

Tutor feedback

Abstracts

Both clear and well written.

Content

Overall, very well written. A pleasure to read.. - - A few more specific points: - -
Difficult/complicated concepts are tackled a few times and invariably explained well.
- - Perhaps a bit more explanation to help the reader understand the results of the study on physical activity would have been useful. - - A good approach to 'indirect factors' by discussing multiple together (one after another) leaving more room/words to discuss 'direct' in a good level of detail. - - Some good critical evaluation, e.g. on p.7 where you appraise a major study that's important to the section (but it would be good to finish here by summarising the main points a bit, signposting etc.) - - I felt that more could be said about the link between stress and depression (but good to have touched on it though).

Use of literature

An excellent range of (mainly quite contemporary) literature cited - all sorts of different primary sources. A huge reference list! And difficult to find any errors - I found one without a year! - - All claims in the text are cited.

Organisation of report

Very well organised throughout. - - Good use of figures - referred to appropriately in the text and described well in the legends (with a good amount of detail). They add to the narrative.

Presentation of report

Excellent use of English, with no misspellings or errors. This helps the essay to flow, along with the linking sentences which guide the reader through, keeping on topic (connecting different aspects to the bigger picture), signposting etc.

The relationship between mental illness and physical health

Tutor name / Student name

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Lay Abstract

This literature review will be focusing on the relationship between mental illness and physical health. The aim of this review is to understand the different factors affecting this relationship in more detail, so that this information can be used to think of ways to improve patient care. It was found that the types of factors affecting mental and physical health could be split into two groups: direct and indirect. Examples of indirect factors are employment and social interactions, and examples of direct factors are stress and genetics. Physical health is affected by many more indirect factors than mental health is, but direct factors have a large effect on both mental and physical health. Research shows that depression's link with long-term physical pain is due to the same disease pathway between the two: long-term inflammation. Long-term inflammation happens when the immune system is not working properly, which could happen because of stress. Lifestyle coaching has been used to help patients with mental illness, to stop their physical health from worsening, and has been successful. More research needs to be done on how physical health and mental health can be checked together in general practice.

Scientific Abstract

This literature review will be analysing the relationship between mental illness and physical health. The aim is to gain insight into the mediators impacting on this relationship and their mechanisms, to inform methods through which patient care can be optimised and physical disease can be prevented. Direct mediators, such as genetics and stress, and indirect mediators, such as employment and social interactions, impact the relationship. The indirect factor with the greatest effect on current physical health was physical activity at 77%, and physical activity was the sole indirect factor impacting on current mental health. Chronic stress affects health by modulating the immune response. Polymorphisms in certain genes, such as the 5-HTT gene, explains the link between cardiovascular disease and depression. The link between depression and chronic pain is proposed to be a common pathological predisposition: chronic inflammation. Lifestyle interventions, focusing on the indirect mediation of physical activity, have shown to be successful in improving the health of mental health patients. Further research is needed into the mediators to create a framework to assess mental and physical health simultaneously in general practice.

1.0: Introduction

In recent years, mental health conditions have increasingly gained acknowledgement as an important public health concern due to their prevalence rising, especially in well-developed, industrialised countries.^{1,2} Currently, it is estimated that one in four people suffer from a mental health problem during their lifetime. It has been calculated, that in the WHO European region, mental health conditions constitute 22% and neurological problems constitute 17% of the total burden of disease.³ Therefore, the likelihood of a physical health problem coinciding with a mental health issue is quite probable⁴ – whether that be coincidental or due to underlying mechanisms.

The significant link between mental and physical health has been well established,^{5,6} but the aim of this literature review will be to further elucidate this and explore the pathways between these two states of health, with a particular focus on depression's association with physical health deterioration. This review is important because it has the capacity to shed light on the complexities of the interactions between physical and mental health, in order to help inform the methods by which the management and prevention of these conditions, on their own and when they co-exist, can be improved.

2.0: Mental and physical health: A complex interplay

The relationship between mental and physical health is complex with a variety of mediators coming together to form a cumulative impact on it. Thus, it is important to gain an insight into each of the main mediators, separately, to understand the mechanism by which physical and mental illness link and manifest on a micro-level. The factors that affect this relationship can be classified into two categories: direct and indirect.

2.1: Indirect mediators

Indirect mediators are those that do not directly lead to a pathological state, but have the capacity to significantly predispose an individual to developing it, by initiating the mechanism of disease via possible impact on another factor. Examples of these mediators include the following: lifestyle choices, social capital, current mental and physical health, certain biological factors and employment.⁷ Lifestyle choices and

social capital are amongst two of the most researched indirect mediators.^{8,9} Social capital consists of factors such as loneliness, social exclusion and social isolation – all significant risk factors for the development of disease – especially in older populations.¹⁰ With regards to lifestyle choices, it has been stipulated that around 55% of the burden of disease in elderly populations – aged 60 and over – can be prevented by certain lifestyle changes in developed countries.¹¹ Furthermore, lifestyle changes have been shown to account for around 70% of the impact of disease when taking into account the general population, irrespective of age.¹²

