

Influence of Acupuncture on Autonomic Balance in Adult Tinnitus Patients: An Exploratory Study*

Jian-feng TU¹, Mirim Kim¹, Jing-wen YANG¹, Qian-qian LI², Gerhard Litscher^{1,3#}, Lu WANG³, Guang-xia SHI², Daniela Litscher³, Cun-zhi LIU^{1#}

¹School of Acupuncture-Moxibustion and Tuina, Beijing University of Chinese Medicine, Beijing 100029, China

²Department of Acupuncture and Moxibustion, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University, Beijing 100010, China

³Research Unit for Complementary and Integrative Laser Medicine, Research Unit of Biomedical Engineering in Anesthesia and Intensive Care Medicine and TCM Research Center Graz, Medical University of Graz, Graz 8036, Austria

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Summary: Acupuncture is an alternative therapy for tinnitus in clinical practice. The mechanism by which acupuncture can alleviate tinnitus is still unknown. Autonomic nervous system was reported to be responsible for tinnitus. The aim of this study was to explore the effect of acupuncture on autonomic balance in adult tinnitus patients. Thirty patients were randomly assigned into either the deep acupuncture (DA) group or the shallow acupuncture (SA) group. Each patient received 6 acupuncture sessions (a-f phase) over three weeks. Measures of heart rate variability and Tinnitus Handicap Inventory (THI) were obtained at baseline and after the sixth acupuncture session in all patients. The results showed that the low frequency/high frequency (LF/HF) pattern was increased at b-f phase until the sixth acupuncture session when compared with that at the first acupuncture session in DA group. However, it continuously increased at b-f phase in SA group even at the sixth acupuncture session, which was not significantly different from that at the first acupuncture session. The decrease in THI in DA group was greater than that in SA group after 3-week treatment ($P=0.043$). Our preliminary study suggests three-week deep acupuncture can improve tinnitus symptoms in adult tinnitus patients, which may be related to the regulation of autonomic nervous system balance.

Key words: tinnitus; acupuncture; heart rate variability; autonomic nervous system

Tinnitus is the perception of sound without an external source^[1]. An estimated prevalence of tinnitus in the population across studies ranges from 10% to 20%; 1% to 3% of those suffer from severe, distressing tinnitus^[2-4]. Despite pharmacological and technological advances, the treatment of tinnitus remains a challenge.

Tinnitus was reported to be etiologically related to ontological, metabolic, dental, cardiovascular, neurological, spinal and psychiatric diseases^[5]. It is suggested that the activation of limbic and autonomic nervous systems (ANS) is responsible for troublesome tinnitus^[6]. Regulation of ANS was demonstrated to

play a useful role in tinnitus therapy since the electrical stimulation of the vagus nerve is frequently used for the treatment of tinnitus and it could greatly improve the clinical outcomes of tinnitus patients^[7,8].

Acupuncture is an alternative therapy for tinnitus according to Traditional Chinese Medicine (TCM). It has been reported that acupuncture could yield immediate relief, both from the loudness and the disturbing quality of tinnitus, significantly improve the quality of life, lessen tension, and provide better sleep^[9-13]. It is not clear whether the acupuncture-induced changes of tinnitus symptoms are mediated by autonomic balance. Heart rate variability (HRV) is a simple and noninvasive marker of autonomic function^[14], and has the potential to evaluate the autonomic status of tinnitus patients^[15]. The effect of acupuncture on HRV has been demonstrated by previous clinical trials in patients with chronic fatigue syndrome, hypertension, and depression^[16-18], but not with tinnitus. Moreover, an increase in parasympathetic tone was found to be associated with successful suppression of tinnitus^[19]. Therefore, in this exploratory study, we evaluated the effect of acupuncture on ANS

Jian-feng TU, E-mail: tujianfeng1@126.com

#Corresponding authors, Gerhard Litscher, E-mail: gerhard.litscher@medunigraz.at; Cun-zhi LIU, E-mail: lcz623780@126.com

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reactivity in patients with chronic tinnitus.

1 SUBJECTS AND METHODS

1.1 Ethical Statement

The trial protocol was approved by the Research Ethical Committee of Beijing Hospital of Traditional Chinese Medicine affiliated to Capital Medical University. We performed the study according to the Declaration of Helsinki and Good Clinical Practice standards. This trial was registered with ISRCTN at Current Controlled Trials (ISRCTN 58013563) and the design had been pre-published^[20].

