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Original Communication

Dietary intake of tryptophan tied emotion-related impulsivity in humans

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Abstract: Emotion-related impulsivity, defined as the tendency to say or do things that one later regret during periods of heightened emotion, has been tied to a broad range of psychopathologies. Previous work has suggested that emotion-related impulsivity is tied to an impaired function of the serotonergic system. Central serotonin synthesis relies on the intake of the essential amino acid, tryptophan and its ability to pass through the blood brain barrier. *Objective:* The aim of this study was to determine the association between emotion-related impulsivity and tryptophan intake. *Methods:* Undergraduate participants (N = 25, 16 women, 9 men) completed a self-rated measure of impulsivity (Three Factor Impulsivity Index, TFI) and daily logs of their food intake and exercise. These data were coded using the software NutriNote to evaluate intakes of tryptophan, large neutral amino acids, vitamins B6/B12, and exercise. *Results:* Correlational analyses indicated that higher tryptophan intake was associated with significantly lower scores on two out of three subscales of the TFI, Pervasive Influence of Feelings scores $r = -.502$, $p < .010$, and (lack-of) Follow-Through scores, $r = -.407$, $p < .050$. *Conclusion:* Findings provide further evidence that emotion-related impulsivity is correlated to serotonergic indices, even when considering only food habits. It also suggests the need for more research on whether tryptophan supplements might be beneficial for impulsive persons suffering from a psychological disorder.

Keywords: Tryptophan, serotonin, diet, impulsivity, emotion

A large body of work indicates that impulsivity is an important predictor of various psychopathologies [1–4]. Nonetheless, it has been increasingly recognized that impulsivity is not a unitary construct, but consists of more multiple, statistically distinguishable facets [5–7]. For example, the Barratt Impulsiveness Scale evaluates different aspects of attentional, motor and non-planning impulsivity [5]. Other scales also consider sensation seeking, difficulty delaying gratification, and poor ability to persevere on difficult tasks [6]. Researchers have also identified a form of impulsivity that occurs specifically during periods of heightened emotion [6–8], defined as the tendency to say and do things that one later regrets [6, 7]. Compared with other forms of impulsivity, emotion-related impulsivity has been found to be more robustly associated with a broad range of psychopathologies including bipolar disorder, borderline personality disorder, post traumatic stress disorder, and major depressive disorder [1, 3, 4, 7].

Previous findings have shown that forebrain serotonin (5-hydroxytryptamine; 5-HT) depletion is related to higher impulsivity level in rodents [9]. In both animal and human models, emotion-related impulsivity has been tied to genetic polymorphisms relevant to serotonergic function [7, 10]. Research has also linked many of the psychological disorders related to this form of impulsivity to serotonergic system impairment [7, 11–13]. Despite the early promising work, no research to date has examined whether emotion-related impulsivity could be tied to current function of the serotonergic system in healthy humans.

Synthesis of 5-HT depends on the availability of the amino acid (AA) precursor, tryptophan (TRP). TRP is an essential AA, meaning it is derived from dietary proteins rather than being synthesized by the human body. TRP is found in almost all proteins but in much lower quantity than other large neutral AAs (LNAAs). Research has shown that saliva, urine, and cerebrospinal fluid 5-Hydroxyindolacetic acid levels (a 5-HT metabolite) can be modestly increased by a specific high TRP diet that includes foods such as soybeans, pumpkin seeds, whole eggs [14–16]. Preliminary studies have shown that increasing intake of TRP via pharmacological or dietary interventions are associated with cognitive and mood benefits [14, 17–19]. These behavioural effects might be explained by an increase of peripheral and central 5-HT synthesis but also by an increase of

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neurotrophic factors (BDNF and IGF-1) acting on neurogenesis and plasticity [20, 21]. Experimentally induced reduction of TRP in healthy subjects has been found to trigger increases in impulsivity-related symptoms [22]. In addition, experimental TRP supplementation has been shown to decrease impulsivity associated symptoms [17, 19, 23]. However, despite the growing body of serious findings from experimental TRP supplementation and depletion, the relationship of naturally occurring dietary TRP intake with emotion-related impulsivity has not been investigated. To be able to realize such analysis, a broad range of covariates influencing 5-HT synthesis and release should be evaluated. For instance, vitamins B (co-factors of TRP to 5-HT conversion) consumption should be assessed [24, 25]. Furthermore, exercise influences the serotonergic function and should also be controlled. In essence, exercise stimulates the catabolism of brain chained AAs (isoleucine, leucine and valine) during and shortly after exercise, with resultant increase in 5-HT synthesis [13, 26, 27]. Moreover, regular exercise has been shown to enhance the 5-HT release in the synaptic cleft by serotonergic neurons [26, 27].

