



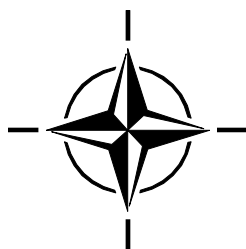
STO TECHNICAL REPORT

TR-HFM-175

Medically Unexplained Physical Symptoms in Military Health

(Symptômes physiques médicalement
inexpliqués dans la santé militaire)

Final Report of the Research and Technology Group HFM-175.



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- SAS System Analysis and Studies Panel
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List of Acronyms

ALA	Allostatic Load Awareness
BMI	Body Mass Index
CBRN	Chemical Biological Radiological and Nuclear
CBT	Cognitive Behavioral Therapy
CCEP	Comprehensive Clinical Evaluation Program
CMH	Central Military Hospital
CNS	Central Nervous System
CRF	Corticotrophin-Releasing Factor
CRP	C Reactive Protein
CT	Computer Tomography
DHEA	Dehydroepiandrosteron
DoD	Department of Defense (United States)
DSM	Diagnostic and Statistical Manual of mental disorders
DTI	Diffuse Tensor Imaging
EEG	Electro Encephalo Gram
EMDR	Eye Movement Desensitisation and Processing
ENT	Eyes Nose Throat
GP	General Practitioner
H/H	High/High
H/L	High/Low
HDL	High-Density Lipoprotein
HDL-C	High-Density Lipoprotein C
HPA	Hypothalamic Pituitary Adrenal
HR	Heart Rate
ICD	International Classification of Disease
IED	Improvised Explosive Device
IGF	Internal Growth Factor
IT	Information Technology
L/H	Low/High
L/L	Low/Low
LDL	Low Density Lipoprotein
LDL-C	Low-Density Lipoprotein Cholesterol
MMHC	Dutch Military Mental Health Care
MOD	Ministry Of Defence (Netherlands)
mTBI	mild Traumatic Brain Injury
MUPS	Medically Unexplained Physical Symptom
NATO	North Atlantic Treaty Organization
NHMRC	National Health and Medical Research Council
OOTW	Operations Other Than War

PDS	Post-Deployment Syndrome
PTSD	Post-Traumatic Stress Disorder
SCEBS	Somatic, Cognitions, Emotions, Behavior, Social system
SCP	Specialized Care Program
SGT	Sergeant
SSRI	Selective Serotonergic Reuptake Inhibitor
STO	Science and Technology Organization
TNF	Tumor Necrosis Factor
U.S./USA	United States of America
UK	United Kingdom
UNPROFOR	United Nations Protection Force
UNTAC	United Nations Transitional Authority in Cambodia
VIP	Very Important Person
VU	Vrije Universiteit [Free University]
WRAMC	Walter Reed Army Medical Center

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Medically Unexplained Physical Symptoms in Military Health

(STO-TR-HFM-175)

Executive Summary

The somatic consequences of exposure to the threat and horror of war have been documented across the millennium. Invariably there is a tension between psychosomatic and physical explanations for post-deployment symptoms. This debate is part of the longstanding quandary in classification about the definitions of functional syndromes in medicine and psychiatry. The terms are often confusing, mixing constructs about description and causation. Every specialty has its explanation and largely ignores the competing hypothesis, which adds to the challenge of managing post-deployment symptom presentations.

The group conducted meetings to explore the topic and contribute research to write a report. Several papers have been produced by team members that have been published in peer-reviewed journals. The essential information that is relevant for this report has been isolated and included. The group began by producing four white papers, which are included in the Annex.

This group focused on:

- The development of an operational definition of MUPS in military setting ('how many specialists do you need to see before the diagnosis MUPS');
- The identification of approaches that NATO partners use to diagnose deployment related health problems ('what is everybody doing');
- The determination of the status of the epidemiology of MUPS among NATO Partners ('what is known');
- The exploration of a consensus on tools of a set of diagnostic tools for diagnosing MUPS ('how can we do better'); and
- The formulation of a set of best practices guidelines for MUPS ('how to identify, treat, manage and return to duty').

