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What is This?

Cultural Differences in the Link Between Supportive Relationships and Proinflammatory Cytokines

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Abstract

Research suggests that inflammation may partially mediate the link between supportiveness of social relationships and physical health. However, cultural differences between Asians and European Americans in the nature of relationships and in seeking social support suggest that there may be cultural differences in the relation between supportive relationships and proinflammatory activity. One hundred and twenty-one young adult participants completed assessments of support from their close relationships (parents, romantic partner, and close friends) and provided oral mucosal transudate samples for assessment of the proinflammatory cytokines interleukin-6 (IL-6) and the type II soluble receptor for tumor necrosis factor- α (sTNF α RII). As predicted, more supportive relationships were related to lower levels of IL-6 among European Americans, but not among Asian Americans. There were no relations to sTNF α RII in either group. We conclude that associations between supportive relationships and inflammatory activity may differ in ways that reflect cultural differences in the construal of relationships and social support.

Keywords

relationships, culture/ethnicity, social support, close relationships, relational factors in health

Humans are social beings and have a need for and are motivated to maintain their social relationships (Baumeister & Leary, 1995). Extensive research documents links between social relationships and physical health. For instance, social isolation and conflict predict higher mortality, whereas social support and social integration predict lower mortality (Berkman & Syme, 1979; Cohen, 2004; Cohen, Doyle, Skone, Rabin, & Swaltney, 1997; De Vogli, Chanodola, & Marmot, 2007; House, Landis, & Umberson, 1988; Kaplan et al., 1988). Having few or less supportive social relationships increases susceptibility to developing disease and is tied to poorer prognosis for existing conditions, such as cardiovascular disease, atherosclerosis, and cancer (Ertel, Glymour, & Berkman, 2009; Everson-Rose & Lewis, 2005; Uchino, 2006). However, the overwhelming majority of these studies have been conducted without consideration of culture, despite the fact that there are well-established cultural differences in the nature of relationships (e.g., Adams & Plaut, 2003; Schug, Yuki, & Maddux, 2010).

Specifically, European Americans construe their supportive relationships as a resource on which they can draw in stressful times. As such, supportive relationships have been consistently found to buffer biological responses to stress among European Americans (Uchino, 2006). Asian Americans, by contrast, are focused on maintaining interconnectedness and social harmony (Heine, 2001; Kim, Sherman, & Taylor, 2008; Taylor et al.,

2004); consequently, they do not extract support from their relationships because they fear disrupting group harmony, burdening others, and losing face (Kim, Sherman, Ko, & Taylor, 2006; Taylor et al., 2004). When facing a stressor, Asians and Asian Americans, compared to European Americans, seek less emotional and informational support, and find support, even from their close ties, to be less effective (Taylor, Welch, Kim, & Sherman, 2007). When important relationships are made salient, Asians and Asian Americans' likelihood of explicitly seeking social support declines (Kim et al., 2006). As a result, relationship closeness does not predict social support provision among Asians, whereas it significantly predicts support provision among European Americans (Chen, Kim, & Sherman, under review). These differences in cultural construals of relationships and social support suggest that relationship supportiveness among Asian Americans may not be linked to health biomarkers and outcomes as strongly as in European American samples. To test this idea, we examined the link between

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perceived supportiveness of close relationships and biological markers of inflammation, a critical biological marker of stress, in European and Asian Americans.

Inflammation is a natural immune response that fights infections and injuries and, as such, is adaptive in the short term. In the longer term, however, inflammation has been implicated in a number of chronic diseases, including diabetes and heart disease (Cesari et al., 2003; Ridker, Rifai, Stampfer, & Hennekens, 2000; Wellen & Hotamisligil, 2005). As such, inflammation may be an important pathway that links relationships to health outcomes. Consistent with this argument, low levels of social support, few social ties, and high levels of social negativity have been related to higher levels of inflammatory activity, including interleukin (IL)-6 and C-reactive protein, a marker of IL-6 activity (Chiang, Eisenberger, Seeman, & Taylor, 2012; Constanzo et al., 2005; Coussons-Read, Okun, & Nettles, 2007; Friedman et al., 2005; Fuligni et al., 2009; Kiecolt-Glaser, Gouin, & Hantsoo, 2010; Miller, Rohleder, & Cole, 2009; Taylor, Lehman, Kiefe, & Seeman, 2006).