In order for TRP to be transformed into 5-HT inside the brain, it must cross the blood brain barrier [14, 23, 28, 29], a process that depends on the large AA transporter (LAT1) [23, 24]. TRP competes with other LNAAs (such as valine, tyrosine [TYR], phenylalanine [PHE], leucine and isoleucine) to use LAT1 [22, 23, 28, 30] such that combined increases in these other LNAAs in the plasma can diminish availability of the transporters. Because of this competition among the LNAAs, a simple increase of high TRP foods consumption is not sufficient to improve behavioural outcomes such as mood in humans. Indeed, high TRP foods are also rich in LNAAs and so greater intake of those foods is not sufficient to change the competition for the blood brain barrier transporters. Rather, the ratio of TRP to other LNAAs in the diet has been shown to be more influential [14, 22, 28, 30].

Beside this, impulsivity has long been related to low levels and function of catecholamines [31, 32] and more specifically with dopamine in the prefrontal cortex [33]. As in TRP metabolism, TYR and PHE use LAT1 to pass across the blood brain barrier; accordingly, AAs that serve as catecholamines (TYR and PHE) should also be considered.

Drawing on this work, we investigated in this study the relationship between the ratio of dietary intake of TRP/LNAAs compared with emotion-related impulsivity in healthy participants. The hypothesis of this study was that greater naturalistically-occurring dietary intake of TRP would be correlated to lower emotion related impulsivity levels. In doing so, we considered the potential confounders of several variables known to influence serotonergic function: exercise, B vitamins intake, competitive AAs, PHE and TYR.

Materials and methods

All procedures were approved by the University of California, Berkeley Institutional Review Board before data collection commenced and were carried out in accordance with the Declaration of Helsinki. All participants completed written informed consent procedures before taking part in the study.

Participants and Procedure

Twenty-five participants (16 women and 9 men) completed this pilot study and were included in analyses. The participants had a mean age of 21 years (SD = 1.92), a mean height of 166.4 cm (*SD = 9.80*), a mean weight of 63.2 kg (*SD = 9.36)*, and a mean body mass index of 22.8 kg/m^2 (*SD = 2.10*).

Students received credits in their undergraduate psychology courses for participation in the study. Potential participants completed an initial informed consent process, and a set of items to verify inclusion/exclusion criteria via a secure Qualtrics survey. Inclusion/exclusion criteria were guided by the goal of reducing individual variability in serotonergic function [34, 35]. Given the evidence that 5-HT synthesis is also blunted by sleep disruption, alcohol use, nicotine, and positively or negatively impacted by specific drug use (e.g. ecstasy) [23, 24], we also excluded individuals who endorsed significant sleep disruption, heavy alcohol or nicotine use, or use of illegal drugs. Inclusion criteria included: age of 18 to 36 years (to avoid age influence in regards of the body energy demand and of participants' proteinogenic character) and body mass index of 18.5 – 24.9 kg/m^2. Exclusion criteria included antidepressant use in the past 3 months [36]; medical condition or psychological disease diagnosed by clinicians, use of any prescription drug (apart from contraceptives), use of illegal drugs, heavy tobacco use (more than one cigarettes pack or 20 cigarettes per day), heavy alcohol use (>210 g/week for women and >280 g/week for men), night shift work during the study period, pregnancy, less than 6 hours of sleep per night on average during the past month, and being an elite athlete. Of the 632 individuals who took the online screening questionnaires, 285 met study criteria and received an email inviting them to take part in the study. Of these, 27 expressed an interest in joining the study and were invited to an initial session. At that session, participants completed written informed consent procedures. Participants consuming dietary supplements were not excluded; rather dietary supplement were recorded as part of food logs.

During the first in-person session, participants received training in how to complete a daily food log. Then, participants were asked to record their food, drink, alcoholic

beverages, and exercise for six days. They were given a choice of when to begin the food recording. They were advised to avoid weeks that would interfere with regular dietary intake patterns such as weddings, graduation, birthday etc. To assess potentially different eating patterns between the week and the weekend, they were required to record diet and exercise for one weekend day.

