RESEARCH SUMMARY

Basal cell carcinoma stressful life events and the tumour environment
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The body's immune system can be clinically significantly altered by stressors and the associated negative emotions they generate. Stressors can affect vaccine responses, wound healing, cause inflammation and affect two different types of immune functions. People who have experienced adverse childhood events are extra sensitive to stress later on in life. Stressful events early in life can affect the regulation of the immune system in the long-term, for example, childhood maltreatment can lead to poorer cellular immune function as well as being linked to diseases such as cancer.

Skin cancer is the most common cancer in the USA and more prevalent than all other malignant tumours combined. Occurrences of the most common skin cancer, basal cell carcinoma (BCC), have been doubling every 14 years. The risk of developing further tumours after the initial one is particularly high, with 44% of people having further tumours within 3 years.The immune system plays an important role in both the appearance and progression of BCC tumours. Chronic stressors can have a strong effect on the immune system in critical developmental periods, affecting future alterations in skin cancer tumours. In studies on mice, which had been subjected to stress, skin cancer developed more rapidly than in non-stressed control mice. They also had a poorer immune response, with their tumours not regressing, even once the stressor had been removed, unlike those of the non-stressed mice. This suggests that stressors early in development affect the immune response long after the stressor is removed.

Other studies on rats exposed young rat pups to varying degrees of shock (escapable, inescapable or no shock). The rats were injected with cancer cells when fully grown and exposed to one of the three shock conditions again. The rats exposed to inescapable shock when young were more likely to develop tumours as adults if also exposed to either escapable or inescapable shock conditions as adults. However, the rats that were not exposed to early inescapable shock were not more likely to develop a tumour as adults. This also suggests that early life stressors can alter the immune response to subsequent stressors later in life, thus decreasing anti-tumour defences.

One common stressor in early childhood is from parental emotional maltreatment. This has been associated with atypical cortisol levels throughout the day, cortisol being the 'stress hormone'. Adults who had experienced difficult parent-child relationships in their infancy are more likely to have emotional difficulties when encountering subsequent stressors than those who had healthy parent-child relationships. This study therefore looked at how parental emotional maltreatment and subsequent stressors could affect the BCC environment. The study hypothesis was that parental emotional maltreatment in childhood would be associated with a poorer immune response to a BCC tumour if it also occurred with a recent stressful event.

Patients were recruited to the study who had had at least one previous occurrence of a BCC tumour, but who had had no other type of cancer. 91 participants were recruited. It was felt that participants who had a previous occurrence of BCC would give a better basis for researching the psychosocial influences on tumours.

Interviews were conducted with patients to assess serious life events in the previous year; the Life Events and Difficulty Schedules (LEDS) tool was used to assess the occurrence of over 200 stressful events in order to understand environmental stressors whilst avoiding interviewer bias. Interviewers also collected data on contextual factors that could intensify the meaning of implications of an event, such as unemployment for someone who is already in debt. The LEDS had been previously used in psychiatric research with severe life events to predict the occurrence of psychiatric disorders. Links have also previously been shown between severe life events and illnesses through using the LEDS tool.

Interview data was also given to a set of raters who were unaware of other data about the participants. The raters assessed the severity of the life events on a scale of one to five, with one representing marked negativity and five representing little or no negativity. They also rated whether events could be related to the BCC itself, such as through medical complications or lifestyle changes. A depression diagnostic tool was applied, as well as an assessment of parental emotional maltreatment. Data on depressive symptoms and sleep quality and sleep deprivation were also assessed, along with data on underlying diseases and associated medication.

The results showed that for participants who had experienced a life stressor in the previous year, those who had been emotionally maltreated by their parents were more likely to have poorer immune responses. Women had a poorer response to the BCC tumour than men, although it is not know whether this is typical as gender has not been assessed in previous studies. Psychological response to stressful life events may have a significant role in the tumour environment and have implications for subsequent BCC tumours.

This study provides an extension to previous work on animals which demonstrated that stress can affect tumour growth and progression, and that early life stress in animals increases vulnerability to tumour development when an additional life stressor is also present in adulthood. This paper is also believed to be the first to demonstrate that early life stressors influence the tumour environment in humans. The research could be relevant to other work linking child maltreatment with cancer incidence.

One of the strengths of the study was that it used the LEDS to asses life events, which meant life events related to underlying medical issues could be excluded and people's ratings of their stress events weren't influenced by biases related to depressive symptoms, as the LEDS used objective ratings of stress severity. The LEDS also meant links between severe stressors and immune function could be assessed. However, there were limitations of the study too, such as potential bias from participants when reporting the degree of parental maltreatment, as well as a lack of other factors such as low socioeconomic status which could affect immune function. Use of solely BCC tumours was also limiting, with future work to assess other types of cancers important in order to generalise the research findings to cancer more widely. Another limitation was that all the participants were white, which was due to the nature of the type of cancer.

BCC tumours are a major public health concern as well as possibly being prognostic for other cancers. Difficult childhood parental experiences are linked to greater stress reactivity and poor immune regulation in adulthood. This was the first study that showed that these experiences, along with recent severe life events, can predict local immune responses to BCC tumours. This paper adds to a growing body of research showing that early problematic parenting has consequences that can severely affect even physical health well beyond childhood.

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