1.2 Patients

Patients were diagnosed as having tinnitus according to Chinese criteria^[21]. A total of 30 patients with tinnitus were recruited from Beijing Hospital of Traditional Chinese Medicine affiliated to Capital Medical University through advertisements, and publicity in outpatient clinics and at community service centers from September 2012 to February 2013.

Patients who fulfilled all of the following conditions were considered for enrollment: typical symptoms of unilateral or bilateral tinnitus; aged 18–65 years, either sex; tinnitus duration of more than 3 months; not receiving any treatment in the last 1 month; normal language and intelligence ability to answer and fill in the questionnaire; written and informed consent obtained.

The exclusion criteria included objective tinnitus (patients with objective tinnitus are audible to the examining/auscultating physician); acute or intermittent tinnitus, history of Meniere disease, or tinnitus induced by middle ear/inner ear/small pons angle tumor; underlying disease or history: otitis media, tympanic membrane perforation, or Eustachian tube function obstacle; acoustic neuroma, intracranial damage or use of any ototoxic drugs; severe dysfunction of the heart, kidneys or liver; the serious original disease of the hematopoietic system or endocrine system; serious aphasia, depression syndrome or mental disease.

1.3 Randomization

SAS software (SAS Institute, Inc., USA) was used to generate a random sequence and the block size was 6. A clinical research coordinator screened and enrolled participants. After the participants completed a baseline evaluation and gave an informed consent, another clinical research coordinator who was not involved in data collection randomly stratified the subjects into deep acupuncture or shallow acupuncture group at a 1:1 ratio according to the random sequence.

1.4 Blinding

The patients, data collection staff, and data analysts were blinded to group allocation. Due to the responsibility of delivering acupuncture, blinding of acupuncturists was quite difficult to achieve. The

patients were only told that they would be randomly provided with one of two acupuncture therapies based on real acupoints. The patients assumed the supine position during acupuncture, so they could not see the depth of acupuncture. The data collection staff and data analysts were not involved in providing interventions.

1.5 Interventions

All of the acupuncture treatment was manipulated by an acupuncturist who was a registered practitioner of Traditional Chinese Medicine with at least 5 years of clinical experience. Single-use sterile needles (0.25 mm × 25 mm; Hwato, China) were used for acupuncture. Acupuncture was conducted over a period of 3 weeks, at a frequency of 2 sessions per week. Multiple sessions in one day were prohibited. No additional treatment was allowed. Acupoints used in the two groups were the same, including *Baihui* (GV20), *Shenting* (GV24), and bilateral *Waiguan* (SJ5), and *Zulingqi* (GB41). Additionally, *Tinghui* (GB2) was bilaterally needled for patients with bilateral tinnitus, whereas only *Tinghui* (GB2) of the affected side was selected for patients with unilateral tinnitus. All acupoints were located according to the World Health Organization Standardized Acupuncture Points Location.

1.5.1 Deep Acupuncture Patients in this group received deep acupuncture by piercing the skin approximately 10 mm to 30 mm into the muscle layer. Quick twirling, lifting and thrusting were manipulated for De qi. De qi is a composite of sensations including soreness, numbness, distention, heaviness, and other sensations, which is believed to be an essential component for acupuncture efficacy.

1.5.2 Shallow Acupuncture Patients in this group received shallow acupuncture by penetrating the skin at approximately 2 mm into the fat layer without any twirling, lifting or thrusting. Procedures were the same as in the deep acupuncture group but with no needle manipulation for De qi.

1.6 Outcome Measures

1.6.1 HRV HRV is the primary outcome and has been used in other trials^[22,23]. It was measured in a quiet room after at least 5 min rest. HRV analysis was conducted using a Medilog AR12 HRV system (Huntleigh Healthcare, UK) provided by the TCM Research Center at the Medical University of Graz. The six measurement phases with 5 min each were as follows: one before stimulation (a), four during acupuncture (b–e), and one after acupuncture (f) (fig. 1). HRV was measured at the first acupuncture session, as well as the last acupuncture session. The sampling rate of the HRV system was 4096 Hz; the raw data were stored on a 32 MB memory card, and were read by a card reader connected with a standard computer after removing the card from the portable system. HRV was displayed in a way to help to judge the function of the ANS^[24]. The researcher performing the HRV testing was blinded to

group assignment. HRV variables were quantified as the low frequency/high frequency (LF/HF) ratio, and mean HR, which was recommended by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology^[25].