The following definitions allow for common understanding and standardization of Medically Unexplained Physical Symptoms (MUPS) across NATO Nations. An agreed-upon definition can also help to coordinate other strategies such as health and environmental surveillance, and the evaluation of deployment health outcomes:

- MUPS may be defined as physical symptoms that prompt the sufferer to seek health care, but remain unexplained after an appropriate medical evaluation.
- MUPS are perceptual (a person feels symptoms), cognitive (the person experiencing symptoms decides they are ominous), and behavioral (the person with symptoms seeks health care for them).
- Patients with MUPS are pervasive in medical practice and perhaps even more so in neurologic settings. Medical science, with its emphasis on identifying etiologically meaningful diseases comprised of homogeneous groups of patients, has split MUPS into a number of diagnostic entities or syndromes, each with its own hypothesized pathogenesis. However, research suggests these syndromes may be more similar than different, sharing extensive phenomenological overlap and similar risk factors, treatments, associated morbidities, and prognoses.

- MUPS tend to occupy a disproportionately large share of physician time and contribute to physician frustration.

MUPS are strongly and consistently associated with:

- Psychosocial distress;
- Psychiatric disorders;
- Decreased quality of life; and
- Increased health care utilization.

Symptômes physiques médicalement inexpliqués dans la santé militaire (STO-TR-HFM-175)

Synthèse

Les conséquences somatiques de l'exposition à la menace et à l'horreur de la guerre ont été documentées tout au long du millénaire. Il existe invariablement une tension entre les explications psychosomatiques et physiques des symptômes post-déploiement. Ce débat fait partie du long dilemme portant sur les définitions qui permettent le classement des syndromes fonctionnels en médecine et en psychiatrie. Les termes sont souvent déroutants, mélangeant des concepts de description et de causalité. Chaque spécialité a son explication et ne tient pas compte de l'hypothèse concurrente, ce qui complique la gestion des symptômes post-déploiement.

Le groupe a organisé des réunions pour étudier le sujet et contribuer aux travaux de recherche afin de rédiger un rapport. Les membres du groupe ont rédigé plusieurs articles qui ont été publiés dans des revues spécialisées. Les informations essentielles pertinentes pour ce rapport ont été identifiées et incluses. Le groupe a commencé par rédiger quatre livres blancs, inclus en annexe.

Ce groupe s'est concentré sur :

- Le développement d'une définition opérationnelle des SPMI dans le contexte militaire ('combien de spécialistes faut-il consulter avant que le SPMI soit diagnostiqué') ;
- L'identification des démarches utilisées par les partenaires de l'OTAN pour diagnostiquer les problèmes de santé liés au déploiement ('ce que fait chacun') ;
- La détermination de l'état de l'art en matière d'épidémiologie des SPMI parmi les partenaires de l'OTAN ('ce qui est connu') ;
- La recherche d'un consensus sur les outils de diagnostic des SPMI ('amélioration possible') ; et
- La formulation d'un ensemble de principes directeurs des meilleures pratiques au sujet des SPMI ('méthode d'identification, de traitement, de gestion et de retour au travail').

Les définitions qui suivent permettent une compréhension commune et une normalisation des symptômes physiques médicalement inexpliqués dans les pays de l'OTAN. Une définition commune peut également aider à coordonner d'autres stratégies telles que la surveillance sanitaire et environnementale et l'évaluation de la santé après le déploiement :

- Les SPMI peuvent être définis comme des symptômes physiques qui poussent le patient à rechercher des soins, mais restent inexpliqués après une évaluation médicale appropriée.
- Les SPMI sont perceptifs (une personne ressent les symptômes), cognitifs (la personne qui ressent les symptômes décide qu'ils sont inquiétants) et comportementaux (la personne qui ressent les symptômes recherche des soins).
- Les patients souffrant de SPMI sont omniprésents dans la pratique médicale et peut-être même davantage dans les contextes neurologiques. La science médicale, qui met l'accent sur l'identification de maladies à l'étiologie explicite composé de groupes homogènes de patients, a divisé les SPMI en un certain nombre d'entités diagnostiques ou syndromes, chacun ayant sa pathogénie hypothétique.

Cependant, la recherche suggère que ces syndromes pourraient avoir plus de points communs que de différences, partageant en grande partie leur phénoménologie et des facteurs de risques, traitements, une morbidité associée et un pronostic similaires.

- Les SPMI tendent à occuper une part disproportionnée du temps des médecins et contribuent à la frustration des praticiens.