The present study examined the association between supportiveness of close relationships (close friends, romantic partner, mother, and father) and levels of the proinflammatory markers IL-6 and the type II soluble receptor for tumor necrosis factor- α (sTNF α RII). Based on previous work showing cultural differences in construals of relationships and social support processes during times of stress, we hypothesized that supportive relationships would be associated with lower levels of proinflammatory cytokine in European Americans, but not in Asian Americans.

Method

Participants

Posters offering \$120 for participation in the study were posted at a large university to recruit participants. Respondents were screened to determine eligibility. Exclusion criteria included: having any major mental or physical health condition, taking any mental health, cardiovascular or neuroendocrine-related medications, and being pregnant and/or lactating. The final sample included 121 students and employees (53 men and 68 women), of whom 38.0% self-identified as European American and 62.0% self-identified as Asian American. Among the Asian Americans, 54 participants were born in the United States and 21 were born in Asia. With respect to family's country of origin, about 61% were of a single ethnicity, 19% were mixed, and 29.3% did not specify a specific country of origin. All participants provided informed written consent.

Procedure

Participants reported to the university's General Clinical Research Center in the afternoon to control for the diurnal rhythm of inflammatory activity. Participants were asked to abstain from eating, exercising, and consuming caffeine an hour before the laboratory session. Upon arrival, information on health status and behaviors (i.e., smoking habits, alcohol and

caffeine consumption, and exercise) that have been shown to influence proinflammatory markers was collected. The Beck Depression Inventory (BDI; Beck, Ward, Mock, & Erbaugh, 1961) was also administered, as depression has been related to elevated inflammation (Miller, Freedland, Carney, Stetler, & Banks, 2003). After a 10-min baseline period, oral mucosal transudate (OMT) was collected. Participants completed subsequent tasks that are not a part of the present study.

Relationship Assessment

Support from partner, close friend, mother, and father was assessed using an 8-item reliable and valid measure (Schuster, Kessler, & Aseltine, 1990) that has been widely used in previous studies. Using a 7-point scale $(1 = not \ at \ all, 7 = a \ lot)$, participants indicated: "How much does your partner/mother/ father/close friend understand the way you feel about things?" "How much do they really care about you?" "How much can you rely on them for help if you have a serious problem?" "How much can you open up to them if you need to talk about your worries?" "How often do they make too many demands on you?" "How often do they criticize you?" "How often do they let you down when you are counting on them?" and "How often do they get on your nerves?" A composite of support from each relationship was formed by averaging the scores of the 8 items after reverse scoring the negatively worded items. An index of supportive relationships was created by averaging the composite scores from mother, father, and close friend. Support from partner was not included, given that fewer than half the participants (n = 54) reported having a romantic partner. There was high internal reliability of all the items inquiring about father, mother, and close friend for both European Americans ($\alpha = .826$) and Asian Americans ($\alpha = .718$).

Inflammatory Activity

Proinflammatory cytokine levels were assessed using OMT, a filtrate of blood plasma that was used in previous studies assessing stress-related inflammatory activity (Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004; O'Connor, Irwin, & Wellisch, 2009). An Orasure collective device was used to collect OMT. Participants placed a pad between their lower cheek and gum for 2 min and then placed the pad into the accompanying vial for storage.

OMT samples were assayed for IL-6 and sTNFαRII at the Center for Interdisciplinary Research in Immunology and Disease at the University of California, Los Angeles. The IMx automated microparticle enzyme immunoassay system was used for IL-6 and the Quantikine Human sTNFαRII enzyme immunoassay kit by R&D Systems was used for sTNFαRII. The inter- and intra-assay coefficients of variation for sTNFαRII were less than 4.1 and 7.5%, respectively, and less than 9 and 3.3%, respectively, for IL-6. The Bradford method using the Bio-Rad protein assay kit with bovine plasma albumin as the standard was used to quantify protein in the oral fluids collected. IL-6 and sTNFαRII results are reported using

