Preliminary communication

A tomato-rich diet is related to depressive symptoms among an elderly population aged 70 years and over: A population-based, cross-sectional analysis

Kaijun Niu [a,b,*], Hui Guo [c], Masako Kakizaki [d], Yufei Cui [b], Kaori Ohmori-Matsuda [d], Lei Guan [b], Atsushi Hozawa [e], Shinichi Kuriyama [f], Toru Tsuboya [d], Takashi Ohrui [g], Katsutoshi Furukawa [h], Hiroyuki Arai [h], Ichiro Tsuji [d], Ryoichi Nagatomi [b]

[a] Department of Epidemiology, School of Public Health, Tianjin Medical University, Tianjin, China
[b] Division of Biomedical Engineering for Health & Welfare, Tohoku University Graduate School of Biomedical Engineering, Sendai, Japan
[c] Tianjin University of Sport, Tianjin, China
[d] Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan
[e] Department of Preventive Medicine and Epidemiology, Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan
[f] Department of Molecular Epidemiology, Environment and Genome Research Center, Tohoku University Graduate School of Medicine, Sendai, Japan
[g] Division of Geriatric Pharmacotherapy, Institute of Development, Aging and Cancer, Tohoku University
[h] Department of Geriatrics and Gerontology, Division of Brain Sciences, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan

ARTICLE INFO

ABSTRACT

Background: Enhanced oxidative stress or defective anti-oxidant defenses are related to the pathogenesis of depressive symptoms. Lycopene is the most powerful antioxidant amongst the carotenoids. The aim of this study was to investigate the relationship between different vegetables, including tomatoes/tomato products (a major source of lycopene), and depressive symptoms in a community-based elderly population.

Methods: We analyzed a cross-sectional survey including 986 community-dwelling elderly Japanese individuals aged 70 years and older. Dietary intake was assessed using a valid self-administered diet-history questionnaire, and depressive symptoms were evaluated using the 30-item Geriatric Depression Scale with 2 cut-off points: 11 (mild and severe) and 14 (severe) or use of anti-depressive agents.

Results: The prevalence of mild and severe and severe depressive symptoms was 34.9% and 20.2%, respectively. After adjustments for potentially confounding factors, the odds ratios of having mild and severe depressive symptoms by increasing levels of tomatoes/tomato products were 1.00, 0.54, and 0.48 (p for trend < 0.01). Similar relationships were also observed in the case of severe depressive symptoms. In contrast, no relationship was observed between intake of other kinds of vegetables and depressive symptoms.

Limitations: This is a cross-sectional study, and not for making a clinical diagnosis of depressive episodes.

Conclusions: This study demonstrated that a tomato-rich diet is independently related to lower prevalence of depressive symptoms. These results suggest that a tomato-rich diet may have a beneficial effect on the prevention of depressive symptoms. Further studies are needed to confirm these findings.

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1. Introduction

For several decades, the health burden of stress-related diseases, including depressive symptoms and anxiety disorders, has been rapidly increasing. The presence of depressive symptoms in later life is recognized as a public health problem. Depressive symptoms contribute a significant independent risk for the onset of coronary disease (Wulsin and Singal, 2003), and disease susceptibility (Zorrilla et al., 2001). Depressive symptoms also worsens the outcomes of many medical disorders, promotes disability and increases mortality (Alexopoulos, 2005).

Several studies have suggested that enhanced oxidative stress or defective antioxidant defenses may be related to affective disorder or the pathogenesis of depressive symptoms (Bilici et al., 2001; Khanzode et al., 2003; Ozcan et al., 2004; Srivastava et al., 2002;

Tsuboi et al., 2004). A longitudinal study in elderly residents showed preventive effects of vitamin E, a dietetically anti-oxidative compound, on the progression of depressive symptoms in male participants (Shibata et al., 1999). On the other hand, lycopene, a carotenoid antioxidant, is the most powerful antioxidant amongst carotenoids and there is no evidence of toxic effects (Heber and Lu, 2002). In vitro study of singlet oxygen quenching action, lycopene was shown to be 100 times more efficient than vitamin E (Atessahin et al., 2005). Thus, we hypothesized that a tomato-rich diet, a major source of lycopene (tomatoes and tomato-based sauces, juices, and ketchup account for more than 85% of the dietary intake of lycopene for most people (Rao and Rao, 2007)) may have a potentially beneficial effect on the prevention of depressive symptoms. However, to our knowledge, only a few studies have investigated the relationship between tomato/lycopene and depressive symptoms (Tsuboi et al., 2004). Moreover, no studies have fully investigated the relationship between a tomato-rich diet and depressive symptoms in a community-dwelling elderly population.

