sprague-Dawley rats weighing 200–250 g (age, 7 weeks) were purchased from the Hyochang Science (Taegu, South Korea). The experimental procedure was conducted in compliance with institutional guidelines of NIH and Daegu Haany University for the Care and Use of Laboratory Animals. The rats were housed 3 or 4 per cage, allowed access to water and food ad libitum, and maintained at an ambient temperature of $21 \pm 2\,^\circ$C with $50 \pm 10\%$ humidity and a 12 h diurnal light cycle (lights on 06:00–18:00 h) prior to testing. The rats were habituated for 5 days before the drug administration. All behavioral experiments were carried out in a room adjacent to the housing room under the same ambient conditions.

2.3. Drug administration

IDC was dissolved in distilled water and scopolamine in saline for use. In the scopolamine-induced memory impairment study (Fig. 1A), IDC (1 ml, 120 or 240 mg/kg, p.o.) or distilled water was administered once a day for 6 days and then given 1 h before the first trial session every consecutive 5 days in the water maze task and 1 h before the acquisition trial and the retention trial in the passive avoidance task for the next 2 days. Memory impairment was induced by scopolamine treatment (0.75 mg/kg, i.p.) 30 min before each task. In control group, vehicle solution (distilled water, p.o. and saline, i.p.) was administered using the same time schedule. Each group contained 6 rats.

In the study to investigate the effect of IDC as a memory enhancer (Fig. 1B), IDC (1 ml, 120 or 240 mg/kg, p.o.) or distilled water (p.o.) was administered once a day for 6 days and then given 1 h before the first trial session every consecutive 5 days in the water maze task and 1 h before the acquisition trial and the retention trial in the passive avoidance task for the next 2 days. In the control group, vehicle solution (distilled water, p.o.) was administered using the same time schedule. Each group contained 7 rats.

2.4. Morris water maze test

The Morris water maze is a circular pool (180 cm in diameter and 60 cm in height) with a featureless inner surface. The pool was filled with water maintained at $21 \pm 2\,^\circ$C. The tank was placed in a dimly lit, sound proof test room with various
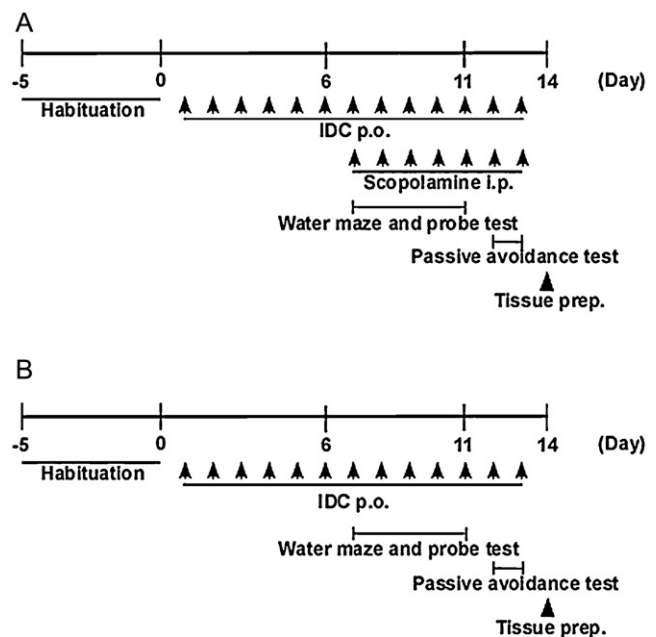

Fig. 1. Experimental schedule to determine the effect of instant decaffeinated coffee (IDC) on memory impairment (A) and memory enhancement (B). (A) After a 5-day habituation period, rats were given IDC (120 or 240 mg/kg, p.o.) for a total of 13 days. IDC alone was treated for 6 days, and then scopolamine (0.75 mg/kg, i.p.) was administered together with IDC for another 7 days. Rats underwent the Morris water maze test for 5 days, and the probe test was conducted after the last training trial of the Morris water maze test. The day after completion of the probe test, the passive avoidance test was conducted for 2 days. The day after passive avoidance test, the rats were sacrificed and hippocampus was removed for Western blot analysis. (B) After a 5-day habituation period, rats were given IDC (120 or 240 mg/kg, p.o.) for a total of 13 days. Rats underwent the Morris water maze test for 5 days, and the probe test was conducted after the last training trial of the Morris water maze test. The day after completion of the probe test, the passive avoidance test was conducted for 2 days. The day after the passive avoidance test, the rats were sacrificed and hippocampus was removed for Western blot analysis.

