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Short communication

Attachment anxiety predicts IL-6 and length of hospital stay in coronary artery bypass graft surgery (CABG) patients

Tara Kidd [a,*], Lydia Poole [a], Elizabeth Leigh [a], Amy Ronaldson [a], Marjan Jahangiri [b], Andrew Steptoe [a]

[a] Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, London WC1E 6BT, United Kingdom
[b] Department of Cardiac Surgery, St. George's Hospital, University of London, Blackshaw Road, London SW17 0QT, United Kingdom

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ABSTRACT

Objective: The mechanisms underlying the association between adult attachment and health are not well understood. In the current study, we investigated the relationship between attachment anxiety, attachment avoidance, inflammation, and length of hospital stay in coronary artery bypass graft (CABG) surgery patients.
Method: 167 CABG patients completed an attachment questionnaire prior to surgery, and blood samples were taken before and after surgery to assess inflammatory activity.
Results: We found that attachment anxiety predicted higher plasma interleukin 6 (IL-6) concentration, and this association was mediated by self-reported sleep quality. Anxious attachment also predicted longer hospital stays following CABG surgery, even after controlling for demographic and clinical factors.
Conclusion: These data suggest that increased levels of IL-6 may be a process linking adult attachment anxiety with health outcomes.

Introduction

Adult attachment is associated with a range of physical illnesses, including cardiovascular disease [1]. Growing evidence suggests that differences in physiological response to stressful situations may be one pathway that links attachment to health outcomes [2,3].

Individuals with high levels of anxious attachment amplify stressful experiences and have greater levels of the stress hormone, cortisol, during acute laboratory stress tasks in young adults [4]. Recently, this pattern of cortisol reactivity was replicated in older anxiously attached adults across the day [5]. Attachment avoidance (minimization of distress) has been implicated in immune responses to acute stressors. Picardi et al. [6] found that attachment avoidance was negatively associated with natural killer cell counts over a one year period, while Jaremka et al. [7] reported that anxious attachment predicted higher cortisol levels and fewer T cells after a marital discussion task in couples. Gouin et al. [8] found that attachment avoidance predicted an increased inflammatory response (IL-6) in couples after a marital conflict discussion.

These studies of biological mechanisms linking attachment to health have mainly been conducted on young, healthy populations, in a laboratory setting using acute stressors to elicit physiological responses. Little is known regarding attachment and the physiological stress response away from the laboratory. It is likely that those who are highly reactive in the laboratory will experience repeated episodes of heightened biological activity in everyday life [5,9]: Chronic activation of the attachment stress response may confer cumulative health risks over the life-course.

We have attempted to expand on existing literature by studying a real life acute stressor, namely CABG surgery in older cardiac patients. Cardiac surgery provokes a vigorous inflammatory response [10], and inflammation is associated with negative health conditions [11,12]. There is significant unexplained variation in inflammation post-surgery [13]. Inflammatory markers such as IL-6, TNF-alpha, and CRP are implicated in recovery from surgery, and length of stay in hospital [10]. In turn, longer hospital stays have been associated with poorer long-term recovery, subsequent hospital readmission, and recurrent cardiac events [14,15]. We hypothesized that high levels of attachment would be associated with an increased inflammatory response following surgery, and consequently a longer length of hospital stay.

Method

Participants

These analyses were carried out on patients in the Adjustment and Recovery after Cardiac Surgery (ARCS) study, as described previously [16,17]. Participants were recruited on average 29 days prior to surgery at a pre-assessment clinic. Inclusion criteria were completion of the attachment questionnaire, blood samples being taken at pre-assessment and 1–3 days after surgery, and participants were undergoing elective

* Corresponding author at: Psychobiology Unit, Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, London WC1E 6BT, United Kingdom. Tel.: +44 2076791846.
E-mail address: T.Kidd@ucl.ac.uk (T. Kidd).

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CABG surgery (+/- valve replacement). 167 participants were eligible to take part in the study (147 males, 20 females, age range: 44–86 years). All procedures were carried out with the written consent of the participants. We obtained ethical approval from the South West London research ethics committee.