Because vegetables are good sources of antioxidant phytochemicals that mitigate the damaging effect of oxidative stress, we designed a cross-sectional study to compare the relationship between intake of several vegetables and tomato products with depressive symptoms in community-dwelling elderly participants aged ≥ 70 years.

2. Methods

2.1. Study participants

The Tsurugaya Project included subjects aged 70 years and older who were living in the Tsurugaya area of Sendai, one of the major cities in the Tohoku area of Japan. The data were obtained in 2002 from 1178 individuals giving their informed consent for data analysis. A detailed description of the methods has been published elsewhere (Niu et al., 2005a). The protocol of this study was approved by the Institutional Review Board of the Tohoku University Graduate School of Medicine.

In this study, depressive symptoms were assessed with the aid of the Geriatric Depressive symptoms Scale (GDS) (Brink et al., 1982). Of the 1178 subjects, 1169 completed the GDS. We also excluded those subjects whose did not have any information on diet ($n=94$). Furthermore, those who reported a history of cancer ($n=89$) and cognitive dysfunction (Mini Mental State Examination [MMSE] Score (Folstein et al., 1975) < 18) ($n=17$) were also excluded. As a result of these exclusions, the final study population included 986 subjects.

2.2. Assessment of depressive symptoms

Depressive symptoms were assessed according to the Japanese version (Niino et al., 1991) of the 30-item GDS using 2 cut-off points (GDS score, ≥ 11 or 14) or the use of anti-depressive agents, indicating relatively mild to severe depressive symptoms or severe depressive symptoms (Brink et al., 1982).

2.3. Assessment of dietary intake

A brief self-administered diet history questionnaire (BDHQ) included 75 food items with specified serving sizes that were described by natural portions or standard weight and volume measures of the servings commonly consumed in this study population. For each food item, participants indicated their mean frequency of consumption over the past year, in terms of the specified serving size by checking 1 of the 7 frequency categories

ranging from "almost never" to "2 or more times/d". The question of tomatoes/tomato products included some commonly eaten tomato foods such as tomato, tomato ketchup, stewed tomato, or tomato stew. According with BDHQ, Other kinds of vegetables were divided into four categories as follow: (1) Green-leaf vegetables, (2) Cabbage and Chinese cabbage, (3) Carrot, onion, burdock, lotus root and pumpkin, (4) Japanese white radish (daikon) and turnips. The mean daily intake of nutrients was calculated using an *ad hoc* computer program developed to analyze the questionnaire. The Japanese food composition tables, 4th edition, and the other sources (Sakai et al., 1995) were used as the nutrient database. The reproducibility and validity of the BDHQs have been described in detail elsewhere (Sasaki, 2005).

2.4. Assessment of other variables

Anthropometrics (height, body weight) were recorded using a standardized protocol. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). Blood pressure (BP) was measured at home using an HEM747IC device (Omron Life Science Co. Ltd, Tokyo, Japan), which uses the cuff-oscillometric method to generate a digital display of systolic and diastolic pressures. The mean of 15.6 ± 10.5 (mean $\pm$ SD) BP measurements was used as the BP value. Participants who did not measure home BP for at least 3 days were treated as having missing information on hypertension. Hypertension was defined as a home systolic BP ≥ 135 mm Hg or a home diastolic BP ≥ 85 mm Hg or the use of antihypertensive agents (Chobanian et al., 2003).

Blood samples were drawn from the antecubital vein of the seated subject with minimal tourniquet use. Specimens were collected in siliconized vacuum glass tubes containing sodium fluoride for blood glucose, and no additives for lipids analyses. Blood glucose concentrations were measured using enzymatic methods (Shino-Test, Tokyo, Japan). Diabetes was defined as a casual blood glucose concentration of ≥ 200 mg/dL or the current use of antidiabetic medication.