visual cues. The pool was conceptually divided into quadrants, and a hidden escape platform (12 cm in diameter and 38 cm in height) was placed in one of the pool quadrants and submerged 2 cm below the water surface so that it was not visible at water level. During the 5 subsequent days, the rats underwent three trials per day with the platform in place. For each training trial, rats were placed in the water facing the pool wall in different pool quadrants, with a variable order each day. When a rat located the platform, it was permitted to remain on the platform for 30 s. If the rat did not locate the platform within 90 s, it was placed on the platform for 30 s. The animal was taken to its home cage and was allowed to dry under an infrared lamp after each trial. During each trial, the time taken to find the hidden platform (latency) was recorded using a video camera-based Ethovision System (Nodulus, Wageningen, Netherlands). Immediately after the last training trial session, rats were subjected to a probe trial session in which the platform was removed from the pool and rats were allowed to swim for 90 s to search for it. A record was kept of the swimming time in the pool quadrant where the platform had previously been placed.

2.5. Passive avoidance test

The passive avoidance test is a well-established experimental procedure used to assess short-term reference memory, which depend on cortical and hippocampal circuitries [17]. The step-through passive avoidance test was performed in identical illuminated and dark chambers (Gemini Avoidance System, San Diego, CA, USA). The illuminated compartment contained a bulb, and the floor of the non-illuminated compartment was composed of stainless steel rods. These compartments were separated by a guillotine door. For the acquisition trial, rats were initially placed in the illuminated compartment and the door between the two compartments was opened 20 s later. When the rats entered the dark compartment, the door closed automatically and an electrical foot shock (0.5 mA) of 5 s duration was delivered through the stainless steel rods. Twenty-four hours after the acquisition trial, the rats were again placed in the illuminated compartment for retention trials. The time taken for a rat to enter the dark compartment after the door opened was measured as the latency time in both acquisition and retention trials, with a maximum of 300 s.
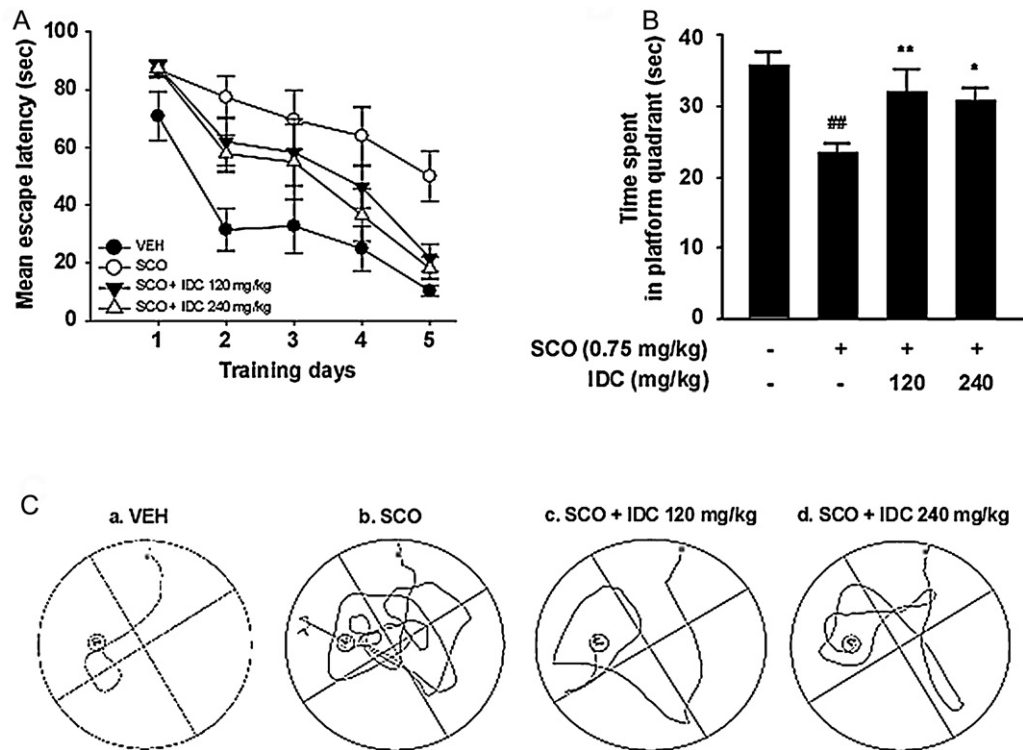
Fig. 2. Effect of instant decaffeinated coffee (IDC) on scopolamine-induced memory impairment in the Morris water maze test. (A) IDC reduced the scopolamine (SCO)-induced escape latency. IDC (120 or 240 mg/kg, p.o.) was administered to rats 1 h before the training trials, and memory impairment was induced by scopolamine treatment (0.75 mg/kg, i.p.) 30 min before the training trials. Data are expressed as mean ± SEM (n = 6). (B) IDC increased time spent in the platform quadrant during the probe test, which had been reduced by scopolamine treatment. Data are expressed as mean ± SEM (n = 6). $^{##}P < 0.01$ versus vehicle–treated group; $^{*}P < 0.05$ versus the scopolamine-treated group; $^{**}P < 0.01$ versus the scopolamine-treated group. (C) Representative swimming paths of rats from each group in the Morris water maze test on the training day 5.