Les SPMI sont fortement et régulièrement associés à :

- Une détresse psychosociale ;
- Des troubles psychiatriques ;
- Une dégradation de la qualité de vie ; et
- Un usage accru des soins de santé.

Chapter 1 – HISTORICAL PERSPECTIVE

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1.1 INTRODUCTION

Every major conflict of the last 150 years brings with it concern about the health of returning veterans [6]. Invariably there is a tension between psychosomatic and physical explanations for post-deployment symptoms [5]. This debate is part of the longstanding quandary in classification about the definitions of functional syndromes in medicine and psychiatry [15], [12]. The terms are often confusing, mixing constructs about description and causation. These problems of definition are exemplified in the post-deployment syndromes where battlefield hazards leave veterans concerned about a range of potential toxic exposures and the effects that they may have on long-term health. These concerns are often further inflamed by confusing scientific disagreements, sensational news media coverage, and rancorous political debate.

The somatic consequences of exposure to the threat and horror of war have been documented across the millennium. Herodotus reported that following his exposure in the Battle of Marathon in 490 BC, Epizelus “... whilst behaving valiantly was deprived of sight although he was wounded in no part of his body, nor struck from a distance” [16]. This report highlights how apparent neurological injury can occur without an obvious wound.

One characteristic is the search for explanation for these symptoms. In the Napoleonic Wars, a condition of cerebrospinal shock was described where individuals suffered tingling of the nerves when they returned from combat. This was attributed to wind contusions caused by a shell passing close by. It was presumed that the patient’s nerves had been bruised by the force of the passing wind [7]. In the Balkans Wars of 1912 to 1913, Dr. Octave Laurent proposed the existence of a condition called “cerebromedullary shock” where the individual suffered from a variety of neurological symptoms from tingling to complete cataplexies. This condition arose when shells caused sudden changes in atmospheric pressure that affected the middle ear [7].

The outbreak of the World War I led to the unexpected emergence of considerable rates of soldiers developing a range of neurological and psychological symptoms, preventing them from fighting. Myers on 15 February 1915 wrote the first known description of shell shock. He attributed the disease to “... the concussive effects of exploding shells”. He emphasised that an important aspect of this condition was where the individual’s normal personality was replaced by the “emotional personality”. An enquiry into this condition at the end of the War concluded that this in fact was not due to neurological injury but an underlying psychiatric disorder [11]. The modern formulation of the potential role of concussive injury is an issue that obviously has been considered repeatedly in the course of history.

In World War I, the impact of gas exposure opened up the problem of determining whether there was substantial physical pathology or whether the soldier had develop effort intolerance due to “occult gas” exposure [1]. These complex clinical diagnostic challenges highlighted the intertwined nature of psychological presentations even when a clear toxic agent was in use on the battlefield. The problem of determining whether clinically significant gas exposure had occurred was exemplified by the fact that the U.S. Forces reported 70,552 gas casualties at the end of the war but by 1925, 300,000 soldiers had applied for war relief alleging “gas disability”. These numbers highlight the potential for the misattribution of causation by veterans, many of whom had substantial legitimate symptoms, many with a psychological origin.

HISTORICAL PERSPECTIVE

A report on the experience of the U.S. Forces into the common psychological presentations in World War I highlights how somatic symptoms were conceptualised as being a core of traumatic neurosis and neurasthenic neurosis [1]. As a matter of diagnostic parsimony, the physical and psychological symptoms were seen as being inseparable. This perspective is one that should be revisited because it does not partition somatic and psychological symptoms and this approach has a utility in wars where blast exposure, chemical weapons and psychological trauma were all seen as intersecting aspects of the combatants' experience.

This formulation was similar to earlier accounts of post-deployment syndromes such as nostalgia [4] which was described amongst the Spanish troops fighting in the Netherlands, included:

- Melancholy;
- Insomnia;
- Weakness;
- Loss of appetite;
- Anxiety;
- Cardiac palpitations;
- Stupor; and
- Fever.

This syndrome had both neurological symptoms, those of autonomic hyperarousal and descriptive elements of the individual's mental state. A committee set up in 1865 investigated a post-deployment syndrome in the UK troops following the Crimean War which was called disordered action of the heart. This concluded that this condition was caused by the belting and tight collars which constricted the action of the heart leading to a change in uniform design. This formulation and approach inevitably was impacted upon by the American Civil War which led to the description of the Da Costa syndrome. This was a constellation of symptoms of tiredness, lethargy, depression, diarrhoea, and breathlessness that was seen to be due to the malevolence of war.