Table 1. Descriptives for Supportive Relationships and Inflammatory Levels

Variable	М	SD	Range
Supportive relationships	5.074	.906	1.58–6.96
Body mass index	22.083	2.729	16.78-34.44
Depressive symptomatology	1.272	.246	I-2.40
Baseline cortisol	.149	.121	.01–1.18
Perceived stress	5.692	.559	1.60-4.40
Multiple Ability Self-Report Questionnaire trait anxiety	1.952	.360	1.06-3.08
Interleukin-6 (pg/ml)	2.301	3.487	.069-26.671
Soluble receptor for tumor necrosis factor- α (pg/ml)	17.842	14.932	1.04-86.34

Table 2. Mean Differences in Supportive Relationships and Proinflammatory Cytokines by Cultural Group

	European	Americans		Asian America	ns
	М	SD	М	SD	t
Supportive relationships	5.350	.777	4.900	.942	2.743**
Body mass index	22.633	2.715	21.746	2.699	1.750
Depressive symptomatology	1.162	.160	1.339	.265	-4.565**
Baseline cortisol	.131	.070	.159	.142	-1.230
Perceived stress	2.492	.529	2.821	.545	-3.254**
Trait anxiety	1.776	.290	2.053	.361	-4.398**
Interleukin-6 (pg/ml)	1.880	1.839	2.557	4.182	-1.222
Soluble receptor for tumor necrosis factor- α (pg/ml)	20.377	16.130	16.287	14.031	1.422

Note. **p < .01.

analyte-to-protein ratios, as they control for differences in salivary flow rate and are therefore more reliable than analyte values alone (Dickerson et al., 2004).

Results

Preliminary Analyses

As shown in Table 1, participants reported generally high levels of support from their close relationships, relatively low levels of perceived stress as indicated by the Perceived Stress scale (Cohen, Kamarck, & Mermelstein, 1983), and relatively low levels of depressive symptoms, as measured by the BDI (Beck et al., 1961). European Americans and Asian Americans reported significant differences in the perceived availability of support from their central ties (Table 2), with European Americans reporting more support than Asian Americans. The groups significantly differed in the amount of stress they perceived, levels of anxiety (measured with the Mood and Anxiety Symptoms Questionnaire [MAS]; Clark & Watson, 1991), and depressive symptoms they experienced, with Asian Americans perceiving more stress and having more depressive and anxious symptoms. There were no differences between the two groups in cortisol levels (see Table 2).

Supportive Relationships and Inflammation

To examine the association between supportive relationships and levels of proinflammatory markers, a series of hierarchical regression analyses were conducted. Gender, body mass

index (BMI), perceived stress, and depressive symptomology were controlled for, given that past research has shown gender differences in relationships, and BMI, stress and depressive symptomology have previously been shown to influence levels of proinflammatory cytokines (O'Connor et al., 2009). Given that European Americans and Asian Americans differed in levels of anxiety, we also included MAS scores as a covariate. We did not include health behaviors as covariates, given the extremely small variability in these behaviors in this sample. We report the results with these covariates. The significance levels of the main results generally hold without them. In analyses for which exclusion of covariates substantially changes the pattern of results, we report the additional results. Dependent variables IL-6 and sTNFαRII were log transformed to correct for non-normality (findings were, nonetheless, similar for raw values and log-transformed values of IL-6 and sTNFαRII).

With culture, relationship support, and their interaction term in the regression model, there was a simple effect of supportive relationships ($\beta = -.599$, p = .001), and culture ($\beta = -1.806$, p = .002), and a significant interaction effect ($\beta = 1.840$, p = .001) on IL-6 (Table 3; Figure 1). Individual comparisons revealed that for European Americans, supportive relationships were significantly associated with lower IL-6 ($\beta = -.567$, p < .001). There was no association among Asian Americans ($\beta = .084$, p = .549). With respect to sTNF α RII, there was no effect of supportive relationships ($\beta = -.106$, p = .334) and there were no cultural differences, as the interaction term was not significant ($\beta = .579$, p = .334; Table 4).

 Table 3. Hierarchical Regression Analyses Predicting Interleukin-6

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383 .459126367 1.840** .788									203	379	.225	–.158	295	.247	201	376	.23
.788												<u>13</u>	383	.459	126	367	.43
															1.840**	.788	.23

Note. *p \leq .05. **p \leq .01.