2.6. Western blot analysis

The rats were anesthetized with pentobarbital (50 mg/kg, i.p.) before being killed by decapitation. The hippocampus was removed from rat brain and homogenized using Ultra Turrax homogenizer (Next Advance, Averill Park, NY, USA) in ice-cold tissue protein extraction solution (Thermo Fisher Scientific, Rockford, IL, USA) containing phosphatase inhibitor cocktail and 0.1 mM phenylmethanesulfonylfluoride (PMSF). The lysate was centrifuged at $16,000 \times g$ for 15 min. The protein concentration of the supernatant was determined using a protein assay kit (Bio-Rad, Hercules, CA, USA). The protein (90 μg) was subjected to 10% SDS-PAGE and electrophoretically transferred to a polyvinylidene fluoride (PVDF) membrane (Millipore, Billerica, MA, USA). The membrane was blocked in 5% fat-free dry milk for 1 h and then incubated with primary antibodies for 2 h at room temperature.

The dilution ratio of all primary antibodies is 1:1000 in TBST with 5% skim milk. The ratio between the amount of loaded protein and the amount of antibody for TNF-α, phospho-p65, and phospho-IκBα were 9:1. The blots were incubated with horseradish peroxidase-conjugated secondary antibodies in TBST with 5% skim milk at a 1:5000 dilution for 2 h at room temperature. The protein bands were detected using an enhanced chemiluminescence (ECL) detection kit (GE Healthcare, St. Giles, United Kingdom).

2.7. Statistical analysis

All analyses were performed using the PASW 18 Statistical Package (SPSS 12.0 KO for Windows, SPSS Inc., Chicago, IL, USA). One-way analysis of variation (ANOVA) and one-way repeated ANOVA were conducted to assess the effects of IDC. Post hoc analyses (Tukey or least significant difference (LSD)) were subsequently conducted to determine the effects of the scopolamine or the IDC treatment. Data were expressed as mean ± standard error of the mean (SEM). $P < 0.05$ was considered significant.