The continued emergence of post-deployment syndromes has continued to dominate the discussions about the veterans of recent wars such as the Gulf War, the Vietnam War and the most recent Middle East conflicts. In the Gulf War there was intense concern about the effects of multiple vaccinations and protective agents for nerve gas agents. The exposure to Agent Orange in the Vietnam War was subject to a Royal Commission in Australia as cause of health problems in veterans with little evidence of any common enduring physical effects. Mild traumatic brain injury in the recent Middle East conflicts highlights how blast exposure has both physical and psychological consequences that are very difficult to disentangle. The inseparable nature of physical and psychological symptoms is almost ubiquitous and a variety of theories about the exposures which have led to these symptoms in the aftermath of conflicts. The public advocacy of veterans groups following these conflicts has led to many large-scale epidemiological and basic science studies being funded to answer some of the central questions of causation. However, the concern about cover-ups and related conspiracy theories has meant that lingering concerns are not easily dispersed.

1.2 LACK OF SYMPTOM SPECIFICITY AND THE PROBLEMS FOR DIAGNOSIS

The classification and clinical management of widespread musculoskeletal pain and related non-specific somatic distress is one of the most vexed conceptual challenges facing clinicians, whether they be physicians or mental

health professionals [8]. The magnitude of this clinical problem is considerable, given that approximately $\frac{1}{4}$ to $\frac{1}{2}$ of all presentations to primary and secondary care are as a consequence of somatic symptoms, that are not well characterised by medical conditions [8]. One of the major difficulties in creating a uniform approach to these patients has been that somatic symptoms are often picked up by various sub-specialties of medicine, which creates idiosyncratic and overlapping approaches that lack consensus [15]. In essence, two competing systems of classification have arisen, the somatoform disorders in psychiatry and functional disorders in medicine, with little cross-reference to each other [12]. This practice is confusing for medical practitioners, a fact that explains why this field is confusing and contradictory for patients, researchers, policy makers and veterans' pension entitlements.

Driving clinical practice in this domain is the important role of doctors in giving diagnoses. This lack of consistent diagnostic practice with patients presenting with MUPS is a major problem of developing broadly accepted consensus approaches. The emergence of special interest groups around the individual syndromes characterised with poorly defined symptoms means that there is little incentive within the medical profession to address the degree of overlap of these syndromes, leading to diagnostic confusion and disagreement [12]. A veteran has to try and adapt optimally in an environment where at times the media coverage of controversial research findings can foster suggestibility. Also, the willingness of some clinicians to act as advocates with special interests in aetiology of particular agents can create hypochondriacal fears among veterans. There is less agreement between the specialities than often presumed by the patient community. Every specialty has its explanation and largely ignores the competing hypothesis [9] which adds to the challenge of managing post-deployment symptom presentations.

1.3 FUNCTIONAL SYNDROMES

The functional syndromes are the group of disorders broadly considered to be different manifestation of MUPS in the practice of physicians [15]. These include:

- Irritable bowel;
- Chronic fatigue syndrome;
- Fibromyalgia;
- Myalgic encephalomyelitis;
- Non-ulcer dyspepsia; and
- Multiple chemical sensitivities.

These are syndromes where particular views about aetiology and treatment are championed by special interest clinicians [13]. The apparent validity of the diagnostic criteria for these syndromes is accepted in the published literature, despite the fact that there is a high degree of overlap between the symptoms of these syndromes. The precise diagnosis that a patient is given has more to do with the clinician who is consulted than the specificity of an individual's complaints. The overlap of these disorders, in other words is considerable.

Diagnosis is ultimately a pragmatic endeavour towards a treatment plan that sometimes gets confused with the issues of explanation or cause. The importance of diagnosis is often over-weighted in the debate treatment plans for somatoform disorders as there are many commonalities in the treatment of these syndromes [10]. The cause ultimately only matters if there is a specific treatment tied to an understanding of the mechanisms of aetiology. Hence with post-deployment syndromes the obsession of some professional and veteran's groups for establishing the cause, if this remains inconclusive and controversial, is ultimately not very relevant to the need for treatment. Hence the definition of entitlements and the need for treatment are often activities that can be contradictory.