Employment has the capacity to act as a mediator between physical and mental health, because of how any type of poor health can potentially impact on an individual's efficiency at work. For instance, if an individual has a labour intensive job and suffers from a decline in physical health, then this could impact on their productivity and could possibly lead to redundancy if they do not report it. The redundancy could be difficult to cope with and lead to the manifestation of a mental health problem, thus exemplifying the relationship between mental and physical health. Employment can also act in the other direction by creating a stressful environment for an individual, who could already be suffering from a mental health condition, and lead to physical health problems such as high blood pressure.^{13,14}

Current mental health issues can impact physical health due to them leading to adverse effects on an individual's decision making capabilities. This can potentially lead to a mental health patient not accessing healthcare information, or healthcare providers, as readily and so not being able to maintain good physical health.¹⁵ Additionally, mental health problems still have a stigma attached to them in various societies, which is another reason why those suffering from them may not access the healthcare they need.

Lifestyle choices have been shown to be very important mediators between the aforementioned states of health,^{12,16} and many studies have shed light on the negative association that depression and poor physical health outcomes have with physical activity.¹⁷⁻²¹ It has been highlighted that an increased amount of exercise can have positive effects on both mental and physical health outcomes, especially in elderly populations.^{22,23} It does have to be noted that there can be a reverse-causal

relationship between high amounts of physical activity and physical and mental health, as those with better health will be more likely to engage in physical activity overall.⁷

Smoking is another key mediator to be observed, as smoking cessation has been shown to have positive effects on stress levels, depression and anxiety²⁴ and decreases the likelihood of developing physical ailments, such as cancer. However, reverse-causality has to be considered once again,⁷ as the amount of people that smoke whilst suffering with depression or anxiety is double the amount that is observed in the general population.²⁵

A bi-directional link can also be seen in the mediating role of alcohol consumption, where a moderate level has been found to have a beneficial effect on both physical and mental health, whilst those with better baseline physical and mental health have been shown to drink moderately.^{16,26} Complete abstinence and excessive drinking have been shown to have negative effects on health outcomes, and pre-existing poor mental and physical health has been demonstrated as a predictor of complete abstinence and excessive drinking.^{27,28}

Dietary choices are significant when assessing physical and mental health, because a poor diet, high in fats and sugar, has a strong association with high mortality risk²⁹ partly due to the implications of an increased likelihood to develop obesity. Food consumption's link with mental health has also been researched, and one particular study highlights the significant association between fruit consumption and overall mental wellbeing and happiness.³⁰ Reciprocally, individuals suffering from depression frequently report loss of appetite as a symptom they experience, and this can have a negative impact on the nutrition their body receives and can potentially affect their physical health.

Lastly, out of all of the lifestyle factors, social interactions are integral to the understanding of the relationship between mental and physical health, because an array of studies have elucidated the strong positive association between social interaction and mental health.^{31,32} The presence of poor social interaction factors, like isolation and loneliness, have been shown to lead to an increase in mortality risk.¹⁰ It

seems maintaining consistent social relationships is very important for physical health, as it has been reported that this significantly decreases mortality risk.⁹ It is important to note that those with poor mental and physical health tend to be more socially isolated overall,¹⁰ which can then further exacerbate physical and mental problems.

One particular longitudinal study comprising data from 10,693 individuals⁷ used an adapted economic framework - which considers health as part of human capital³³ - to mainly analyse the indirect factors linking physical and mental health [Figure 1]. The study did this by carrying out an interview every two years and measured the outcome variables of mental and physical health on relevant scales. A total of six waves of data was utilised and the factors investigated were employment, current mental health issues and lifestyle choices such as smoking, physical activity, diet and alcohol consumption.⁷