3. Results

3.1. IDC inhibited scopolamine-induced memory impairment

To determine the effects of IDC on memory impairment, rats treated with IDC (120 or 240 mg/kg, p.o.) and scopolamine (0.75 mg/kg, i.p.) underwent the Morris water maze test (Fig. 2A). One-way repeated ANOVA showed that the interaction effects

between the group and the training session were not significant ($F_{(12,80)}$ = 0.877, n.s). On the other hand, the between group effects were significant ($F_{(3,20)}$ = 10.286, $P < 0.001$) as were the training session effects ($F_{(4,80)}$ = 36.563, $P < 0.001$). As shown in Fig. 2A, the vehicle-treated rats (VEH) quickly became proficient at locating the submerged platform during the training sessions; however, the scopolamine rats (SCO) did not show much improvement over the course of training when compared with the vehicle-treated rats (VEH) (P = 0.0002). The scopolamine-treated rats that were administered IDC (120 or 240 mg/kg, p.o.) showed significantly better performances than the scopolamine rats (P = 0.038 or P = 0.009, respectively). Fig. 2C depicts the representative swim paths of these rats on the 5th day of the Morris water maze test. Vehicle-treated rats (a, VEH) swam a shorter distance to find the platform compared to scopolamine-treated rats (b, SCO). IDC treatment at 120 mg/kg (c, SCO + IDC 120 mg/kg) or 240 mg/kg (d, SCO + IDC 240 mg/kg) shortened the distance needed to find platform.

Spatial learning was also assessed by the probe test, in which the platform was removed from the pool and rats were given 90 s to look for it. We measured how long rats spent in the quadrant that had previously held the platform (Fig. 2B). The one-way ANOVAs on the probe test showed that the between group effects were significant ($F_{(3,20)}$ = 5.919, $P < 0.01$). The vehicle-treated rats were found to have the spatial bias when compared with the scopolamine rats (P = 0.001). Vehicle-treated rats spent about 37.4 s in the platform quadrant, whereas scopolamine rats spent about 22.6 s in that quadrant. Scopolamine rats treated with IDC (120 or 240 mg/kg, p. o.) did show statistically significant ameliorative effects on spatial learning when compared with scopolamine rats (P = 0.009 or P = 0.02, respectively). The speed of rats was measured for 5 days during the training trials of the Morris water maze test and the between group effects were not significant (data not shown).
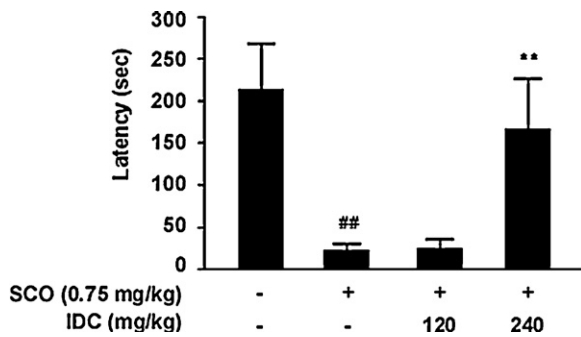
Fig. 3. Effect of instant decaffeinated coffee (IDC) on scopolamine-induced memory deficits in the passive avoidance test. IDC increased the step-through latency of scopolamine (SCO)-treated rats. IDC (120 or 240 mg/kg, p.o.) was administered to rats 1 h before the acquisition trial and the retention trial, and the memory impairment was induced by scopolamine treatment (0.75 mg/kg, i.p.) 30 min after IDC treatment. Data are expressed as mean ± SEM ($n = 6$). ##$P < 0.01$ versus vehicle-treated rats; **$P < 0.01$ versus scopolamine-treated rats.

Retention of the passive avoidance response was measured to confirm the effects of IDC on memory impairment (Fig. 3). Scopolamine (0.75 mg/kg, i.p.) was administered 30 min before the acquisition trial and the retention trial. The one-way ANOVAs on the passive avoidance test showed that the between group effects were significant ($F_{(3,20)} = 31.157$, $P < 0.001$). Scopolamine-treated rats had a significantly shorter step-through latency compared to the vehicle-treated rats ($P = 0.000001$). Administration of IDC (240 mg/kg, p.o.) 30 min before the scopolamine treatment significantly lengthened the step-through latency ($P = 0.00007$). Latency times during the acquisition trial were not affected by any of these drugs (data not shown). These observations suggest that IDC acted as a memory stabilizer against scopolamine-mediated deficits.