In the post-deployment setting diagnosis serves the role of acknowledgment to the veteran for the sacrifice of their health for the nation and purposes of compensation. Deferring to the causal model should be understood for its distraction from the primary need for care. There are multiple agendas that impinge on this setting where there is the challenge of integrating the debates from the research literature with agreed clinical interventions that do not harm through false attributions. There are a number of examples in medicine of the importance of not to get distracted by the competing agendas in the scientific literature about aetiology such as with cancer where the cause has little impact on the treatment regime selected. This pragmatic approach works for other real diseases such as multiple sclerosis and cardiac failure.

A longstanding issue which has never been resolved in psychiatry is the extent to which somatic distress is a distinct but inescapable dimension of psychiatric disorder [2]. Just as anxiety and depression are highly correlated, so are somatic symptoms, in psychiatric disorders such as depression and post-traumatic stress disorder, somatic distress is almost a ubiquitous component including symptoms such as fatigue and pain [3]. A further analysis of these questions in the respective national comorbidity studies has demonstrated that back pain and joint pain have a strong relationship with the presence of psychological disorders [14]. However, this overlap has not been systematically addressed in psychiatric classification and has put to one side the significant degree of correlation between somatic distress, anxiety, and depression [2].

One of the difficulties is that different diagnostic categories depend upon symptoms being able to separate disorders. However, the specificity and sensitivity of many symptoms is relatively low and subtle clinician preferences that can influence the history taking process leads to substantial variances in diagnostic practice. However, the use of structured diagnostic interviews in epidemiological studies does provide a basis where some of this overlap can be addressed.

The clinical challenge that is often inadequately addressed is the differentiation of the acute response, i.e., concussion, and the prolonged and delayed effects. One of the critical challenges for the clinician is to validate the acute concussion of the patient, while creating a positive expectancy about the outcome, rather than focusing on the potential that the concussion may later lead to disorder symptoms.

1.4 REFERENCES

- [1] Schaller, W.F., Diagnosis in Traumatic Neurosis. *Jama*. 1918;71(5):338–347. doi:10.1001/jama.1918.02600310016006.
- [2] Goldberg, D., A dimensional model for common mental disorders, *Br J Psychiatry Suppl*: 44-9, 1996.
- [3] Henningsen, P., Zimmermann, T. and Sattel, H., Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review, *Psychosom Med* 65:528-33, 2003.
- [4] Hofer, J. (1688), *Medical Dissertation on Nostalgia*, The Institute of the History of Medicine, 1934, pp. 376-391.
- [5] Hyams, K.C., Wignall, S. and Rosewell, R. (1996), War syndromes and their evaluation: from the US Civil War to the Persian Gulf War, *Annals of Internal Medicine*, 125, pp. 398-405.
- [6] Ikin, J.F., Sim, M.R., Creamer, M.C., Forbes, A.B., McKenzie, D.P., Kelsall, H.L., Glass, D.C., McFarlane, A.C., Abramson, M.J., Iltak, P., Dwyer, T., Blizzard, L., Delaney, K.R., Horsley, K.W.A.,

- Harrex, W.K. and Schwarz, H., War-related psychological stressors and risk of psychological disorders in Australian veterans of the 1991 Gulf War, *British Journal of Psychiatry*, 2004, 185(2):116-26.
- [7] Jones, E. and Wessely, S., *Shell Shock to PTSD: Military Psychiatry from 1900 to the Gulf War*, Maudsley Monograph 47, Hove: Psychology Press, 2005.
- [8] Kroenke, K. and Price, R.K., Symptoms in the community: prevalence, classification, and psychiatric comorbidity, *Arch Intern Med* 1993, 153:2474-2480.
- [9] Schur, E.A., Afari, N., Furberg, H., Olarte, M., Goldberg, J., Sullivan, P. F. and Buchwald, D. (2007). Feeling bad in more ways than one: comorbidity patterns of medically unexplained and psychiatric conditions. *J Gen Intern Med*, 22(6), 818-821. doi: 10.1007/s11606-007-0140-5.
- [10] Sharpe, M. and Mayou, R., Somatoform disorders: a help or hindrance to good patient care? *Br J Psychiatry*, 2004, 184:465-467.
- [11] Southborough, Lord. Report of the War Office Committee of Enquiry into "Shell-Shock", London, His Majesty's Stationery Office, 1922.
- [12] Strassnig, M, Stowell, K.R., First M.B. and Pincus, H.A., General medical and psychiatric perspectives on somatoform disorders: separated by an uncommon language, *Curr Opin Psychiatry*, 2006, 19:194-200.
- [13] Talley, N.J. and Spiller, R., Irritable bowel syndrome: a little understood organic bowel disease?, *Lancet* 2002, 360:555-564.
- [14] Von Korff, M., Crane, P., Lane, M. *et al.* (2005), Chronic spinal pain and physical-mental comorbidity in the United States: results from the national comorbidity survey replication, *Pain*, 113:331-9.
- [15] Wessely, S. (2006), Introduction. The health of Gulf War veterans, *Philos Transactions of Royal Society London Biological Science*, 361:531-2.
- [16] Anonymous, War Neurosis in the Battle of Marathon, 1919, *Mental Hygiene* 3:676.