We controlled the influence of physical activity by recording exercise time and intensity. At the end of the week, participants were asked to return the food and physical activity logs to the research office and to complete the Three Factor Impulsivity index (see section "Three-Factor Impulsivity Index"). Two participants did not complete measures after the first appointment. Participants were removed from the study.

Measures

Three-Factor Impulsivity Index [7]

The Three Factor Impulsivity (TFI) index is a well-validated 54-item composite self-report measure of multiple dimensions of impulsivity [7]. The questionnaire covers 11 components of impulsivity that have been shown in factor analysis to load on three separate subscales [7]. Most items are rated from 1 ("I disagree a lot") to 5 ("I agree a lot"). The three different factor subscales are labelled Pervasive Influence of Feelings, (lack of) Follow-Through and Feelings Trigger Action. Items on the second factor, (Lack of) Follow-Through, cover issues such as lack of perseverance and distractibility that are not emotion related. The first and the third factor are emotion-related. Pervasive Influence of Feelings covers how (mostly negative) emotions tend to shape thoughts and motivations. Feelings Trigger Action covers impulsive speech and behaviour in response to positive and negative emotions. Whereas Pervasive Influence to Feelings is robustly tied to depression and suicidal ideation, Feelings Trigger Action is more directly tied to externalizing disorders, manic tendencies, and suicidal action [37]. Factor scores were constructed using the rotated factor weights published in the validation article [7]. Higher scores reflect more impulsivity. All scales were standardized to z-scores for ease of comparison and interpretation within the pre-screening sample. Internal consistency was good for the Feelings Trigger Action (Cronbach's $\alpha = 0.791$), (lack of) Follow-Through (Cronbach's $\alpha = 0.886$), and Pervasive Influence of Feelings (Cronbach's $\alpha = 0.899$). TFI factors have been shown to be related to a polymorphism of the 5-HT transporter gene, to early adversity and to both internalizing and externalizing syndromes [7, 38, 39]. The subscale Feelings Trigger Action, considered as the main emotion-related factor was used as a pre-screening tool to recruit individuals of varying impulsivity levels. The hypotheses, however, focused on both emotion-related subscales—Feelings Trigger Action and Pervasive Influence of Feelings. Consistent with validation work, these two emotion-related factors, were highly correlated, $r = .501; p < .011, N = 25$ among our participants [7]. Lack of Follow-Through was also significantly related to Pervasive Influence of Feelings, $r = .639$, $p < .001$, $N = 25$, and not significantly related to Feelings Trigger Action, $r = .187$; $p = .371$, $N = 25$.

Daily Diet and Activity Log

Participants recorded on paper the type and quantity of food consumed, and cooking methods for those foods (e.g., fried with canola oil, baked). Data were extracted and coded using NutriNote software professional version (from Nutriworx Juergen Abeln, Cologne, Germany). NutriNote software was used to code intake of LNAAs and other nutrients consumed on each of the 6 full days logged. These LNAAs intake estimations were calculated as the average daily milligram of intake per kilogram of body mass. Nutrinote software uses the United States Department of Agriculture database that provides levels of 131 nutrients for over 7500 foods. Because many natural protein sources provide a full range of essential AAs, the levels for all LNAAs were highly intercorrelated, all $r's > .968$, $p's < .001$; $N = 25$. For analysis, TRP levels were divided by the intake of all other LNAAs (Table 1); this ratio score has been validated as more predictive of central nervous system levels than a non-ratio score [22, 25, 28]. Key variables were the mean (across 6 days) TRP/LNAAs, with secondary analyses of (TYR + PHE)/LNAAs; these two variables showed a correlation of $.726$, $p < .001$, $N = 25$.

On the first daily log, participants were asked if they were vegan or vegetarian; one participant reported being vegan. On their last food log (day 6), participants were asked if they considered the study week typical in terms of physical activity and food consumption. Four participants reported modest differences between their food log and their usual eating pattern.