3.2. IDC did not enhance memory per se

To know whether IDC per se enhances memory, rats were treated with IDC (120 or 240 mg/kg, p.o.) without scopolamine and underwent the Morris water maze test (Fig. 4A and B). One-way repeated ANOVA showed that the interaction effects between the group and the training session were not significant ($F_{(8,72)} = 0.463$, n.s.). The between group effects were not significant ($F_{(2,18)} = 1.574$, n.s.), either, even though the training session effects were ($F_{(4,72)} = 41.505$, $P < 0.001$). As shown in Fig. 4A, the vehicle-treated rats (VEH) became proficient at locating the submerged platform during the training sessions, and the IDC (120 or 240 mg/kg, p.o.)-treated rats did not show much difference over the course of training when compared with the vehicle treated rats (VEH). There were no significant differences between the vehicle-treated rats (VEH) and IDC (120 or 240 mg/kg, p.o.)-treated rats ($P = 0.097$ or $P = 0.275$), indicating that IDC does not enhance spatial memory per se.

We also measured how long rats spent in the quadrant that had previously held the platform after IDC treatment by the probe test (Fig. 4B). Vehicle-treated rats and IDC-treated rats spent similar times in that quadrant. The one-way ANOVAs on the probe test showed that the between group effects were not significant ($F_{(2,18)} = 0.511$, n.s.). The speed of rats was measured for 5 days during the training trials of the Morris water maze test and the between group effects were not significant (data not shown).

The effects of IDC as a memory enhancer were tested by the passive avoidance test. The one-way ANOVAs on the passive avoidance test showed that the between group effects in step-through latency were not significant ($F_{(2,18)} = 0.143$, n.s.) (Fig. 4C). During the acquisition trial, no differences in latent time were observed
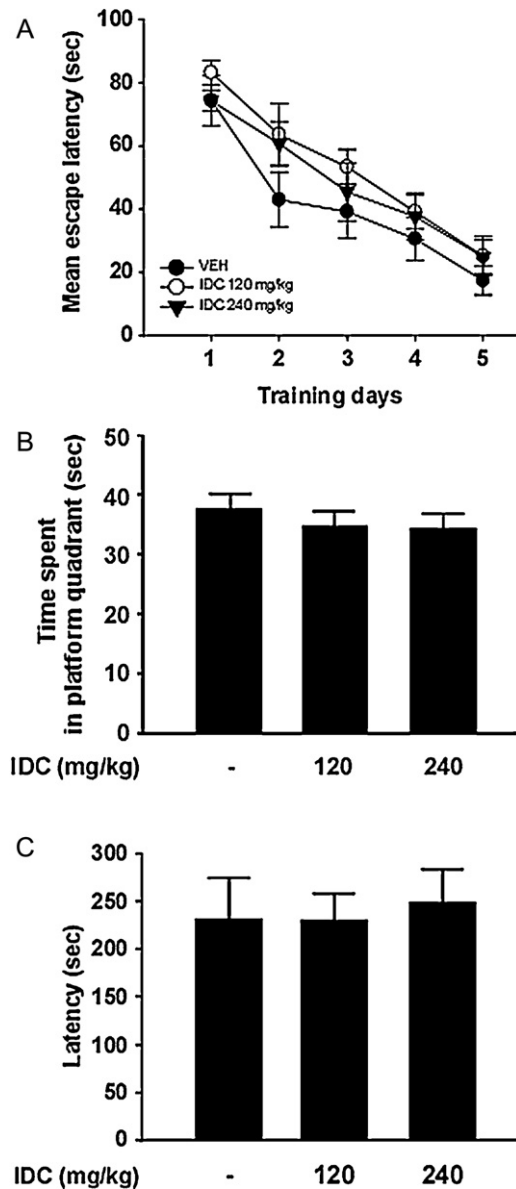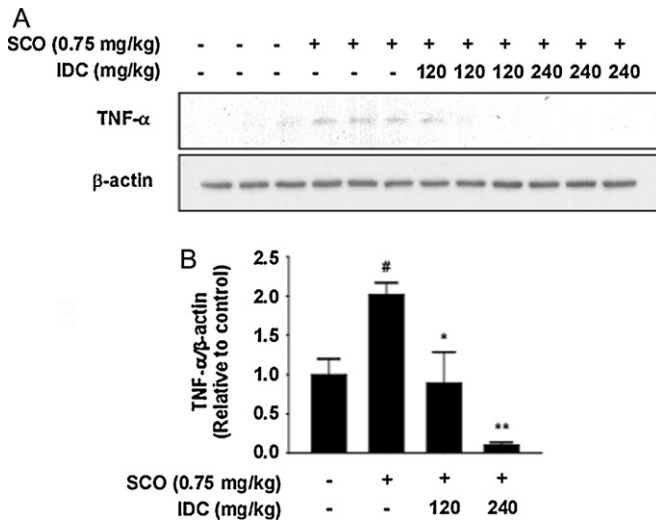