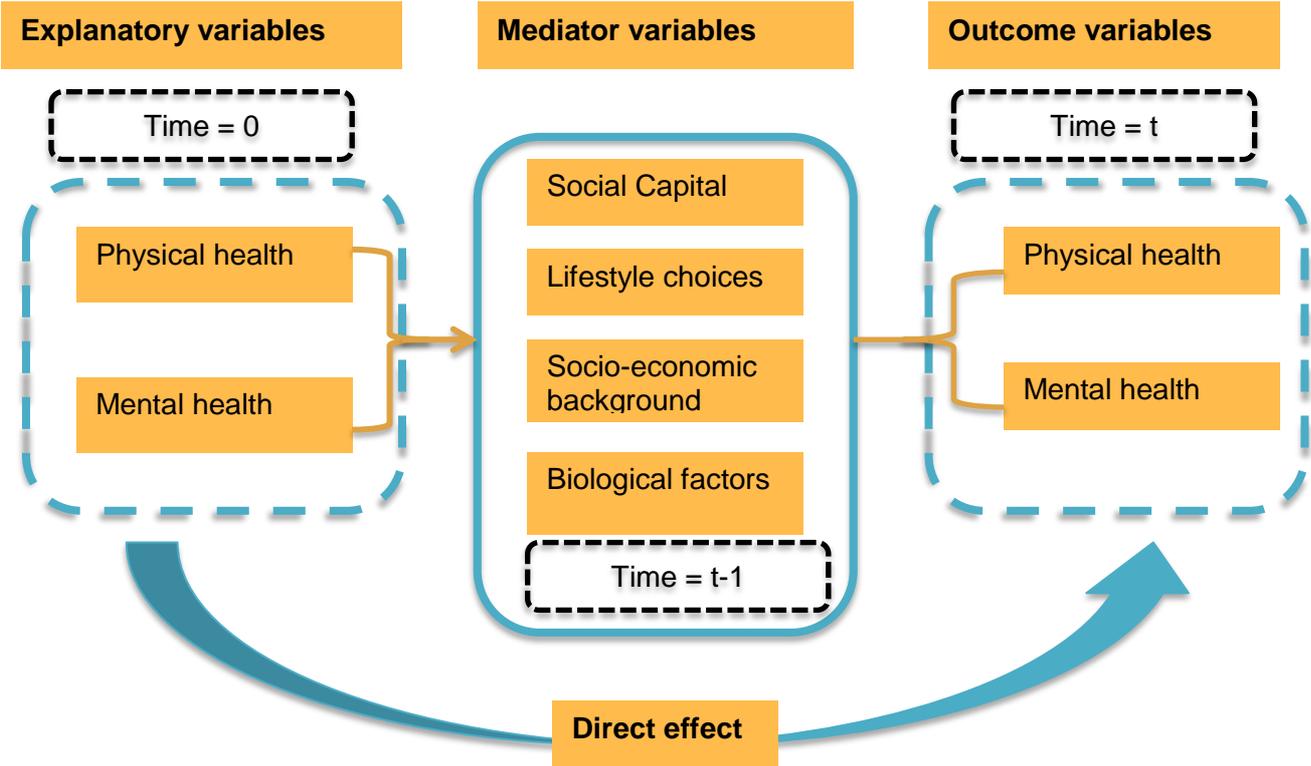


Fig. 1 – Representation of the indirect and direct effects between mental and physical health, adapted from Ohrnberger J et al.⁷ Social capital consists of social interactions, loneliness and social isolation. Lifestyle choices consist of diet, physical activity, smoking and drinking. Biological factors consist of cognitive skills and stress, and socio-economic background consists of income/wage, job conditions and retirement.

A mediation analysis was carried out focusing specifically on physical activity, smoking and social interactions, due to them being amongst some of the most important predictors of mortality within the lifestyle choices.^{9,10, 12, 34,35} The study found that indirectly mental health had an effect of 9.7% out of its full effect on current physical health, physical activity had a 77.27% indirect effect and social interaction had a 13.63% total indirect effect. Furthermore, physical activity had a greater effect on the higher age group of 80+ years in comparison to the 50-60 years age group, and a stronger effect was also seen on males in comparison to females.⁷

The only mediator observed to have a significant positive association with current mental health from baseline physical health was physical activity. Higher baseline physical health held a positive correlation with levels of physical activity, which can explain its link with improved current mental health. The total amount that baseline physical health affected present mental health indirectly was 8%. The total effects of the factors increased with age and were more significant in females.⁷

The aforementioned study provided important insight into the mediation between physical and mental health, because the presentation of a physical or mental health problem is a summation of a wide range of indirect and direct effects. The results revealed that in comparison to current mental health, a wider range of indirect factors impacted current physical health.⁷

However, the study did have certain shortcomings, as it did not take into account other lifestyle factors such as medical care or socio-economic background.⁷ It also collated data from six waves of surveys and refreshed the sample three times, which disrupts continuity and can introduce a degree of transfer bias, despite the researchers aiming to negate that by keeping the sample size randomised and maintaining the same amount of participants in each wave. Nevertheless, the study had a considerable amount of internal validity as many variables were controlled, such as age and ethnicity, but because the study was undertaken with participants aged 50+ the results cannot be applied to the general population.

2.2: Direct mediators

In order to acquire the full picture of what affects the relationship between mental and physical health, it is imperative that the knowledge of indirect mediators is supplemented with the knowledge of direct ones – which can directly lead to a pathological state. Biological factors like stress and genetics mainly act as direct mediators, but have the ability to act indirectly too.

Stress is defined as a collation of events that contains a stimulus – stressor – which is processed by an individual, dependent on their unique outlook, and elicits a reaction in the brain: stress perception. Subsequently, the stress perception then activates the physiological fight-or-flight systems, known as the stress response.³⁶ The main chemical constituents of stress are epinephrine and norepinephrine that are released from the adrenal glands as part of the sympathetic nervous system, and cortisol, adrenocorticotropin and corticotropin releasing hormone – the release of which is followed by the activation of the hypothalamic-pituitary-adrenal (HPA) axis. The effects of stress lead to biological changes being triggered on a large scale, because most of the cells in the body have receptors for the stress hormones.³⁷

Stress can be acute or chronic with the latter being deemed as detrimental to health,³⁸⁻⁴¹ mainly due to its effects on the immune system, and the former being deemed as potentially beneficial for health.³⁷ Stress is classified as ‘chronic’ if it lasts for several hours per day for a long period of time, ranging from weeks to months.³⁶ One of the key mechanisms hypothesised to explain the damaging effects of chronic stress is the dysregulation of the circadian cortisol rhythm,^{36,42,43} which is also thought to be a contributor to the pathophysiology of depression and so this indicates how integral stress can be to the development of mental illness.