Sociodemographic variables including gender, age, educational level, and perceived social support (PSS) were also assessed. Educational level attained was assessed by determining age at completion of schooling and was divided into 2 categories: ≤ 12 or > 12 years. PSS was evaluated on the basis of responses ("yes" or "no") to the following 5 questions: "Do you have someone to whom you can talk when you are in trouble?" (PSS1); "Do you have someone to whom you can talk when your physical condition is not good?" (PSS2); "Do you have someone who can help you with daily housework" (PSS3); "Do you have someone who can take you to hospital when you do not feel well?" (PSS4); and "Do you have someone who can take care of you when you are ill in bed?" (PSS5). These questions were extracted from a previous study regarding social support and elderly depressive symptoms in a rural community (Muraoka et al., 1996). A single summed score was calculated based on the PSS 1–5. The lack of PSS was defined as PSS score$=0$.

Health-related variables assessed included history of physical illness, pain, cognitive function, instrumental activities of daily living (IADL), and current use of medication. History of physical illness was evaluated on the basis of responses ("yes" or "no") to questions. Pain within the previous 4 weeks was assessed by the question, "Have you had any pain recently? If so, how intensely do you feel such pain?" Possible answers were "no pain," "very mild pain," "mild pain," "moderate pain," and "severe pain." A subject who reported "mild" to "severe" pain was considered to have pain. Cognitive function was assessed on the basis of the MMSE and was classified into 2 categories: 18–23 and ≥ 24. IADLs were assessed using the Rouken–Shiki scale (Koyano et al., 1987) and a cut-off point of 10/11 was used to determine

impairment in IADL. The drug information was confirmed by a well-trained pharmacist.

Information on smoking status and drinking status were obtained from the questionnaire survey. Physical activity (PA) was assessed first by a self-reported single-item question on whether the participant undertook any PA during the past year. If yes, questions were asked about the frequency and duration of walking, brisk walking, and sports. PA was then classified into 3 categories, based on frequency and duration: (1) "High," at least 3–4 times per week for at least 30 min each time; (2) "Low," reporting some activity in the past year, but not enough to meet high levels; and (3) "None," no PA. Furthermore, PA was classified into 6 levels based on the above 3 categories and the type of physical activity, such as walking, brisk walking, and sports: (1) "Level 1," no walking, no brisk walking, no sports; (2) "Level 2," low walking, no brisk walking, no sports; (3) "Level 3," high walking, no brisk walking, no sports; (4) "Level 4," any walking, low brisk walking, no sports; (5) "Level 5," any walking, high brisk walking, no sports; (6) "Level 6," any walking, any brisk walking, low or high sports. Detailed information has been provided in previous reports (Niu et al., 2005b). Finally, subjects were divided into 2 categories: $\leq$ level 3 or $>$ level 3.

2.5. Statistical analysis

Descriptive data are presented as mean (95% confidence interval [95% CI]) or percentages. Depressive symptoms were used as the dependent variable and the tomato/tomato product and other vegetable intake level as the independent variable. Multiple logistic regression analysis was used to examine the relationship of tomato/tomato product and other vegetable intake with depressive symptoms after adjustment for age, sex, BMI, hypertension, diabetes, history of cardiovascular diseases,

smoking and drinking habits, physical activity, cognitive status, impaired IADL, self-reported body pain, educational level, living alone, marital status, lack of PSS, total energy intake, and intake of all kinds of fruits (tertiles), green tea (tertiles) (Niu et al., 2009), and mutual other kinds of vegetables. The odds ratios (ORs) and 95% CIs for depressive symptoms for increasing tomato/tomato product and other vegetable intake levels, with the lowest level as the reference, were also calculated using multiple logistic regression analysis. Interactions between tomato/tomato product and other vegetable intake levels and confounders of depressive symptoms were tested by the addition of cross-product terms to the regression model. A significant difference was defined as $p < 0.05$. All statistical analyses were performed using a Statistical Analysis System 9.1 edition for Windows (SAS Institute Inc., Cary, NC, USA.).

3. Results

Among 986 subjects who were available to be analyzed, 34.9% and 20.2% were classified as having mild and severe and severe depressive symptoms, respectively.