Fig. 4. Effects of instant decaffeinated coffee (IDC) on memory enhancement in the Morris water maze test and the passive avoidance test. IDC (120 or 240 mg/kg, p.o.) was administered to rats 1 h before the trials. (A) IDC did not alter escape latency per se in the water maze test. (B) IDC did not increase time spent in the platform quadrant during the probe test. (C) IDC did not increase the step-through latency in the passive avoidance test. Data are expressed as mean ± SEM ($n = 7$).

either. Overall, these observations suggest that IDC has no effect as a memory enhancer in itself.

3.3. IDC suppressed scopolamine-induced TNF-α production

Accumulating evidence suggests that inflammation is involved in impaired learning and memory [18–21]. Pro-inflammatory cytokine such as TNF-α is up-regulated in brains affected by dementia [22]. To determine the effects of IDC on TNF-α production, we performed Western blot analysis of proteins from the hippocampus of rats treated with IDC and scopolamine (Fig. 5A and B). One-way ANOVA analysis of the TNF-α showed that the between group effects were significant ($F_{(3,8)} = 12.326$, $P < 0.01$). The hippocampal TNF-α levels in the scopolamine (0.75 mg/kg, i.p.)-treated rats were strongly up-regulated when compared with the vehicle rats (Fig. 5B; $P = 0.020$). These increases induced by scopolamine were

Fig. 5. Effects of instant decaffeinated coffee (IDC) on scopolamine (SCO)-induced TNF-α production. (A) IDC suppressed the scopolamine-induced increase in TNF-α production in the hippocampus of rats. Levels of TNF-α were determined by Western blot analysis. β-actin was used as a loading control. (B) TNF-α protein levels of (A) were quantified. Data are expressed as fold increase relative to vehicle-treated group (mean ± SEM; $n = 3$). #$P < 0.05$ versus vehicle-treated rats; *$P < 0.05$ versus scopolamine-treated rats; **$P < 0.01$ versus scopolamine-treated rats.

attenuated by treatment with IDC (120 or 240 mg/kg, p.o.; $P = 0.023$ or $P = 0.002$, respectively). These results suggest that IDC significantly inhibited scopolamine-induced TNF-α production.

3.4. IDC suppressed scopolamine-induced NF-κB activation

To determine the inhibitory mechanism of IDC on TNF-α production, we evaluated the nuclear factor-κB (NF-κB) signaling molecules in the hippocampus by Western blot analysis (Fig. 6A–C). One-way ANOVA analysis of protein levels of p-p65 and p-IκBα showed that the between group effects were significant ($F_{(3,8)} = 14.973$, $P < 0.01$, and $F_{(3,8)} = 27.098$, $P < 0.001$, respectively). Hippocampal p-p65 and p-IκBα levels in the scopolamine-treated rats were strongly up-regulated when compared with the vehicle rats (Fig. 6B and C; $P = 0.003$ and $P = 0.028$, respectively). Increase in the level of p-p65 induced by scopolamine was attenuated by treatment with IDC (240 mg/kg, p.o.; $P = 0.004$, Fig. 6B) and the scopolamine-induced phosphorylation of IκBα was also inhibited by treatment of IDC (120 or 240 mg/kg, p.o.; $P = 0.0004$ or $P = 0.0002$, respectively, Fig. 6C).