Blood collection and analysis

A 20 ml blood sample was taken at pre-assessment and two further samples were drawn at 7.00 am on days 1 and 3 after surgery. We analysed IL-6, CRP, and TNF-alpha. Assays were performed at St George's Healthcare NHS Trust, using commercial automated immunoassay (Immulite 1, Siemens Healthcare Diagnostics, Frimley, Surrey).

Measures

Attachment was measured using the *Revised Adult Attachment Scale* [18]. Higher values indicate higher attachment anxiety and avoidance. Cardiac risk was assessed using the European System for Cardiac Operative Risk Evaluation (EuroSCORE) [19]. Sleep disturbance was assessed using an adapted 5-item version of the Jenkins Sleep Problems Scale [20]; higher scores indicate greater sleep disturbance. Socioeconomic status was assessed using yearly household income. Body mass index (BMI) was assessed at the pre-operative clinic and calculated using the standard formula (kg/m^2). The number of days patients stayed in hospital after surgery was recorded.

Statistical analysis

Associations between attachment anxiety, avoidance, inflammatory response, and post-operative length stay were analysed using hierarchical linear regression models. We entered BMI, smoking status, income, EuroSCORE, diabetes and hypertensive status, baseline inflammatory markers, and sleep quality in model 1. These demographic and clinical factors were included since they are known to be associated with immune functioning and post-operative stay [21,22]. Age and sex are included in EuroSCORE so were not entered separately to avoid double adjustment. Attachment anxiety and avoidance were then entered in model 2 to see if they explained any additional variance over and above demographic and biological factors. Adjusted R^2 and unstandardized B values with 95% confidence intervals are presented. Normality, linearity, and multi-collinearity assumptions were met. Mediation was examined using Preacher and Hayes SPSS macro to calculate the indirect effect, using bootstrapping procedures [23]. A resample procedure of 5000 bootstrap samples was performed (bias corrected and accelerated estimates and 95% CI).

Results

The participants were predominantly white British men (Table 1). The majority of patients were overweight, hypertensive, and approximately one third of patients suffered from diabetes. Most participants (80%) had on-pump cardiopulmonary bypass surgery. Correlational analyses found that attachment anxiety was correlated with baseline sleep reports ($r = 0.16$ $p = 0.01$), but no other significant relationships were found between BMI, EuroSCORE, age, or SES, and attachment.

Attachment and inflammatory response

The inflammatory variables showed substantial increases between baseline assessment and post-operative samples, as shown in Table 1. Because associations with attachment were only observed for IL-6, results for TNF alpha and CRP are not presented. In the fully adjusted model greater anxious attachment was significantly associated with higher concentrations of IL-6 after surgery, but avoidant attachment was not ($p = 0.35$, see Table 2). Poor sleep was also a significant predictor of IL-6 following surgery. As sleep was associated with both attachment anxiety and IL-6 following surgery, mediation analyses were conducted [23]. As the confidence interval does not contain zero (0.04 to 5.73), we concluded that poor sleep quality mediated the association between attachment anxiety and IL-6 after surgery.

Table 1
Participant characteristics n = 167.

	Mean (SD) or N (%)
Demographics	
Age	67.73 (6.90)
Male	147 (89%)
BMI (kg/m^2)	29.10 (4.19)
Married/cohabitating	126 (76%)
Ethnicity — White British	143 (86%)
Yearly household income	
<£10.000	23 (13.8%)
£10,000–£20,000	51 (30.5%)
£20,000–£30,000	37 (22.1%)
£30,000–£40,000	24 (14.4%)
>£40,000	32 (19.2%)
Smoker (current)	15 (5%)
Co-morbidities	
Diabetes	55 (33%)
Hypertension	133 (80%)
Clinical factors	
EuroSCORE	4.33 (3.24)
No. of grafts	3
Length of stay (days)	7
IL-6 baseline	6.25 (12.58)
IL-6 1–3 days post-surgery	197.13 (68.39)
CRP baseline	7.30 (5.92)
CRP 1–3 days post-surgery	84.94 (81.46)
TNF-alpha baseline	5.87 (2.74)
TNF-alpha 1–3 days post-surgery	6.41 (3.19)
Baseline measures	
Attachment anxiety	1.91 (0.91)
Attachment avoidance	2.46 (0.54)
Sleep disturbance	9.34 (7.04)

Attachment and length of hospital stay

Attachment anxiety, EuroSCORE, BMI, but not attachment avoidance, were significant independent predictors of hospital stay in the fully adjusted model (Table 2). There were no significant interactions between the anxiety and avoidance dimensions of attachment in any analyses. The results are also independent of depressive symptoms (results not shown).