Age- and sex-adjusted participant characteristics according to tomato/tomato product status are presented in Table 1. The proportion of male, current smoker, lower educational level, and widowed or divorced status were significantly lower across the tomatoes/tomato products groups (p for trend ≤ 0.03). The proportion of subjects who were married was significantly higher across the tomatoes and tomato products groups (p for trend $= 0.04$). Mean total energy intake was significantly higher across the tomatoes/tomato products groups (p for trend < 0.0001). The mean GDS score was significantly lower across the tomatoes/tomato products groups (p for trend < 0.0001). Otherwise, no significant difference

Table 1
Age- and sex-adjusted characteristics according to categories of tomato/tomato product consumption.

	Tomatoes/tomato products consumption			p for trend
	≤ 1 time (wk)	2–6 times (wk)	≥ 1 time (d)	
No.	139	325	522	–
Age (year)	75.5 (74.7–76.3)	75.9 (75.4–76.4)	76.1 (75.7–76.5)	0.45
Sex (male)	49.6	48.3	36.2	< 0.001
BMI (kg/m^2)	23.5 (23.0–24.1)	23.8 (23.5–24.2)	23.9 (23.6–24.2)	0.42
Diabetes	7.9	9.2	9.4	0.70
Hypertension	71.2	68.6	69.0	0.62
History of CVD	14.4	16.0	14.8	0.80
Smoking status	–	–	–	–
Current smoker	25.9	12.9	9.8	< 0.001
Ex-smoker	26.6	35.1	25.9	0.41
Drinking status	–	–	–	–
Current drinker	44.6	44.3	35.8	0.32
Ex-drinker	9.4	12.0	12.3	0.17
PA ($>$ level 3)	38.1	37.9	37.9	0.60
Self-reported total number of physical illness (≥ 2)	63.3	68.6	69.9	0.26
Cognitive ability (18 $\leq$ MMSE < 24)	5.8	9.9	7.1	0.61
Impaired IADL	12.2	14.2	10.5	0.19
Self-rated health (yes)	79.1	82.5	81.8	0.44
Body pain (yes)	70.5	81.2	77.4	0.23
Lack of PSS (total score$=0$)	15.1	14.8	13.4	0.34
Educational level (≤ 12 years)	79.1	71.1	67.8	< 0.001
Living alone (yes)	28.1	21.5	25.1	0.13
Marital status married	59.0	63.4	60.5	0.04
Widowed or divorced	37.4	33.2	34.9	0.03
Total energy intake (kcal/d)	1841.7 (1768.4–1915)	1976.7 (1928.8–2024.6)	2084.4 (2045.8–2123)	< 0.0001
GDS	10.9 (10.1–11.8)	9.1 (8.5–9.7)	8.4 (7.9–8.8)	< 0.0001

BMI, body mass index; CVD, cardiovascular diseases; PA, physical activity; PSS, perceived social support; MMSE, Mini Mental State Examination; IADL, Instrumental Activity of Daily Living; GDS, Geriatric Depression Scale.
Variables are presented as mean (95% confidence interval).

Table 2
Adjusted association between consumption of tomatoes/tomato products and other kinds of vegetables and depressive symptoms [a].