4. Discussion

We found that IDC-treated rats without scopolamine did not improve the learning and memory compared to vehicle-treated rats, suggesting that decaffeinated coffee is not a general memory bolsterer (Fig. 4). Instead, IDC attenuated scopolamine-induced purported memory deficit (Figs. 2 and 3). Oral administration of IDC at 120 or 240 mg/kg in rats, which is equivalent to approximately three or six cups of coffee, respectively, in a 60 kg human, prevented the effects of scopolamine on memory impairment, indicating that IDC acted as a memory stabilizer against scopolamine.

Results of recent studies have indicated that decaffeinated coffee is neuroprotective. For example, decaffeinated coffee attenuated H_2O_2-induced oxidative neuronal cell death by inhibiting the accumulation of intracellular reactive oxygen species (ROS) [23]. Decaffeinated coffee up-regulated NADPH:quinone oxidoreductase 1 (NQO1) expression and prevented H_2O_2-induced apoptosis in primary cortical neuron [24]. In the transgenic fly models of
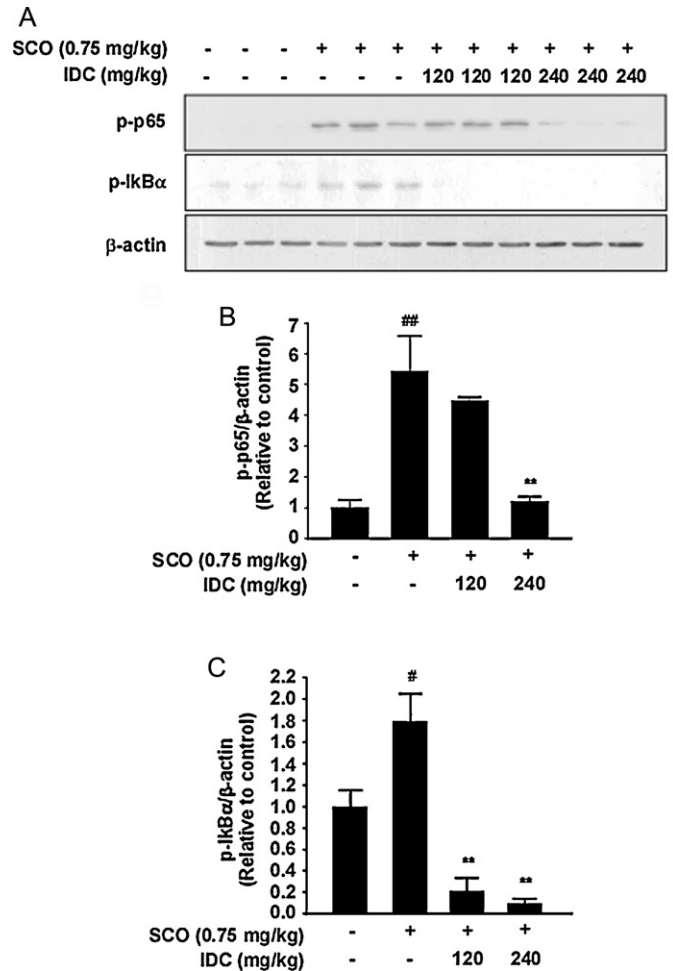
Fig. 6. Effects of instant decaffeinated coffee (IDC) on scopolamine (SCO)-induced activation of the NF-κB pathway. (A) IDC inhibited scopolamine-induced phosphorylation of p65 and IκBα in the hippocampus of rats. Levels of phosphorylated p65 and IκBα were determined by Western blot analysis. β-actin was used as a loading control. (B and C) Protein levels of phosphorylated p65 and IκBα (A) were quantified. Data are expressed as fold increase relative to vehicle-treated group (mean ± SEM; $n = 3$). #$P < 0.05$ versus vehicle-treated rats; ##$P < 0.01$ versus vehicle-treated rats; **$P < 0.01$ versus scopolamine-treated rats.