Participants also logged the time and the type of athletic activities they practiced. Scores were logged using the NutriNote software. Because participants practiced different types of sports with distinct intensities, exercise levels were coded using the Metabolic Equivalent of Task (MET), MET is a physiological measure of the energy cost of physical activity, calculated as the rate of energy consumption during a specific physical activity to a reference metabolic rate (set by convention to 3.50 ml O_2. kg^{-1}. min^{-1}) [40]. Moderate intensity exercise is defined by MET scores of 3 to 6 (e.g. cycling <16 km/h for a recreationally active man), and high intensity exercise is defined by MET scores of 6 and higher (e.g. high intensity running <16 km/h for a recreationally active man) [40]. Total

Table 1. Participants' LNAAs and Vitamins B intakes, physical exercise reports and Three Factor Impulsivity Index scores (N = 25). Means, minimum, maximum, standard deviation, kurtosis and skewness are presented for each variable

	Minimum	Maximum	Mean	Standard deviation	Skewness	Kurtosis
Pervasive Influence of Feelings	−4.85	4.46	.31	2.53	−.68	−.33
(Lack of) Follow-Through	−4.72	5.48	−.31	2.96	.44	−.55
Feelings Trigger Action	−1.94	2.38	.06	1.16	.17	−.76
Daily TRP intake (mg/kg)	8.39	23.68	13.38	4.18	1.22	.75
Daily PHE intake (mg/kg)	33.95	92.38	53.45	16.58	1.22	.66
Daily TYR intake (mg/kg)	24.60	74.56	40.00	13.60	1.22	.99
Daily Valine intake (mg/kg)	38.77	112.19	60.46	20.62	1.43	1.53
Daily Leucine intake (mg/kg)	58.64	173 .38	93.20	31.46	.46	.90
Daily Isoleucine intake (mg/kg)	32.08	102.08	53.91	18.74	1.45	1.78
TRP/LNAAs	.039	.060	.045	.004	1.64	4.43
(TYR + PHE)/LNAAs	.397	.578	.436	.043	2.24	5.26
Vitamin B6 (mg/day)	2.02	181.50	19.88	44.52	3.31	9.99
Vitamin B12 (mg/day)	.75	6.69	2.23	1.34	1.95	4.36
Total time of moderate exercise: 3MET < X < 6MET (min)	0	820	126.60	200.62	2.28	5.39
Total time of vigorous exercise: >6MET (min)	0	840	81.80	184.59	3.41	12.54
Total exercise time (min)	0	840	208.4	240.07	1.59	1.90[1]

[1]TRP: Tryptophan; PHE: phenylalanine; TYR: Tyrosine; LNAA: large neutral amino acid; MET: Metabolic equivalent of task.

exercise times at moderate and high intensities, as well as total time were summed across the logged days.

Statistical analyses

All statistical analyses were conducted using SPSS software, version 23.0 (IBM, Armonk, New York). The distribution of each variable was evaluated with the test of Shapiro-Wilk. A logarithmic correction was applied when required. Spearman (non-parametric) and Pearson (parametric) correlations were used to evaluate links between variables. Partial correlation was conducted controlling for variables that were significantly related to impulsivity and/or AA ratio scores. All tests were two-tailed. As we considered three impulsivity factors, a Bonferonni correction was applied to the α ($.05/3 = .017$). Post experiment power analysis was realised using the software GPower 3.1.9.2 (A. Buchner, E. Erdfelder, F. Faul, A.G. Lang)

Results

Means, variability, kurtosis, skewness and distributions for all key variables were reviewed before conducting tests of hypotheses (Table 1).

Analyses of Possible Confounds

Correlations were conducted to examine whether the significant correlation between TRP/LNAAs ratios and the impulsivity scores, was confounded with gender, age (despite the limited range [*21 ± 2 years*]) weight, vitamin B6 intake, vitamin B12 intake or levels of activity with 3 to 6 MET and higher than 6 MET. TRP ratios were not significantly related to gender, age, weight, vitamin B12 and B6 intake, vitamin C intake or moderate and vigorous physical activity (Table 1), all $r's < |.178|$, *all* $p's > .524$, $N = 25$. The same 8 confounds were considered in relation to impulsivity scores. All covariates were not correlated to impulsivity scores, $r's < |.300|$, *all* $p's > .170$, $N = 25$.

Table 2. Bivariate Spearman correlation of amino acid ratio scores with the impulsivity scores (N = 25)

	TRP/LNAAs	(TYR + PHE)/LNAAs
Pervasive Influence of Feelings	−.502**	.052
(Lack of) Follow-Through	−.407*	−.135
Feelings Trigger Action	−.115	−.174

*$p < .050$; **$p < 0.010$.