Studies have shown that a stress-driven rise in levels of corticosteroids can lead to structural brain abnormalities in processing centres, such as the amygdala. Abnormalities in the amygdala, due to its major role in emotion processing, as well as its minor role in the stress response,^{44,45} can consequently lead to the display of mental pathophysiology in the form of depressive symptoms.

Furthermore, after the administration of corticosteroids, the hippocampus of the brain has been shown to have a noticeable reduction in volume.⁴⁶ The hippocampus is the region of the brain which houses long term memory, and so a reduction in its volume can lead to cognitive deficits, further exacerbating any possible mental health issues. In relation to the mediation between mental and physical health, these stress-related cognitive deficits can cause physical health problems, as an individual can have difficulty keeping track of any health changes - due to memory problems - and so may not seek appropriate medical help.

The magnitude of the impact that stress can have on a person is dependent on their stress perception, processing, appraisal and coping.^{47,48} These factors are key to acknowledge because they have significant effects on the peak levels of stress hormones in the blood, and the total amount of time that these hormone levels increase.³⁷ Chronic levels of stress, affecting mental and physical health, can lead to the continuous long-term activation of the fight-or-flight response³⁷ and this has been shown to substantially transform the function and distribution of immune system components; a mechanism that is worthwhile understanding.^{49,50}

In general, the immune system's responses can be categorised into the following: immunoprotective, immunopathological or immunoregulatory.^{51,52} Immunoprotective responses are usually intertwined with acute stress, and comprise of the responses involved in efficient wound healing, clearing out toxins, obliterating infections and cancer and mediating vaccine-induced immunological memory.^{51,52} Innate and/or adaptive immunity can demonstrate immunoprotective characteristics: consistently active immune surveillance, swift identification of pathogens and rapid clearance of the pathogen to arrive at a successful resolution.³⁷

Immunoregulatory responses are involved in regulating, mostly suppressing, the actions of particular cells in the immune system.^{51,52} Immunoregulatory responses are generally supposed to have a positive impact on the body's defences by regulating inflammation, autoimmune and hypersensitivity reactions.^{53,54} However, some research has suggested that this is not always the case, as immunoregulatory cells do have the capability of suppressing anti-tumour immunity and so can impact negatively on cancer prognosis.^{43,55}

Immunopathological responses, the category of responses associated with chronic stress and linked pathologies, is defined as reactions that work against one's own body. It is linked to autoimmune diseases such as lupus, multiple sclerosis and psoriasis, innocuous antigens that can cause hypersensitivity reactions and asthma and chronic inflammation.^{51,52} Generally, inflammation does not need to be high grade and widespread in order to cause damage, as low-level and long-term increases in local inflammatory mediators can contribute to an array of diseases: obesity, cardiovascular disease and depression.⁵⁶⁻⁵⁸ Thus, any modulation of the immune system that can exacerbate its immunopathological capabilities can mediate the onset of both physical and mental illness – clearly exemplifying the role of stress as a direct mediator between the two.

Stress-induced immunosuppression, involving mechanisms that inhibit prostaglandin synthesis, cytokine production and recruitment of leukocytes,⁵⁹ demand a longer time duration than the amount of time that elapses in an acute stress situation.³⁷ This emphasises that stress does not have to be universally damaging to health and that acute stress may indeed be exempt from producing lasting, adverse effects like immunosuppression. There is an 'energy-conservation' hypothesis, which suggests that acute stress may work by suppressing the secondary adaptive immune response – thus conserving energy - and enhancing the innate immune response.^{60,61}

When trying to ascertain whether stress will have pathological or protective consequences, via the immune system, it is important to consider the following factors: the duration of the stress, the changes in the distribution of leukocytes systemically, the differing effects of pharmacological glucocorticoid levels and endogenous glucocorticoid levels in the blood and the time that elapses between the exposure to the stressor and the activation of the immune system.³⁷

Alongside these factors, it is also imperative to take into consideration the genetics, age, route of administration of glucocorticoids, if synthetic, and the point in the circadian cycle where the individual was exposed to the stressor, because all of these affect how an individual uniquely modulates stress. For the sake of clarity, the immune system's responses have been neatly categorised into the three aforementioned categories. However, the 'good' and 'bad' effects are not mutually

exclusive and so to conclude whether a stressor has enhanced or suppressed immune function, one must focus on the overall end-effect [Figure 2].³⁷