Alzheimer's disease, Parkinson's disease, and Huntington's disease, decaffeinated coffee activated cytoprotective transcription factor NF-E2-Related Factor 2 (Nrf2) and showed neuroprotective effects [14]. Dietary supplementation with decaffeinated green coffee improved diet-induced brain energy metabolism dysfunction in a high-fat diet mouse [25]. On the other hand, acute i.p. treatment with decaffeinated coffee compared to caffeinated coffee did not change the plasma levels of granulocyte-colony stimulating factor (GCSF), which was previously reported to enhance cognitive performance, in both AbPPsw + PS1 transgenic mice and non-transgenic littermates. These reports suggest that further studies are required to understand the neuropharmacological effects of decaffeinated coffee.

Accumulating evidence suggests that increased inflammation and microglial activation is associated with cognitive deficits [18]. High level of pro-inflammatory cytokines including TNF-α, interleukin (IL)-6, and IL-1 are shown in the brains of dementia [22,26,27]. TNF-α and inducible nitric oxide synthase (iNOS) are required for amyloid β (Aβ)-induced learning and memory impairment [28]. In particular, TNF-α participates in the Aβ-induced inhibition of long-term potentiation, a form of synaptic plasticity closely associated with learning and memory [29]. Therefore,

inhibiting TNF-α production and neuroinflammation may be a promising strategy to prevent memory impairment [30,31].

We found that IDC attenuated the scopolamine-mediated up-regulation of TNF-α in the hippocampus. Muscarinic receptors in the central nervous system inhibit systemic inflammation in endotoxemic rats and activation of muscarinic cholinergic transmission in the central nervous system lowers serum TNF levels [32]. Since scopolamine is a non-selective muscarinic receptor antagonist, blockage of muscarinic receptor by scopolamine might increase the expression of TNF-α in the hippocampus. It has been reported that coffee contains cholinomimetic compounds distinct from caffeine [33], and the compounds might act as a muscarinic receptor ligand and inhibit the scopolamine-mediated induction of TNF-α. IDC pre-treatment also significantly decreased the phosphorylation of IκBα and p65 in scopolamine-treated rats, suggesting that the ability of IDC to lower the level of TNF-α might be mediated by suppressing NF-κB activation.

On the other hand, coffee is a rich source of chlorogenic acids and contains many bioactive phenolic phytochemicals [9,10]. It has been reported that chlorogenic acid inhibits staphylococcal exotoxin-induced proinflammatory cytokines TNF-α, IL-1β, and IL-6 [34]. Caffeic acid lowered renal and cardiac levels of TNF-α, IL-1β, and IL-6 in diabetic mice and inhibited lipopolysaccharide-induced TNF-α release from human monocytes [35,36]. These results suggest that coffee phenolic phytochemicals including chlorogenic acid and caffeic acid might also be the bioactive neuroprotective candidates in IDC that attenuate TNF-α levels in the rat hippocampus.

It should be considered that decaffeinated coffee actually has caffeine, albeit in lower amounts than regular coffee. Apart from caffeine, decaffeinated coffee contains several other xanthines that can interfere with the function of adenosine A2A receptors [37,38]. It cannot be excluded that other components present in decaffeinated coffee might be antagonists of adenosine A2A receptors. Antagonists of adenosine A2A receptors in IDC might also be the candidates to prevent learning and memory impairment.

5. Conclusion

In conclusion, our findings demonstrate that IDC did not enhance memory per se, however, stabilized the memory impairment induced by scopolamine. The memory stabilizing effects of IDC in scopolamine-treated rats appeared to be mediated by suppressing NF-κB activation, thereby reducing TNF-α levels in the hippocampus. IDC might protect brain against memory impairment by attenuating NF-κB-TNF-α-mediated tissue injury in the hippocampus. These results suggest that regular consumption of decaffeinated coffee might be beneficial on brain health.

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