1.6.2 Tinnitus Handicap Inventory (THI) THI consists of 25 questions^[26]. Each question of the THI was answered by the patient as “often” (4 points), “sometimes” (2 points), or “never” (0 point) with a maximum total score of 100 indicating most severe suffering from tinnitus. The assessment was at baseline (before treatment initiation) and 3 weeks later (after the last acupuncture treatment).

1.6.3 Adverse Events Participants also reported adverse events, including discomfort or bruising at the sites of needle insertion, nausea, or feeling faint and so on.

1.7 Data Analysis

Repeated-measures analysis of variance (ANOVA) was used for analysis of HRV. Student’s *t* test was used for analysis of age and THI. Baseline characteristics between groups were compared using χ^2 test for sex, tinnitus side, pure tone, and frequency of tinnitus, and Kruskal-Wallis test for tinnitus duration. Continuous variables were described using the mean (standard deviation), or the median (minimum value, maximum

value) if the normality assumption was violated. Categorical variables were described using the frequency (percentage). The criterion for significance was $P<0.05$. The main analysis of this study was to evaluate the impact of deep acupuncture on the HRV in tinnitus patients. The efficacy measure was defined as the decrease in the THI score. Data analysis was conducted by statisticians who were independent of the research team. Every analysis was conducted using SPSS software (SPSS 16.0 for Windows).

2 RESULTS

Fifteen patients with tinnitus received deep acupuncture (8 females, 7 males, 55.13±11.62 years) and 15 were given shallow acupuncture (10 females, 5 males, 51.27±9.98 years). The flow diagram is shown in fig. 2. The duration of tinnitus ranged from 6 months to 15 years. There was no statistical difference between two groups in terms of demographic data (table 1).

Fig. 3 shows changes in LF/HF of the deep acupuncture group and the shallow acupuncture group during the six measurement phases (a–f). Compared with the baseline, LF/HF showed significant increases during and after the first treatment session in both groups. After 3-week deep acupuncture treatment, the LF/HF pattern did not show a significant increase at b–f phases compared with that at a phase. In the shallow acupuncture group, the LF/HF pattern continually increased during a–f phases.

Fig. 4 shows the mean HR of all 30 patients with tinnitus during the six measurement phases. There was no significant change in the mean HR before, during, or after deep acupuncture either in the first or last