Chapter 2 – THE NO-MAN’S LAND OF POST-DEPLOYMENT SYNDROMES: THE CURRENT ATTEMPTS TO CAPTURE THIS TERRITORY AND THE UNCERTAINTIES ABOUT MTBI

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ABSTRACT

Mild traumatic brain injury is considered the current signature injury of the Wars in Iraq and Afghanistan but has been conceptualised differently in the Western major allies. This chapter addresses the historical context of post-deployment syndromes and suggests that the current debate about the conflicting perspectives of mTBI must be addressed with caution informed in the context of this history. An examination of the literature of medically unexplained symptoms also highlights the risks to the health of veterans if individual medical specialities vie for supremacy of their formulation of this complex issue. The lack of consensus of the definitions and the absence of specific treatment approaches directed by a particular diagnosis highlights the risks of presuming there is a specific disease-based treatment. The differences in the formulations also are influenced to a significant degree by the structure of the health systems and definition of diseases required for compensation entitlements explains some the divergent literature. While psychiatric disorders such as PTSD may explain some of this morbidity, the limitations of psychological constructs need to be acknowledged. Equally the non-specific nature of the post-concussion symptoms means that their sole attribution to a brain injury ignores the substantial association PTSD and depression with these symptoms. Allostatic load and sensitization are constructs that may progress the understanding of the mechanism of the syndromes and the aetiological role of stress in physical and psychological symptoms.

2.1 INTRODUCTION

This chapter will review the different conceptual approaches which have been taken in the past to explore the nature of post-deployment syndromes and propose a method of approaching the emerging data from the studies conducted of veterans from the most recent conflicts in Iraq and Afghanistan. Kardiner and Spiegel [31] characterised the investigation of this area with the following summary. “These conditions are not subject to continuous study ... but only to periodic efforts which cannot be characterised as very diligent ... though not true in psychiatry generally, it is a deplorable fact that each investigator who undertakes to study these conditions considers it his sacred obligation to start from scratch and work at the problem as if no one had ever done anything with it before”.

This statement should be taken as a warning for any researcher or clinician who wishes to discuss this domain and highlights the importance of careful scrutiny of often a forgotten literature of previous wars to distil past lessons which may have been forgotten in the fog of time. Glass [20] similarly in summarising the mental health programs in the U.S. Forces from a historical perspective cautioned (page 804) that “... *practically all available psychiatric diagnoses indicate the existence of organic or intrapsychic pathology ... as yet there is little usage of diagnostic designation for failure of adaptation, which would include both external and internal determinants of behaviour*”. This formulation is relevant to the psychosomatic syndromes arising from the exposure to combat.

These warnings emphasise the particular responsibility of all those involved in formulating and understanding of post-deployment syndromes of carefully attending to the earlier mistakes and knowledge derived from earlier conflicts.

2.2 THE THREAT OF CURRENT WAR

The question about the nature post-deployment syndromes which has gained greatest attention, in the aftermath of the studies of troops, deployed to Iraq and Afghanistan is the extent to which the symptoms and syndromes are either explained by mild traumatic brain injury or post-traumatic stress disorder [25]. This concern has arisen in the light of the threat and mortality arising in these conflicts from the use of the Improvised Explosive Devices (IEDs). For example, the figures from the UK Military¹ provided information that emphasises the reality of this apprehension. On the occasion of the death of the 300th British individual in active service in Afghanistan, it highlighted that 205 had been killed by explosions, 57 by small arms fire, 26 by accidents, 9 by friendly fire, 1 had been murdered, and 2 suicided.