Odds ratio (95% confidence interval)	Tomato and tomato product consumption			*p* for trend[b]
	≤ 1 time (wk)	2–6 times (wk)	≥ 1 time (d)	
Tomatoes and tomato products	–	–	–	–
No. of participants	139	325	522	–
No. of mild and severe depressive symptoms, defined as GDS of ≥ 11 or use of antidepressants	70	111	163	–
Crude	1.00	0.51 (0.34–0.77)	0.45 (0.31–0.66)	< 0.001
Age- and sex-adjusted	1.00	0.49 (0.33–0.74)	0.40 (0.27–0.59)	< 0.0001
Multiple adjusted [c]	1.00	0.54 (0.35–0.85)	0.48 (0.31–0.75)	< 0.01
Green-leaf vegetables	–	–	–	–
No. of participants	188	523	275	–
No. of mild and severe depressive symptoms, defined as GDS of ≥ 11 or use of antidepressants	80	179	85	–
Crude	1.00	0.70 (0.50–0.99)	0.60 (0.41–0.89)	0.01
Age- and sex-adjusted	1.00	0.69 (0.49–0.97)	0.58 (0.39–0.85)	< 0.01
Multiple adjusted [c]	1.00	0.78 (0.51–1.19)	0.72 (0.45–1.15)	0.19
Cabbage and Chinese cabbage	–	–	–	–
No. of participants	200	605	181	–
No. of mild and severe depressive symptoms, defined as GDS of ≥ 11 or use of antidepressants	78	203	63	–
Crude	1.00	0.79 (0.57–1.10)	0.84 (0.55–1.27)	0.37
Age- and sex-adjusted	1.00	0.78 (0.56–1.09)	0.79 (0.51–1.20)	0.24
Multiple adjusted [c]	1.00	1.07 (0.71–1.64)	1.46 (0.85–2.50)	0.18
Carrot, onion, burdock, lotus root and pumpkin	–	–	–	–
No. of participants	102	556	328	–
No. of mild and severe depressive symptoms, defined as GDS of ≥ 11 or use of antidepressants	42	199	103	–
Crude	1.00	0.83 (0.60–1.15)	0.61 (0.41–0.92)	0.02
Age- and sex-adjusted	1.00	0.78 (0.56–1.09)	0.56 (0.37–0.85)	< 0.01
Multiple adjusted [c]	1.00	1.31 (0.77–2.27)	1.34 (0.74–2.45)	0.44
Japanese white radish (daikon) and turnips	–	–	–	–
No. of participants	265	519	202	–
No. of mild and severe depressive symptoms, defined as GDS of ≥ 11 or use of antidepressants	105	178	61	–
Crude	1.00	0.80 (0.59–1.08)	0.66 (0.45–0.97)	0.03
Age- and sex-adjusted	1.00	0.78 (0.57–1.06)	0.61 (0.41–0.90)	0.01
Multiple adjusted [c]	1.00	0.94 (0.65–1.37)	0.70 (0.43–1.13)	0.17

[a] GDS, Geriatric Depression Scale.
[b] Obtained by using multiple logistic regression analysis.
[c] Adjusted for age, sex, BMI, hypertension, diabetes, history of cardiovascular disease, smoking and drinking habits, physical activity, cognitive status, impaired instrumental activities of daily living (IADL), self-reported body pain, educational level, living alone, marital status, lack of perceived social support (PSS), total energy intake, all kinds of fruits, green tea, and mutual other kinds of vegetables.

was observed among tomatoes/tomato products groups (*p* for trend ≥ 0.13).

Table 2 shows the adjusted relationship between tomatoes/tomato products and other kinds of vegetables and mild and severe depressive symptoms. The ORs for mild and severe depressive symptoms decreased across the levels of tomato/tomato product intake. Age- and sex-adjusted ORs (95% CI) for depressive symptoms across tomato/tomato product intake levels were 1.00, 0.49 (0.33–0.74), and 0.40 (0.27–0.59) (*p* for trend < 0.0001). These results were unchanged when adjusted for multiple confounding factors. Similar relationships were also observed when males and females were analyzed separately (*p* for interaction=0.08). Of the other covariants, smoking/drinking status and educational level were related with depressive symptoms. The tests for interactions between the categories of tomato/tomato product intake and these potential confounders in the final models were not found to be significant. Furthermore, because depressive status is also related to unhealthy eating habits and appetite (Andreasson et al., 2007; Cassano and Fava, 2002), a sensitivity analysis was added to assess the relationship between tomatoes/tomato products and depressive symptoms, excluding those who had very low (under 2.5%) or high (upper 2.5%) energy intake. However, this exclusion did not change the

above results. Similar results were also observed when a cut-off of ≥ 14 or the use of antidepressants was used to indicate severe depressive symptoms. In the final model, the ORs (95% CI) for severe depressive symptoms across tomato/tomato product intake levels were 1.00, 0.64 (0.39–1.08), and 0.60 (0.37–0.99). In contrast to tomato/tomato product intake, no relationship was observed between intake of other kinds of vegetables and the prevalence of depressive symptoms (Table 2). Similar results were also observed when a cut-off of ≥ 14 or the use of antidepressants was used to indicate severe depressive symptoms (data not shown).

4. Discussion

This study examined the relationship between the intake of various vegetables, including tomatoes/tomato products, a main source of lycopene, and depressive symptoms among a community-dwelling elderly population aged 70 years and over. These results suggest that a high intake of tomatoes/tomato products was independently related to a lower prevalence of depressive symptoms. In contrast to tomato/tomato product intake, no relationship was observed between intake of other kinds of vegetables and depressive symptoms.