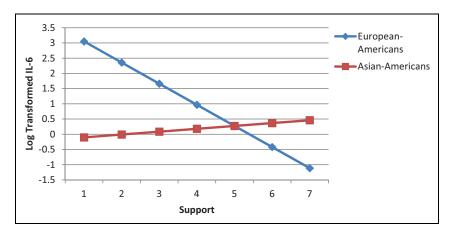


Figure 1. Supportive relationships predicted levels of IL-6 only in European Americans. The more supportive European Americans found their close relationships to be, the lower their levels of IL-6.

Social Support Versus Social Strain

Previous work suggests that social strain and social support may have different effects on health (Brooks & Dunkel-Schetter, 2011; Rook, 1984). Thus, we examined the supportive items (i.e., positively worded items from the relationship assessment questionnaire) and the social strain items (i.e., negatively worded items) separately.

There was no main effect of support on IL-6 ($\beta = -.099$, p = .378), but the interaction term was marginally significant ($\beta = 1.279$, p = .081). Tests of simple effects revealed no significant association in either group between support and IL-6 (European Americans: $\beta = -.252$, p = .169; Asian Americans: $\beta = .062$, p = .670).²

There was a simple effect of social strain on IL-6 (β = .421, p = .033) and a significant effect of the interaction term (β = -.887, p = .037). More strain was related to greater levels of IL-6 among European Americans (β = .396, p = .051). Social strain did not predict IL-6 among Asian Americans (β = -.068, p = .610). Neither support nor social strain was predictive of sTNF α RII for both European and Asian Americans.³

Parental Ties Versus Friendship Ties

Given that the benefits of social support may vary across sources (Walen & Lachman, 2000) and given differences in the parent–child relationship between East Asians and European Americans (Chao, 1994), we examined the effects of parental relationships and close friendships separately on proinflammatory markers. There was a significant simple effect of parental relationships on IL-6 ($\beta = -.441$, p = .021). In addition, the interaction term was marginally significant ($\beta = 1.155$, p = .063). Supportive parental relationships were related to (marginally) significantly lower levels of IL-6 among European Americans ($\beta = -.319$, p = .053), but not among Asian Americans ($\beta = -.015$, p = .912).

There was a marginally significant simple effect of close friendship ($\beta = -.262$, p = .065) and a significant interaction

between culture and supportive close friendship ($\beta = 1.419$, p = .007) on IL-6. Among Asian Americans, supportive close friendship was associated with marginally greater levels of IL-6 ($\beta = .269$, p = .052), but supportive close friendship did not predict IL-6 among European Americans ($\beta = -.257$, p = .123). For sTNF α RII, support from parental relationships and close friendships were not predictive of inflammatory levels in models both with and without covariates. There were no cultural differences in this finding as well.

U.S.-Born Versus Asia-Born Asian Americans

Supplemental analyses revealed that, consistent with the overall analysis, supportive relationships were not predictive of IL-6 either among Asian Americans born in the United States ($\beta = -.126$, p = .493) or among those born in Asia ($\beta = .383$, p = .166). Similarly, supportive relationships did not determine levels of sTNF α RII for U.S.-born Asian Americans ($\beta = .110$, p = .532) and Asia-born Asian Americans ($\beta = -.099$, p = .735).

Romantic Partner

Although fewer than half of the students reported having a romantic partner, we examined the association between supportive relationship and the two pronflammatory cytokines. There were no main effects of support from partner on levels of proinflammatory cytokines, and there was no interaction between support from partner and culture on inflammatory cytokines.