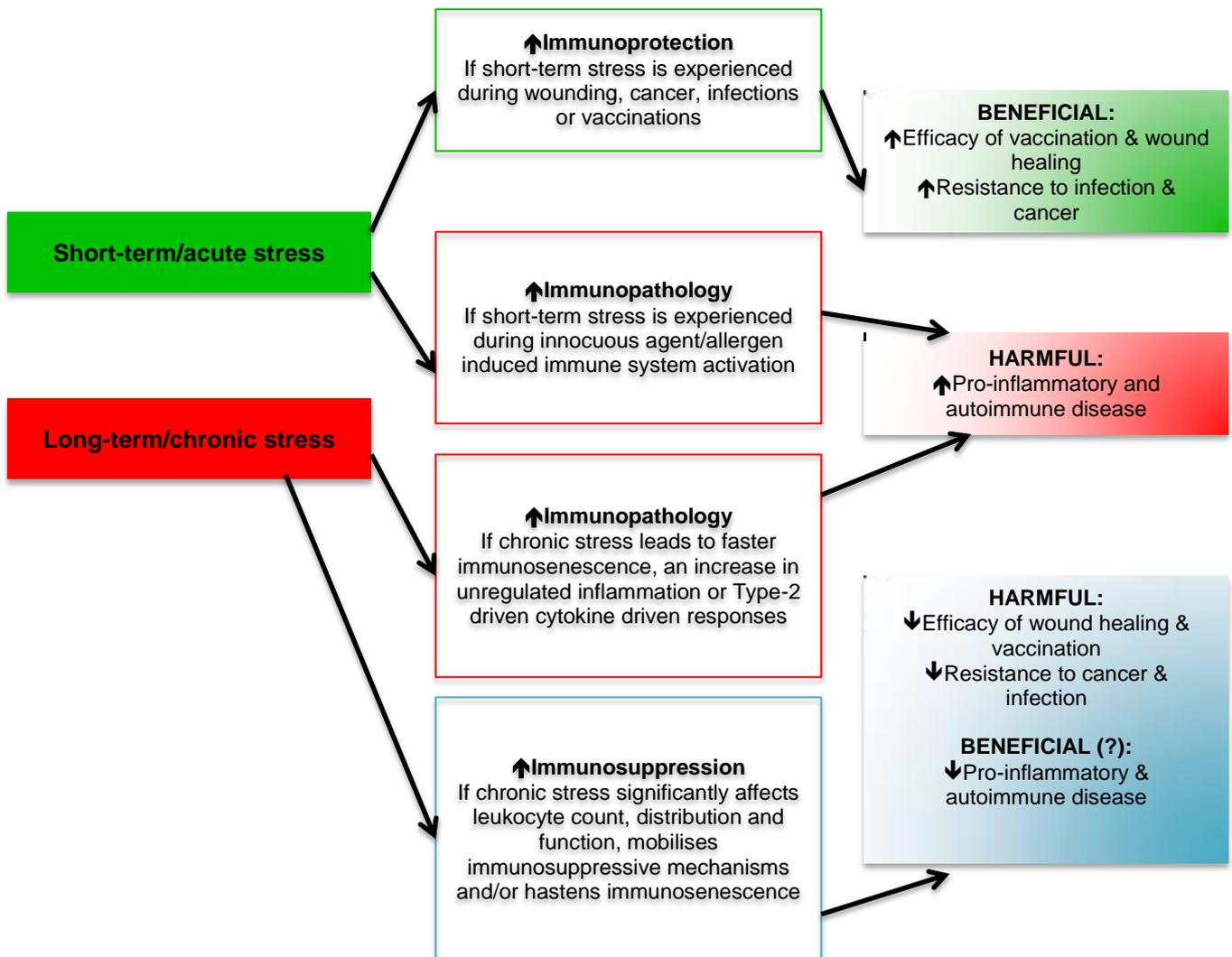


Fig. 2 – Adapted from Dhabhar FS.^{37,51} A representation of the enhancing vs. the damaging effects of stress and the positive and negative health outcomes it can produce via interaction with the immune system.

To expand further on chronic stress, the proposed mechanisms by which it dysregulates the immune system have been ascertained through a combination of human and animal studies. These studies have shed light upon the following mechanisms: a decrease in leukocyte mobilisation from the blood to other bodily compartments,³⁶ suppression of antibody production,⁶² increase in leukocyte count,^{63,64} natural killer cell activity³⁹ and virus-specific T cell and natural killer cell activity.⁶⁵

Another key immune effect of chronic stress, explored by a study on women,⁶⁶ was that it accelerated immune cell ageing. The blood lymphocytes and monocytes from female participants, who reported experiencing a high level of chronic stress, had significantly shorter telomeres in comparison to women who were experiencing low levels of stress.⁶⁶ Thus, chronic stress has a significant effect on the aging process of immune cells, which effectively shortens their cell cycle and limits their function. Further research has illustrated that the rate of telomere shortening observed in chronic stress had a strong association with mortality risk from cardiovascular disease⁶⁷ – once again another lucid exemplification of how stress links to the deterioration of physical health.

In addition to the various mental and physical effects of stress on the body already mentioned, the relationship between chronic stress and cancer has been widely investigated as well.⁶⁸⁻⁷⁰ Research has drawn links between chronic stress and cancer development and progression,⁴³ as well as its impact on the immune system leading to cell-mediated immunity not being able to work as effectively to defend the body against cancer. This impact is especially important when considering immunoresponsive tumours like squamous cell carcinoma (SCC), as the disease progression of SCC can be somewhat controlled by a functional and strong immune defence.⁷¹

In the first half of this section of the review, it was highlighted that physical activity in the form of exercise was a significant indirect mediator between mental and physical health. Exercise's potent effect on health can be explained through its link with stress, as when undertaking exercise the body undergoes a physiological change and the levels of stress hormones rise.⁷²⁻⁷⁴ The rising levels of epinephrine, norepinephrine and cortisol during exercise mirror an acute stress response, and so it can be suggested that regular exercise can refine the short-term stress response, to gain all of its immunoprotective assets and fundamentally keep the body healthy.⁵¹

To summarise, stress acts in an encompassing manner, impacting on various physiological mechanisms to affect the relationship between mental and physical health – mainly through the immune response. It is extremely vital to understand how

stress manifests in different individuals, so that healthcare providers can promote effective stress management strategies as part of endorsing a healthy lifestyle.