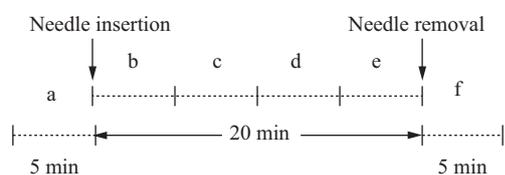


Fig. 1 Experimental protocol for needle acupuncture

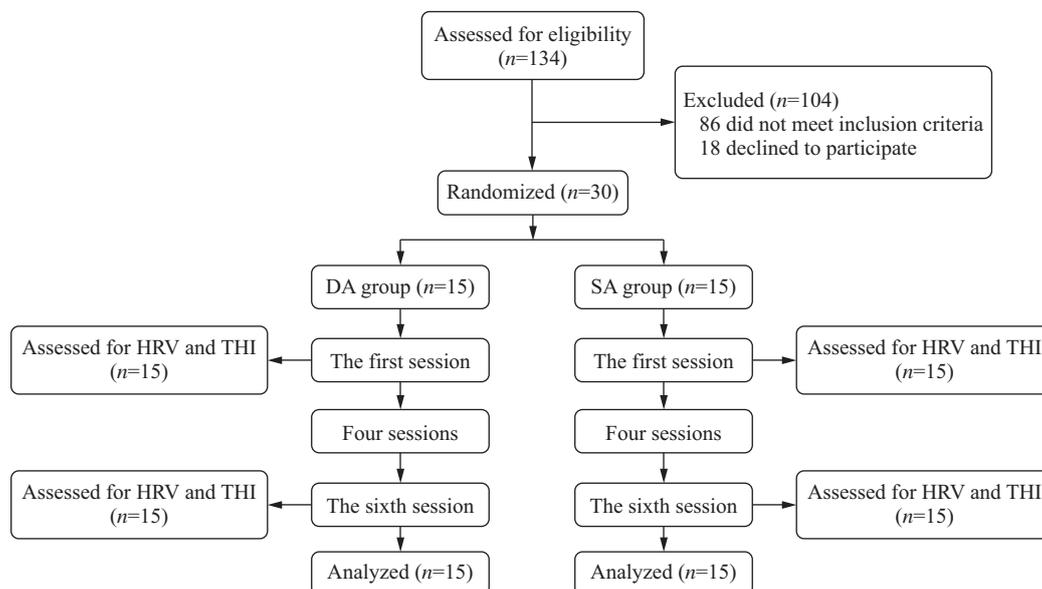


Fig. 2 Flow diagram

DA: deep acupuncture; SA: shallow acupuncture; HRV: heart rate variability; THI: Tinnitus Handicap Inventory

Table 1 Baseline demographics

Variables	Deep acupuncture (n=15)	Shallow acupuncture (n=15)	P
Age (years)	55.13±11.62	51.27±9.98	0.34
Sex			
Male	7	5	0.46
Female	8	10	
Tinnitus side			
Right	1	2	0.50
Left	3	1	
Bilateral	11	12	
Duration (months)	24 (9–180)	30 (6–120)	0.26
Pure tone			
<60 dB	9	7	0.46
≥60 dB	6	8	
Frequency of tinnitus			
<1 kHz	5	3	0.68
1–4 kHz	2	3	
>4 kHz	8	9	
THI	54.00±1.58	55.87±1.29	0.82

Data are given as mean±standard deviation or median (range). THI, Tinnitus Handicap Inventory

treatment. Similar results were found in the shallow acupuncture group.

The THI scores of the participants before and after 3-week treatment are shown in table 2. The THI of the deep acupuncture group was significantly improved after 3-week treatment compared with that of the shallow acupuncture group ($P=0.043$).

Table 2 THI values for the different interventions

	Deep acupuncture (n=15)	Shallow acupuncture (n=15)	P
Baseline	54.00±1.58	55.87±1.29	0.82
Three weeks	37.33±1.68	52.73±1.74	–
<u>Change from baseline</u>	<u>16.67±1.11</u>	<u>3.13±1.21</u>	<u>0.04</u>

THI, Tinnitus Handicap Inventory. Data are reported as mean±standard error.

During the study, 6 participants in the deep acupuncture group reported adverse events: subcutaneous hematoma ($n=4$) and post-needling persistent sensation ($n=2$); 4 participants in shallow acupuncture group had such adverse events as subcutaneous hematoma ($n=2$), post-needling persistent sensation ($n=2$). All adverse events were relieved spontaneously in subsequent 2–7 days. There was no occurrence of serious adverse events.