Discussion

Our results suggest that attachment anxiety predicts IL-6 responses and longer hospital stay following CABG surgery, tentatively supporting the idea that attachment anxiety augments inflammatory responses to a stressor. Research has demonstrated that high levels of anxious attachment are associated with pronounced HPA reactivity to stress [3]. Although cortisol inhibits the immune response, chronically high levels of cortisol may lead to glucocorticoid insensitivity and subsequently an unregulated immune system producing increased levels of cytokines

Table 2
Predictors of IL-6 levels following surgery and length of hospital stay.

Model	Adj R^2	F	B	95% CI	p value
IL-6 1–3 days post-surgery					
Baseline adjusted[a]	0.03	1.96			0.06 ns
Fully adjusted model[b]	0.06	2.12			0.03
Attachment anxiety			18.18	2.20–4.17	0.02
Sleep			2.06	0.43–3.70	0.04
Hospital stay					
Baseline adjusted[a]	0.10	5.54			0.001
Fully adjusted model[b]	0.17	5.87			0.004
Attachment anxiety			0.83	0.41–1.61	0.03
EuroSCORE			0.53	0.36–0.69	0.001
BMI			0.22	0.10–0.35	0.001

[a] Baseline adjustments: BMI, smoking status, income, EuroSCORE, diabetes, baseline IL-6 levels, baseline sleep quality.
[b] Fully adjusted model: Attachment anxiety and avoidance are added to the model.

such as IL-6 [24]. There has been growing interest in the link between attachment anxiety and sleep disturbance [25]. It is believed that attachment anxiety is associated with increased sleep disturbance resulting from hyper-vigilance with increased physiological and emotional arousal [26]. Moreover, sleep disturbance has been associated with increased circulating levels of IL-6 [21]. This has important implications, as inflammation is associated with poorer recovery from CABG surgery, and longer hospital stay [16].

Interestingly, we found that anxious attachment also predicted longer hospital stay. Recovery from surgery is largely explained by clinical factors and in line with this, we found that BMI and EuroSCORE predicted duration of stay. However, the additional involvement of attachment anxiety in significantly contributing to length of stay is an exciting finding, as it supports the hypothesis that attachment anxiety is important in physical recovery from surgery.

Limitations

As our sample was relatively homogenous and no subjective stress measure was taken during the hospital stay, we are limited in making claims regarding emotional-regulatory processes and generalising to other groups. Based on existing work, we believe emotional-regulatory strategies are likely to contribute to length of hospital stay, as IL-6 did not [27,28]. The association between inflammation and attachment anxiety was based on one single marker, and the variance accounted for by attachment anxiety on IL-6 was small.

Unlike previous acute stress studies [8], we found no evidence of any association between avoidant attachment and IL-6. One explanation may be that we were studying a very profound stressor in an older population. Our results may reflect cumulative exposure to attachment-driven biological response to stress, perhaps not apparent in younger samples [2]. Gender may also contribute to our findings. The majority of our patients were men, and previous studies have found that avoidant attachment in women is associated with greater physiological responses [4,5]. Future work is needed to examine further the role of context, age, and gender on attachment and response to stress.

Despite these limitations, our results build on the existing literature and support an association between attachment anxiety, inflammation, and post-surgery stay in older adults. Moreover, our findings suggest that inflammatory pathways may be one way through which attachment anxiety confers risk to health in patients with cardiovascular disease, and that disturbed sleep may influence this association.

Conflict of interest

All authors declare they have no conflict of interest.

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Informed consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

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