In this study, we have hypothesized that the intake of tomatoes/ tomato products may have a potentially beneficial effect on the prevention of depressive symptoms. Although several studies have investigated the relationship between dietary antioxidant nutrients, such as folic acid and vitamin E, and depressive symptoms, few studies have reported the relationship between intake of tomatoes/ tomato products and depressive symptoms (Alpert et al., 2000; Maes et al., 2000; Miyake et al., 2006; Shibata et al., 1999; Tsuboi et al., 2004). Only one study has assessed the correlations between serum lycopene and depressive score, in subjects consisting of 66 healthy female volunteers aged 38–70 years (Tsuboi et al., 2004). However, in that study, many confounding factors were not considered and the results have not suggested a significant correlation between lycopene and depressive score. In this larger community-based population study we adjusted for a considerable number of confounding factors. The current results suggest that high tomato/ tomato product intake levels are independently related to a lower prevalence of depressive symptoms. Moreover, we also conducted a stratified analysis for sex. Similar relationships were also observed when males and females were analyzed separately.

Lycopene is the red-colored carotenoid predominantly found in tomatoes, but in few other fruits or vegetables (Bramley, 2000). Lycopene has the strongest antioxidant activity of various common carotenoids (Di Mascio et al., 1989). Oxidative stress may accelerate aging and increase the risk of chronic diseases, such as coronary heart disease, cancer, and rheumatoid arthritis; dietary intake of tomatoes/tomato products containing lycopene have been shown to be related to decreased risk of these chronic medical illnesses (De Pablo et al., 2007; Heber and Lu, 2002). Since these chronic medical illnesses are also related to the occurrence of depressive symptoms, particularly in elderly people, the presence or degree of these chronic medical illnesses may be a potential mechanism linking intake of tomatoes and tomato products to depressive symptoms. Furthermore, since enhanced oxidative stress or defective antioxidant defenses may be related to depressive symptoms, lycopene may directly link tomato and tomato product intake to depressive symptoms because of their anti-oxidative effect. Further study is needed to confirm these findings.

In the present study, lycopene concentration from tomatoes/ tomato products was not calculated. In fact, food frequency questionnaires generally used in epidemiological studies vary greatly in their usefulness in estimating the true variation in lycopene intake among individuals. A review indicated that dietary intake of tomato/ lycopene is difficult to quantify precisely for several reasons: different food habits, inaccurate estimation of dietary intake, the quality of the food database used, and variation of lycopene concentration within a given food (Porrini and Riso, 2005). Moreover, since lycopene is predominantly found in tomato and tomato-based products (at least 85%) (Bramley, 2000), but only in a few other fruits or vegetables (e.g., watermelon, pink grapefruit, guava, and papaya), the frequency of eating tomatoes/tomato products was used to assess the relationship between tomatoes/lycopene and depressive symptoms in this study.

This study had several limitations. First, the GDS has been designed for measuring the intensity of depressive symptoms and not for making a clinical diagnosis of depressive episodes. Therefore, a larger sample population using a standardized comprehensive structured diagnostic interview should be studied to confirm the effect of depressive symptoms on functional decline. Second, because this study was a cross-sectional study, we could not conclude that lower tomato and tomato product intake increased the occurrence of depressive symptoms or that depressive symptoms lead to a decline in tomato/tomato product intake. Therefore, a prospective study or trial should be undertaken to confirm the relationship between tomato/tomato product intake and depressive symptoms. Moreover, although we adjusted for a considerable number of confounding factors, we cannot exclude the possibility that depressive symptoms are affected by other dietary habits correlated with habitual dietary intake of tomatoes/tomato products. Therefore, an intervention study is necessary to establish a causal relationship between tomato/tomato product intake and depressive symptoms.

In conclusion, this study demonstrated that the intake level of tomatoes/tomato products, as measured by a self-administered questionnaire, is independently related to a lower prevalence of depressive symptoms in a community-dwelling older population. These results suggest that a tomato-rich diet may have a beneficial effect on the prevention of depressive symptoms. Further studies are needed to confirm these findings.

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