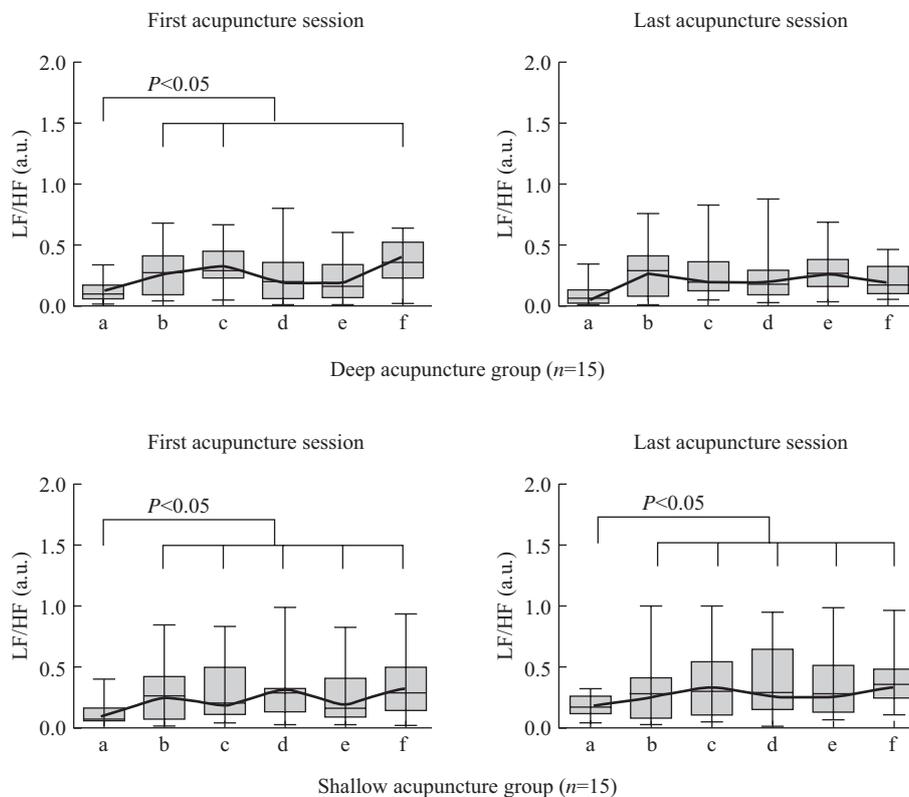


Fig. 3 Box plots of low frequency/high frequency ratio

The ends of the boxes indicate the 25th and 75th percentiles with a line at the median. Six measurement phases were compared: one before stimulation (a), four during acupuncture (b–e), and one after acupuncture (f). Compared with the baseline, LF/HF showed significant increases during and after the first treatment session in both groups. After 3-week deep acupuncture treatment, the LF/HF pattern did not show a significant increase at b–f phases compared with a phase. In the shallow acupuncture group, a significant increase was found during the last treatments, which was not significantly different from that during the first treatment.

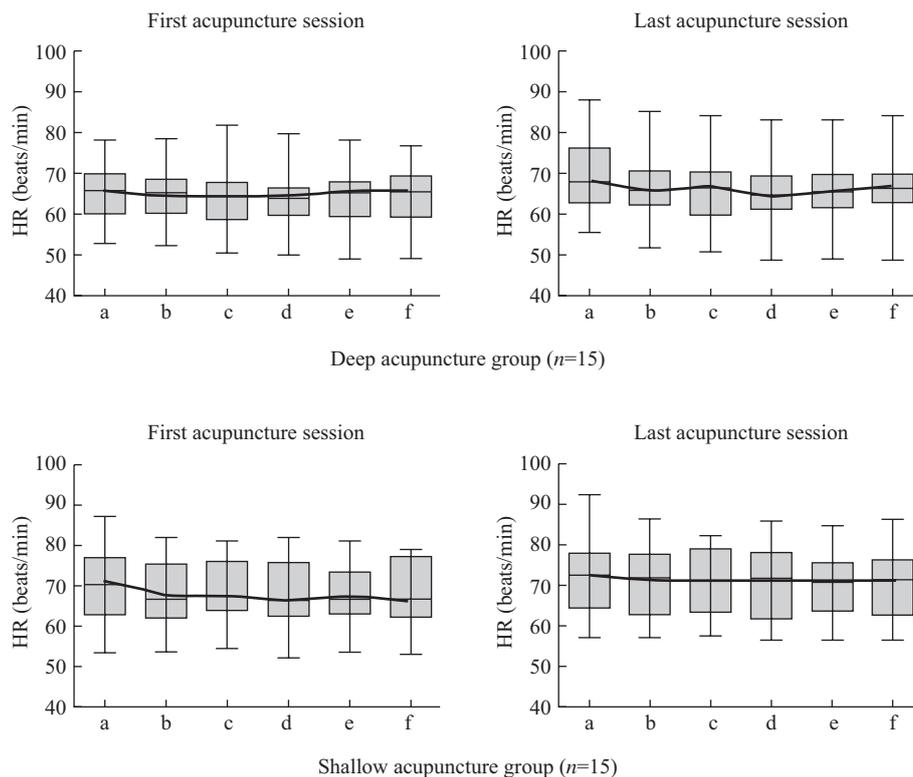


Fig. 4 Box plots of heart rate

The ends of the boxes indicate the 25th and 75th percentiles with a line at the median. Six measurement phases were compared: one before stimulation (a), four during acupuncture (b–e), and one after acupuncture (f). There was no significant change of the mean HR before, during, or after acupuncture either in the first or last treatment in both groups.