Discussion

The present study examined cultural differences in the link between supportive relationships and levels of proinflammatory cytokines. Controlling for a number of potentially confounding variables, perceived support in one's close relationships was associated with lower levels of

Table 4. Hierarchical Regression Analyses Predicting Type II for Tumor Necrosis Factor-∝

Model																		
		_			2			8			4			2			9	
	β	В	SE	β	В	SE	β	В	SE	β	В	SE	β	В	SE	β	В	SE
Intercept		3.208**	.456		4.055**	.732		4.452**	.923		4.685**	.952		4.607**	970		5.276**	161.1
Culture	058	093		065	105	.157		075	.162		063	.163		071	164		-1.016	988
Support	<u>10</u>	–.087	.082	079	068	.083		098	.093		093	.093		09I	.094		209	.I54
Gender	143	222	•	<u>186</u>	289	.I 54		281	.155		254	.157		255	.158		281	091:
Body mass index				–.146	0 4	.028	139	039	.028	156	044	.028	156	044	.028	—· 168	047	.029
Depressive symptoms								012	.017		00 	.020		007	.024		003	.024
Perceived stress											<u>168</u>	.167		203	.185		226	981.
Trait anxiety														.157	.343		991.	.343
Support \times Culture																	970	.334
																		ĺ

Note. ** $\rho \leq .05$.

proinflammatory cytokines among European Americans, but not among Asian Americans.

The results for European Americans are consistent with a large body of research conducted primarily with European Americans that relates supportive relationships to biological markers and to lower biological indicators of stress and illness likelihood. In that literature, social support has been found to buffer the effects of stress, for example, by keeping cardiovascular reactivity (Gerin, Pieper, Levy, & Pickering, 1992; Kamarck, Manuck, & Jennings, 1990) and cortisol responses to stress at low levels (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003).

The findings also suggest that European Americans' biological well-being may depend on supportive relationship more than is true for Asian Americans, at least in the way in which supportiveness is commonly operationalized (e.g., Sarason, Sarason, Shearin, & Pierce, 1987; Sherbourne & Stewart, 1991; Walen & Lachman, 2000). This raises the question of whether supportive relationships are defined and function differently in Asian cultural contexts. East Asian culture emphasizes social harmony, and relationships tend to be oriented toward relational goals, including maintaining closeness, harmony, and interdependence; as such, East Asians do not explicitly draw on their close relationships for support. European Americans, by contrast, regard social support as a personal resource and actively recruit it in times of need (Chen, Kim, Mojaverian, & Morling, 2012). Thus, explicit support (i.e., social support an individual recruits from his or her supportive ties) buffers European Americans against biological responses to stress, but does not do so for Asian Americans (Taylor et al., 2007). Consistently, then, perceiving support as available in one's central ties is related to lower inflammatory activity among European Americans, but this factor does not tap whatever aspects of social relationships buffers Asian Americans' inflammatory activity. Identifying ways to assess implicit support (the emotional support that one receives without raising or discussing problems or stressful situations), as perhaps through a sense of harmony or interconnectedness, may prove to be useful for assessing the links between Asian Americans' social relationships and biomarkers prognostic for poor health.

Interestingly, social strain, more than support, was predictive of IL-6 among European Americans. The positive relation between social strain and IL-6 is consistent with previous work demonstrating that social strain can be detrimental to health and well-being. In particular, social strain has been associated with depressive symptoms (Rook, 1984), cardiovascular disease (De Vogli et al., 2007), and inflammation (Fuligni et al., 2009). The lack of a significant association between support and IL-6 among this sample of European Americans is somewhat surprising, given research that relates supportive relationships to biological markers and to lower illness likelihood (e.g., Gerin et al., 1992; Heinrichs et al., 2003; Kamarck et al., 1990). However, the effects of strain on health are often found to be stronger than the effects on health (e.g., Rook, 1984).

Among European Americans, demands and criticism from social ties are construed negatively, leading to interpersonal stress that can be harmful to health. The fact that we observed no association between social strain and inflammation among Asian Americans implies that Asian Americans may not perceive criticism and demands from their close relationships as negatively as European Americans do. Asians tend to use their failures to meet expectations and obligations of their particular social group in order to improve their subsequent behavior and actions (Kitayama, Markus, Matsumoto, & Norasakkunkit, 1997). Criticism from and demands made by others, then, may not be interpreted as strain and thus may not threaten health-related indicators among Asian Americans as it appears to do among European Americans (Fuligni et al., 2009). Rather, Asian Americans may view criticism and relationship demands as opportunities to fulfill relational obligations, which can enhance belongingness to a group and social harmony (Heine, Kitayama, & Lehman, 2001).