Moving on, the other key direct mediator to be discussed, which impacts on the relationship between mental and physical health, is genetics. There is currently a growing bank of research highlighting certain genes/polymorphisms that have a strong association with both a physical and mental disease: the genetic link between depression and cardiovascular disease being one of the most thoroughly researched.⁷⁵

Depression and some cardiac disease risk factors have an integral genetic component,⁷⁶⁻⁷⁹ alongside other interacting factors, leading to their manifestation [Figure 3].⁸⁰ Various studies have been undertaken to explore any mutual genetic factors between these two conditions. One particular study of 2731 male-male twin pairs,⁸¹ in Vietnam, revealed that there may indeed be common genetic risk factors that can predispose an individual to developing both depression and cardiac disease. In relation to hypertension, coronary heart disease and depression, significant genetic correlations were observed, and a further statistical model undertaken showcased that coronary heart disease shared a similar genetic variance with depression as it did with hypertension.⁸¹

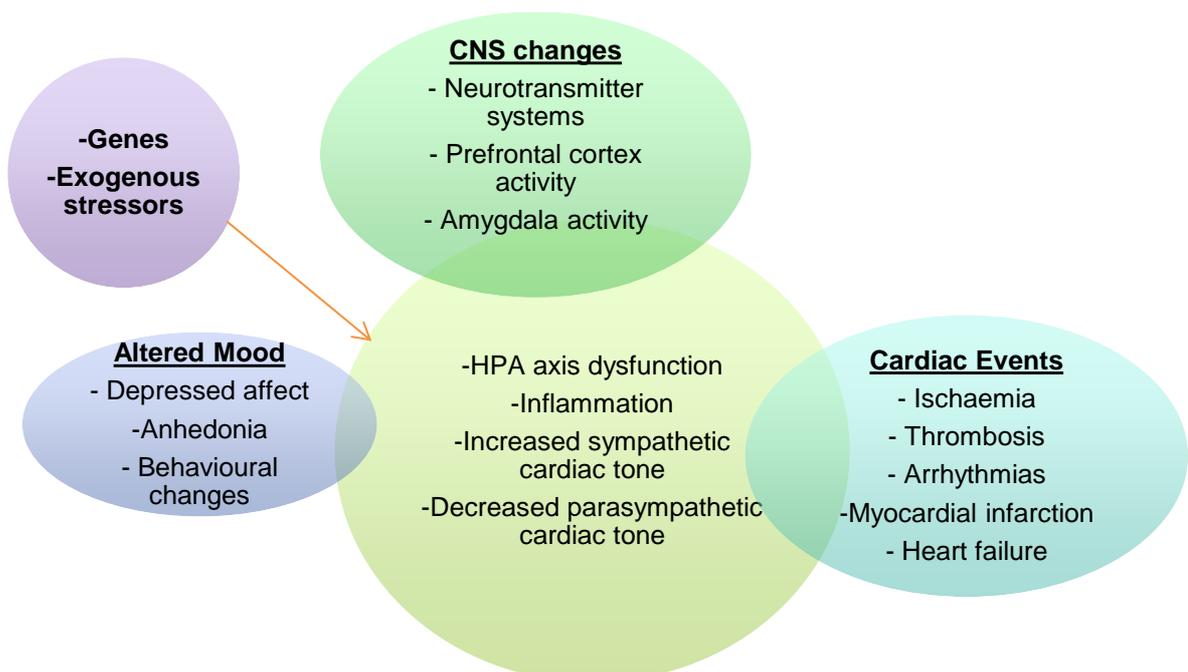


Fig. 3 – A representation of the pathophysiological mechanisms that directly and indirectly interact between depression and CVD, adapted from Bondy B.⁸⁰

The fact that a mental and physical disease can have a similar genetic variance to two pathologically related physical diseases, emphasises how intrinsically linked mental and physical health can be and how important it is to assess both states of health together. This research could also suggest that coronary heart disease and depression may be differing phenotypes of the same genetic code,⁸² however this cannot be concluded as of yet, because further research is needed into the role of environment in the expression of these genes and any other mediating factors. Additionally, this study only had male participants and so it would be helpful to gain further insight into whether this genetic link between cardiovascular disease and depression is as evident and prevalent in females.

A specific gene implicated in the link between depression and cardiovascular disease is the gene for the 5-HT transporter (5-HTT).⁸⁰ Due to 5-HTT being expressed on both neuronal tissue and on the surface of platelets, where it works to maintain homeostatic balance of 5-HT in the blood,⁸³ the gene coding for it can fundamentally affect serotonin levels in both regions. A mutation in this gene can predispose an individual to mental pathology – depression – and vascular pathology – cardiovascular disease – simultaneously.