3 DISCUSSION

This study aimed to explore the effect of acupuncture on ANS reactivity in patients with chronic tinnitus. The results indicated that deep acupuncture, compared with shallow acupuncture, led to different changes of the LF/HF pattern and decline of THI in the tinnitus patients; acupuncture had no substantial impact on mean HR.

Mounting evidence showed that acupuncture can influence the balance of ANS^[16–18]. Generally, acupuncture enhances either vagal or sympathetic tone, depending on which acupoints are stimulated^[27]. In the present study, LF/HF was significantly increased during and after the first acupuncture compared with baseline values before treatment. One possible reason might be that both deep acupuncture and shallow acupuncture, as an external stimulation, are able to stimulate the body to produce its own defense reflex alarm reaction. However, induced-stress response by deep acupuncture could gradually disappear, and translate into a benign stimulation.

Acupuncture has frequently been used to treat tinnitus^[13–15]. The mechanism may be related to activating endogenous opioid and neuropeptides by stimulating specific brain structures^[28, 29]. As a complementary and alternative medicine, acupuncture has been reported to

relieve the loudness and disturbing quality of tinnitus, and improve the quality of life^[30].

The ANS has two components, the sympathetic nervous system and the parasympathetic nervous system. The sympathetic nervous system is responsible for flight and stress responses, while the parasympathetic nervous system is dominant when a person is relaxed. LF (0.04–0.15 Hz) mainly reflects the sympathetic nerve activity, whereas HF (0.15–0.4 Hz) is considered as an index of parasympathetic nerve activity. The LF/HF ratio is considered to reflect sympathovagal balance.

Tinnitus patients exhibit impairments in the ANS. A study showed that the LF/HF was significantly increased in chronic tinnitus patients^[31], which suggested a state of the sympathovagal imbalance. The results of the current study that the LF/HF ratio but not the mean HR component could be modulated by acupuncture were similar to previous works. ANS modulation is also linked to ANS tone (HR mean) and, as a consequence, an increase in the sympathetic activity and a decrease in the vagal tone are related to an increment in the HR and a reduction in its variability. This implies that there is a physiological correlation between HRV and HR. However, a simulation study suggested the changes in ANS modulation are independent of changes on mean HR^[32]. This is consistent with our results. Thus, deep

acupuncture can modulate the ANS by activating the sympathetic and parasympathetic nervous balance.

There were several limitations in this study. First, the sample size is limited. The relatively small sample size limits the power to detect a differential effect of the two acupuncture methods, which should be considered in the interpretation of data. Because there are few similar studies reported previously, we could not calculate the sample size on the basis of the differences of HRV modulated by deep acupuncture or shallow acupuncture in tinnitus patients. The sample size of 30 was pre-specified according to common practice of exploratory trial and also was reported in the published protocol^[20] to avoid data-driven analysis and enhance the transparency. Second, an error was made in the registration, in which the control group was laser acupuncture, but actually, shallow acupuncture was used in the control group. This was explicitly specified in the protocol^[20]. Third, the influence of treatment duration on the results was not determined in this study. It is likely that prolonged acupuncture treatment would be of greater benefit for the relief of tinnitus. Fourth, shallow acupuncture may have some physiological effects, which is also a limitation of the study. Fifth, the aim of this exploratory study was to evaluate the effect of acupuncture on autonomic balance in adult tinnitus patients. We just used THI, a commonly used measure, to detect the clinical effect of acupuncture on symptoms. Other outcomes should be adopted to evaluate the long-term effect of acupuncture on tinnitus in future trials. Furthermore, relevant animal experiments should be carried out for further verification.

In conclusion, our preliminary study suggested deep acupuncture improves tinnitus symptoms as evidenced by a significant decrease in THI, and the mechanism seems to be related to modulating the imbalance of ANS. Different brain activities between deep and shallow acupuncture and the effect of non-acupoint stimulation on autonomic nervous activity warrant further investigation in the future.

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Conflict of Interest Statement

The authors have no conflict of interest.

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