Tests of Hypotheses

As shown in Table 2, higher TRP/LNAAs ratios were significantly related to lower Pervasive Influence of Feelings scores $r = -.502$, $p < .010$, and (lack-of) Follow-Through scores, $r = -.407$, $p < .050$. Further analysis revealed the existence of an outlier (TRP/LNAA = .060) that once excluded of the analysis strengthened the correlation with Pervasive Influence of Feelings scores $r = -.540$, $p < .010$ and decreased the correlation with (lack-of) Follow-Through score, $r = .401$, $p = .051$ (Figure 1). After alpha

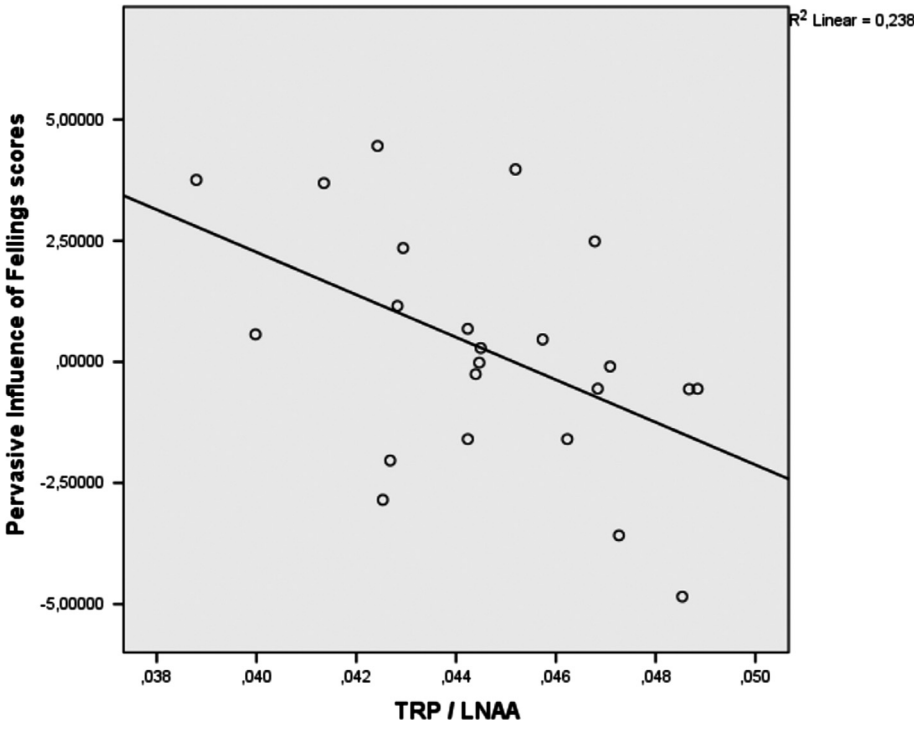

Figure 1. Dots plot of the ratio of TRP/LNAA and the Pervasive Influence of Feelings scores (N = 24).

correction the first factor remained significantly correlated with the TRP/LNAAs ratio (Figure 1). The Feeling Trigger Action scores were not correlated with the AA intakes.

Secondary analyses indicated that (TYR + PHE)/LNAAs ratio was not significantly correlated to any of the three impulsivity scores (Table 2).

Discussion

Given the broad evidence that TRP is related to both mood and impulsivity, the current study aimed to examine how naturalistically occurring variations in dietary intakes of TRP and LNAAs assessed via a six-day food diary might be associated to emotion-related impulsivity. Our findings provided support for our hypotheses in that the daily average intake TRP in ratio to other LNAAs was correlated to one form of emotion-related impulsivity, Pervasive Influence of Feelings (Figure 1). However, in healthy humans our results suggest that only a non-significant trend with the other form of emotion-related impulsivity (Feelings Trigger Action). The effects of TRP/LNAAs ratio appeared to be relatively specific, in that dietary intake of the catecholamine precursors, TYR and PHE ratio did not relate to impulsivity.

One question is why dietary TRP/LNAAs ratio was correlated significantly with the Pervasive Influence of Feelings, but not with the Feelings Trigger Action scale. Although this differentiation of the two impulsivity scales was not predicted, the first scale covers difficulties with negative emotions guiding thought and motivation, and has been more closely tied to depression [1, 7]. This coincide with findings linking depression to poor serotonergic function [12, 24, 30].

The current study is distinguished by the careful assessment of a number of potentials confounds. Although participants showed relatively little variability on many of these characteristics (likely limiting any downstream effects on impulsivity), total physical activity was tied to dietary intake patterns. None of the confounders assessed statistically explained the effects of TRP/LNAAs ratio on impulsivity shown in this investigation.