In analyses of source of support, more supportive relations with friends among Asian Americans were marginally associated with elevated levels of IL-6. The reason for this pattern is not fully known. It may be that friend relationships marked by explicit support produce ambivalence among Asians/Asian Americans, which may be harmful to physiological functioning (Holt-Lunstad, Uchino, Smith, & Hicks, 2007).

Why IL-6 but not tumor necrosis factor- α (TNF- α), as indicated by sTNFRII α , was sensitive to relationship quality remains unknown. TNF- α and IL-6 are both acute phase proteins released in response to microbial challenge. They have common effects on biological responses, including stimulating T- and B lymphocyte responses (Peters, 1996). However, different cytokines have different functions and effects on various cells. Thus, the differential effects of relationships on the two cytokines may be due to biological factors that modulate cytokine activity. However, knowledge of the causes and timing of increases in inflammatory activity in response to social stimuli is not yet well understood, and it may be that the procedures of the present study were more suitable for capturing the dynamics of IL-6 activity than for TNF- α .

Some limitations of the current study warrant caution in interpreting the results. First, causal inferences cannot be drawn, given the correlational nature of the study. It is possible that higher levels of proinflammatory cytokines might lead to more supportive relationships. However, previous prospective studies have linked supportive relationships to inflammatory markers (Chiang et al., 2012; Friedman et al., 2005; Miller et al., 2009) and thus suggest support for this direction of causality. A second limitation is that a third variable might be implicated in the link between relationship quality and inflammatory levels in European Americans'. A likely candidate for such a variable would be depression, as depressed individuals tend to have greater levels of proinflammatory cytokines (Miller et al., 2003) and poorer relationships (Pearson, Watkins, Kuyken, & Mullan, 2010; Stice, Ragan, & Randall, 2004). However, depressive symptoms were controlled for in the present analyses, indicating that relationships predict inflammatory activity over and above depressive symptoms. A third limitation is that the present study used self-identified ethnicity as a proxy for culture, rather than

measuring culture directly. However, previous research provides considerable evidence that Asian Americans are exposed to and adhere to Asian cultural meaning systems, leading to significant cultural differences between Asian and European Americans (e.g., Heine, Lehman, Markus, & Kitayama, 1999; Kim & Markus, 2002; Taylor et al., 2004).

Implications for health are unknown. That is, it is unknown whether inflammation assessed at one time point in healthy young adults has any health implications. However, it is clear that chronic sustained inflammation and inflammation in the absence of injury can have adverse health implications. The use of OMT in assessing inflammatory markers may limit the generalizability of the findings. IL-6 from OMT has only been modestly correlated with plasma levels of IL-6 (Fernandez-Botran, Miller, Burns, & Newton, 2011). Nonetheless, inflammatory markers, as measured by OMT, at least reflect localized inflammation of the mouth, a primary avenue by which bacteria and viruses enter and affect the body.

Despite these limitations, the current findings provide evidence that more supportive relationships are linked to lower inflammatory activity in European Americans, but not in Asian Americans. Controls for a number of potential confounders suggest that this pattern is robust. Thus, the link between support in close relationships and biomarkers prognostic for poor health is not universal but may vary in ways that reflect cultural differences in the uses of relationships.

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Notes

- 1. In the sample, 26.7% were Chinese/Taiwanese, 12% Korean, 8% Indian, 6.7% Vietnamese, 4% Thai, 1.3% Japanese, and 2.6% Philippino.
- 2. In a model without the covariates, more support was marginally related to lower levels of IL-6 ($\beta = -.089$, p = .061), but culture did not interact with support to predict IL-6 ($\beta = .577$, p = .401).
- 3. Without any covariates in the model, there was a simple effect of social strain on IL-6 (β = .358, p = .048), but culture did not interact with social strain to alter IL-6 (β = -.542, p = .174).
- 4. In the periphery, macrophages and monocytes secrete IL-6 in order to activate natural killer cells and to facilitate B cell differentiation and proliferation (Peters, 1996). IL-6 also acts as a growth factor for T cells. Secreted by macrophages, mast cells, and natural killer cells, TNF-α activates neutrophils, moderates acute-phase protein transcription, and stimulates secretion of other proinflammatory cytokines and other inflammatory mediators.

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