IED blasts have been estimated to account for about 40% of all United States military casualties in the Iraq and Afghanistan conflicts (Brookings Institution, 2007 as cited in Ref. [61]) and “*appears to account for a larger proportion of casualties than it has in other recent US wars*” (Ref. [43], p. 2044). IEDs pose a particular concern to soldiers and other combatants because they are difficult to identify and military personnel are unable to act in a proactive manner in the face of a blast event. Although IEDs are associated with a large number of military casualties, the estimated ratio of individuals wounded by IEDs to fatalities in Iraq and Afghanistan is relatively high [61]. For every nine wounded, there is approximately one fatality. In contrast, Tanelian and Jaycox [61] calculated that the ratio of battle deaths to wounded in World War II was 1:2.4 and the fatality to wounded ratio in Vietnam was 1:3 (data cited from Ref. [17]). Although the mortality rate is low, injuries resulting from IED blasts can be multiple and can involve severe injuries to extremities, particularly for those in close proximity to the blast.

The risks of being exposed to the hidden and unpredictable threat of the IEDs inevitably pervade the mind of combatants. Every individual who has fought must be vigilant and preoccupied about the threat of these hidden weapons. It is therefore not surprising that the consequences of explosions and particularly head injuries have come to preoccupy the debate about the consequences of this conflict. Developments in body armour means that individuals are now surviving a catastrophic explosion often with multiple limb amputations and the threat of significant head injury at rates that previously were unknown in a combat environment. In this setting, it is important to revisit previous debates about this question, as well as data obtained from civilian studies to optimise a formulation of the best way to understand the health outcomes of those exposed.

One important aspect of the impact of an IED is that the experience of the moment of the loss of consciousness is a central to any traumatic memory. For a person who dies this moment of losing consciousness is the memory

¹ The Guardian, 25 June 2010.

of death. The potential of such an experience to cause PTSD is obvious. At this moment of losing consciousness it is unknown to the soldier whether he/she will live or die. Subsequently any reminder of this moment will be a critical aspect of a traumatic memory that provokes anxiety. Hence any introceptive experience that subtly or unconsciously evokes concerns such as subtle disturbances of awareness may bring back this fear memory about the state of mind at the point of the explosion. Dissociative symptoms (amnesia or derealisation) [7] or disordered memory and concentration may be traumatic triggers. This context is critical in differentiating the effects of unconsciousness in a sports injury as against war. The media also has emphasised the risk of IED exposure with the graphic images that readily capture the public's attention and concern about the risks of IED exposure.

The impact of mTBI on executive function may result in unregulated recall of the trauma that may also exacerbate PTSD symptoms. There may also be reduced facility to cope with PTSD as a result of mTBI-induced neuropsychological changes that impact cognitive resources. For example, the damage caused by mTBI may impede the ability of an individual to helpfully appraise the event and find strategies to prevent rumination, as well as engage in coping strategies more generally [6], [66]. There may also be increased risk of PTSD as a result of mTBI interrupting the way in which the memory of the trauma is laid down. Some studies have shown that lack of memory of a traumatic event (e.g., as a result of peritraumatic amnesia and/or dissociation) has been associated with worse PTSD outcomes [7], [40], [64].

Individuals with mTBI demonstrate decreased activation in the hippocampus, which is responsible for memory processes (see Ref. [66] for a review). Such an injury may impact the ability to accurately encode the memory of the trauma and also impact the subsequent processing of the trauma event [66]. Cognitive deficits that result following mTBI interfere with the formation of coherent and well-integrated memories which is likely to impact PTSD severity if present [66].