Emotion-related impulsivity is a distinct form of impulsivity linked with a broad range of psychopathology [1, 3, 4, 7]. Although research has shown that this form of impulsivity is related to a polymorphism of the 5-HT transporter gene [7], no previous research had considered how this form of impulsivity related to other indices of 5-HT. Our preliminary results showing a correlation of higher emotion-related impulsivity with lower dietary intake of TRP in healthy humans are encouraging.

Several limitations are important to consider in this study. Of most importance, all participants consumed levels of AAs, including TRP, that exceeded intake guidelines set by the World Health Organization (WHO) by at the least

50 percent [41]. These limits are understanding of how deficits in AA intake might influence impulsivity. It is important to note that WHO recommendations on needs have been established to satisfy nitrogen and energy balances without regard to behavioural outcomes [41]. In addition, dietary intake levels are only one component of healthy serotonergic function. For example higher cerebrospinal TRP levels do not always yield more 5-HT release [13, 24, 29]. Synthesis and release are distinct processes that are not necessarily correlated. Moreover, we were not in a position to consider complex interactions of dietary intake on multiple neurotransmitter systems. All monoamines have a common final rate-limiting enzyme (aromatic AA decarboxylase) [25, 29]. Therefore, a major increase of TRP might elevate 5-HT level but decrease the level of catecholamines [42].

Even at the level of uptake into the body, TRP and LNAAs intake levels may not be closely correlated with plasma levels for several reasons. Firstly, there is a potential error existing between the food reported in the diary (or the way it is reported) and the TRP and LNAAs levels assessed. This error has been evaluated going up 14% of underreport when considering the energy intake [43, 44]. Secondly, the absorption of AAs by the intestine depends on protein quality and on the meal composition [22, 30]. Thirdly, some of the TRP absorbed by the intestines is bound to albumin and does not pass through the blood brain barrier[13, 24]. Fourthly, the conversion of TRP to 5-HT also relies on a number of factors, including free fatty acid levels, competitive AAs concentration, TRP hydroxylase saturation and aromatic AA decarboxylase saturation [13, 18, 24, 28].

Beyond the lack of plasma measures, this pilot study included only 25 participants. Adequate power (*.90*) to detect moderate effect size, $r = .40$, would typically require 58 participants (*Actual power: .904*). Given the small sample size and that diary food records provide only a rough approximation of AA plasma levels, dietary logs of TRP intake were bound to our impulsivity index. It is important to remember that the reliance on an undergraduate sample with small age variability restricts our conclusions to a specific population subset.

Notwithstanding the limitations, these preliminary findings suggest several goals for future research. We would recommend incorporation of behavioural indices of impulsivity [8]. Previous work has shown that early adversity, which was not considered here, may amplify the effects of 5-HT related genetic polymorphisms on impulsivity [7], and early adversity could be included in building a more integrative model.

Future research should consider forms of diet as a potential influence of impulsivity, including vegan and vegetarian diets that might promote a higher TRP ratio [45]. Experimental research using TRP supplements is also recommended, as this research would more directly change the TRP balance which has been shown to have few side effects [17, 46–48].

The serotonergic system is complex, with effects throughout the whole brain and multiple interactions with other neurotransmitters systems [12, 13, 49]. Deciphering those effects with Positron Emission Tomography indices of 5-HT would be warranted if current findings replicate.

Conclusion

In summary, findings of the current study suggest that dietary intake of TRP, assessed using a 6-day food diary in undergraduate students is tied to lower levels of one form of emotion-related impulsivity (Pervasive Influence of Feelings). This relationship was independent of medical disease, medication, exercise, vitamin, or other lifestyle factors controlled through exclusion criteria or statistical analysis. Despite limitations, the findings are relying on self-reports instead of biological tests, it agrees with previous research suggesting that polymorphisms related to 5-HT also relate to this form of impulsivity. This suggests the importance of future research on dietary manipulations, as well as neurobiological research on 5-HT. If these findings can be replicated and generalized with larger samples and more refined methods, this has important implications, given that this form of impulsivity has been related to a very broad range of psychopathology syndromes, to aggression, and to suicide. To date, treatments do not appear to be available to directly target this form of impulsivity. Taken together, the current work suggests the promise of ongoing work on the role of 5-HT in impulsivity.

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Conflict of interest
The authors declare that there are no conflicts of interest.

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