The 5-HTT gene has a polymorphic site located in its promoter region, which has been investigated on multiple occasions, with a deletion/insertion variation that creates short (S) or long (L) alleles.⁸⁴ The S allele is associated with decreased 5-HT uptake and decreased transcriptional activity.⁸⁵ This subsequently leads to 5-HT being active in the synapses of the brain and in the bloodstream for a longer period of time than normal,⁸⁵ and the L allele essentially has the opposite effects of this.

With regards to the S allele, research has shown that the presence of at least one S allele in individuals leads to the exhibition of maladaptive behaviour such as 'harm avoidance'.⁸⁶ In addition to this, there are higher levels of a personality trait, associated with psychopathology, known as neuroticism and an increased display of depressive symptoms overall – in comparison to those that are homozygous for the L allele.⁸⁶

Building on this, many recent meta-analyses have stipulated that there is a strong association between the S allele and increased neuroticism,^{87,88} which clearly highlights how genetics can work directly and indirectly to impact on the relationship between mental and physical health. This is due to the fact that neuroticism has been extensively researched, and has been found to be significantly associated with a wide variety of mental and physical conditions ranging from atopic eczema⁸⁹ and irritable bowel syndrome⁹⁰ to antisocial personality disorder⁹¹ and schizophrenia.⁹² Thus, if neuroticism is significantly associated with the S allele, then the presence of this genetic polymorphism can indirectly increase the likelihood of developing both mental and physical diseases in the future.

In relation to cardiovascular disease, polymorphisms of the 5-HTT gene that produce the S and L allele have both shown associations with the development of disease. The L allele is associated with an increased level of transcriptional activity, and so those that are homozygous with this polymorphism would exhibit higher blood 5-HT concentrations, due to rapid 5-HT uptake and storage in the dense granules of platelets.⁹³ This notion was consolidated by a study in geriatric depressed patients that were homozygous for the L allele, as they showed prominent platelet activation, thromboglobulin levels and increased platelet factor 4.⁹⁴

Thus, it can be inferred that increased platelet activity, which would be followed by increased 5-HT release, in those homozygous with the L allele can predispose them to a higher risk of thrombus formation. This inference was reinforced by a large multicenter study carried out on more than 600 carriers of the LL genotype, who were coronary artery disease patients, and it was found that they had a greater risk for myocardial infarction than those that did not have the genotype.⁹⁵ This research, once again, cements the importance of genetics as a factor that impacts significantly on the relationship between mental and physical health.

The S allele works differently to the L allele, in relation to cardiovascular disease, as it mainly affects emotion processing and has been shown to have a significant impact on the risk for cardiac events through this mechanism.⁸⁰ This was exemplified in a prospective study undertaken with patients, after they had suffered from a myocardial infarction, and the presence of the S allele was shown to increase the risk of further

cardiac events. This increased risk was proposed to be due to the exhibition of depressive symptoms in the patients, which were significantly higher in those of the patient population that were S allele carriers.⁹⁶

To sum up, stress and genetic factors work through clear physiological mechanisms to impact on the relationship between mental and physical health. The indirect mediators such as lifestyle choices and employment accentuate these factors; in order to produce a health outcome. Once basic knowledge of the mediators is acquired, the next task is to be able to apply it in the context of a specific disease, so that it can be prevented from developing alongside its associated comorbidities.

3.0: Depression and chronic pain – a bidirectional relationship rooted in common pathological predisposition?

Depression has been shown to have significant associations with physical disease; its relationship with chronic pain being one of the most prominent ones.⁹⁷ Studies exploring the clustering of the two conditions have revealed that they occur together at a high prevalence ranging from 30% to 60%,^{98,99} which highlights this as a considerable public health problem to tackle.

Research has been undertaken showing that common treatment strategies are used to ameliorate the symptoms of the two conditions, such as the widely used typical antidepressants that successfully treat chronic pain.¹⁰⁰ The use of common treatment regimens may hint at the same pathological mechanism underlying the relationship between the two diseases, perhaps rooted in chronic inflammation.⁹⁷

However, when typical antidepressants are prescribed for chronic pain, they are not exclusively targeting the underlying inflammation. Thus, recognition of the neuro-immune mediated mechanisms, that drive the pathology of chronic pain and depression, could aid in boosting the efficacy of therapeutic options available currently.⁹⁷ The current pharmacological agents prescribed to treat chronic pain and depression, such as SSRIs, SNRIs and traditional opioids, have each been shown to have an efficacy lower than 50%.¹⁰¹ This fact prompts the need for developing new treatments that are more specifically targeted to the mutual mechanism of disease.

It was highlighted in the first part of this review that stress can trigger an immune response, and act as a significant contributor to inflammation and subsequent mental and physical disease. The process of inflammation in the body initiates a cascade of reactions between the brain and the immune system. With regards to the link between chronic pain and depression, important components of the inflammatory response – cytokines – have been shown to interact with neural pathways, causing abnormal restructuring of important neurotransmitter pathways.⁹⁷

For example, inflammatory signals can transform GABAergic neurotransmission from inhibitory to excitatory and can also disrupt the excitation of NMDA receptors in the brain. The aforementioned neural restructuring can then potentially lead to an acute inflammatory response prompting the progression of sickness to depression and from acute to chronic pain, even after the initial event has elapsed [Figure 4].⁹⁷ Thus, it can be suggested that the inflammation underlying the pathology of depression and chronic pain establishes a bidirectional link of causality between the two diseases, in order to explain their significant clustering.

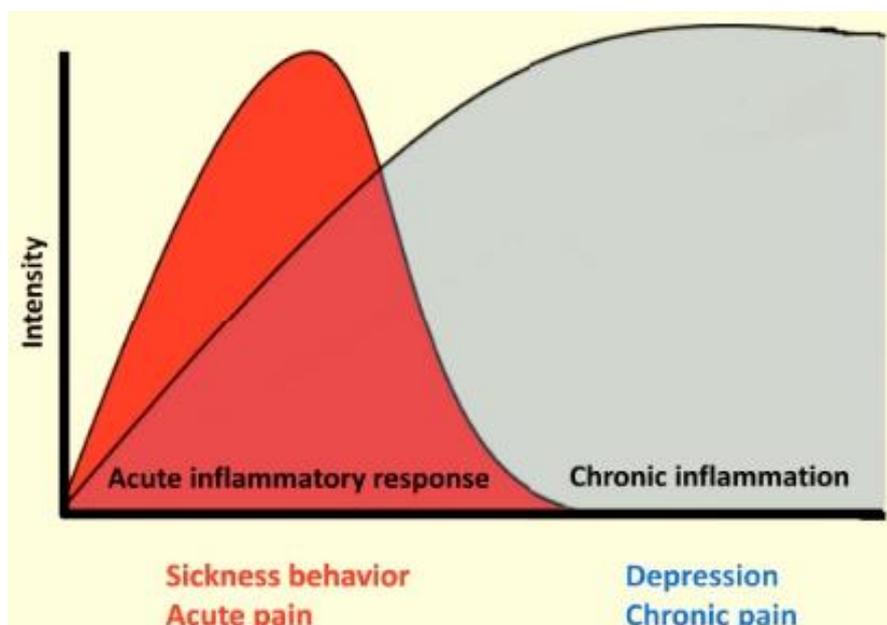


Fig. 4 – Graphical representation, taken from Walker AK et al,⁹⁷ which depicts the timing and overlapping interaction of acute pain and sickness with depression and chronic pain.

4.0: Clinical Implications

Research has shown that those experiencing severe mental illness have a two to three fold higher associated mortality burden in comparison to the general population.^{102,103} A large proportion of this mortality burden – 60 % - is attributed to physical illness.^{104,105}

It is evident that the relationship between physical and mental health has significant clinical implications, and yet research shows that mentally ill patients prevalently do not receive the holistic care they need. This has been exemplified by research that showed many patients were not being tested for metabolic risk factors – a common associated physical comorbidity with severe mental illness – at an alarmingly high rate.¹⁰⁶

This literature review has highlighted the importance of a variety of direct and indirect factors that affect the development of mental and physical disease. It is important to put the knowledge of these into practice, by facilitating discourse with patients and deciding on effective lifestyle interventions, to help them keep both their mental and physical state healthy.

A lifestyle intervention programme carried out on a Canadian population clearly illustrated the efficacy of incorporating this approach into disease management. A total of 110 patients diagnosed with schizophrenia, bipolar disorder or schizoaffective disorder took part in the study, with 59 in the experimental group and the rest in the control group. All of the patients in the study were being treated with atypical antipsychotics - pharmacological agents known to cause substantial weight gain and thus an increase in physical health complications.^{107,108}

Those in the experimental group were given dietary education, physical activity counselling and a structured exercise programme for 18 months. At the end of the study, those in the experimental group showed significantly positive mean differences in their lipid profiles, body weight, BMI and waist circumference, clearly exemplifying the beneficial impact of a programme like this.¹⁰⁸ Furthermore, a recent systematic review exploring workplace physical activity, found that yoga practice had strong associations with the reduction of anxiety symptoms.¹⁰⁹

Psychiatrists, general practitioners and healthcare workers need to work cohesively within their multidisciplinary teams to help mentally ill patients to easily access healthcare, overcome societal stigmas and participate in intervention programmes. Patients should be guided to interventions that specifically target their personal risk factors for developing physical disease, such as their employment, physical activity levels or social interactions.

5.0: Conclusion

In conclusion, this literature review has attempted to elucidate the complex relationship between mental and physical health, and cement the notion that they cannot be assessed as two separate systems. Direct mediators and indirect mediators of the relationship, and the usefulness of targeting these mediators through intervention programmes have been highlighted.

In the UK as the ageing population continues to grow, and with it the amount of chronic comorbidities, the importance of a medical practitioner's holistic approach increases in preventing the personal and economic burden of comorbid physical and mental disorders. Future research should explore whether a specific framework could be used to assess physical and mental health together in general practice, within a short ten-minute consultation, and whether it could be successful enough to impact on health policy associated with chronic conditions.

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