In contrast, the threats in the First Gulf War were less graphic, such as the complications of multiple vaccinations and the threats from invisible biological and chemical weapons. The use of protection measures such as alarms were also associated with the risk of adverse health outcomes. The many false alarms created conditioned response between the threat and the attendant vigilance about the physical symptoms emerging as a consequence of the attack that had not eventuated [9]. In that war, the duration of the combat exposure was brief in contrast to the prolonged exposure to threat and the consequence of necessary hypervigilance that occur prior to the commencement of conflict. When the health consequences were initially discussed, PTSD was seen to be a minimal possibility due to the brief duration of the combat phase which encouraged the emergence of other diagnostic hypotheses to explain the multiple somatic symptoms that many veterans presented with [32]. The most evocative images of that war were of gassed Kurdish civilians and oil well fires in Kuwait which further added to the concerns about the threats from environmental exposures.

2.3 THE CURRENT PROBLEM

One of the current difficulties in the literature is the strikingly different emphasis that has emerged from the studies conducted in the United States and the United Kingdom. Most studies examining deployment-related mTBI and associated post-deployment functioning in Afghanistan and Iraq veterans have been conducted by American researchers (e.g., Refs. [5], [26], [44], [45], [52] and [62]). There has been a major focus on the neural and cellular consequences of mTBI in the U.S. literature (e.g., Ref. [11]). The high profile of mTBI in the U.S. has also influenced health care provision and compensation policies for American military personnel [25].

One notable change has been that in the U.S., deployment-related mTBI is now recognised as an injury for which a Purple Heart may be awarded. A Purple Heart is a military decoration awarded to any member of the

U.S. Defense Force who is wounded or killed during service as a result of enemy action [1]. These social forces have driven a greater propensity to attribute the non-specific symptoms in veterans to mTBI rather than depression or PTSD. Also the substantial differences in veterans' entitlements in the United Kingdom, United States, Canada and Australia may account for the different focus of this debate. The lack of alternative universal health care insurance and care in the U.S. and the necessity of a U.S. veteran to have sustained disability is critical to the focus of the differences in emphasis in the literature.

This matter is not a trivial issue due to the dangers of "pseudodiagnosis and pseudodisability" in populations where it difficult to objectively define damage or disease in compensation settings [35]. The central issue is the mTBI in the U.S. has a unique currency as a diagnosis where the doctor uses this label to validate payment for diagnostic and therapeutic services and access to disability pensions. The excessive focus on one possible explanation with the aggregations of symptoms that are currently being attributed to mTBI fails to heed the well-established knowledge about the overlap between functional somatic symptoms [68], [53].

Researchers from the United Kingdom have published on head injury in military personnel from Iraq [16] and have also recently published data relevant to military personnel in both Iraq and Afghanistan [50]). These studies have highlighted the non-specific nature of post-concussion symptoms and the fact that other exposures readily explain their occurrence. This emphasis is similar to the Canadian [69] and Dutch [14] research that has published data related to military personnel in Afghanistan.

The difference between the United States and United Kingdom position is perhaps best characterised by the conclusion stated in the review of the UK group about the history of shell shock and mild traumatic brain [28]. They concluded: *"Despite a vigorous debate, physicians failed to identify or confirm characteristic distinctions. The experiences of the armed forces of both the United States and the United Kingdom during World Wars I and II led to two conclusions: that there were dangers in labeling anything as a unique "signature" injury and that disorders that cross any divide between physical and psychological require a nuanced view of their interpretation and treatment. These findings suggest that the hard-won lessons of shell shock continue to have relevance today."* This review highlights the importance of the propensity for the possibility of concussive injury to be the cause of post-deployment symptoms.

There is a need to face these differences of approaches is critical if the mistakes of the past are not to be repeated. The research agenda and literature about mTBI needs to consider the substantial background literature of identifying *"controversial idiopathic controversial symptom syndromes associated with every modern war, suggesting that war typically sets in motion interrelated physical, emotional and fiscal consequences of the veterans and society"* (Ref. [12], p. 707). The weight of evidence strongly argues for the public health prevention approach to these syndromes to prevent iatrogenic illness [13]. Hence there is a need to face inherent risks exist about the premature attribution of unexplained symptoms which are very common in deployed personnel to particular causes [18].

These symptoms are very common in the general population and are an area of medical practice that eludes clear elucidation and creates *"disagreements between competing medical disciplines and between clinicians and affected patients"* [12]. Furthermore, much of the current states based on a symptom-based diagnosis of mTBI fail to address the fundamental limitation articulated by Hyams [27] about the need to ensure homogeneity of the populations. In essence this problem arises from that the conclusions cannot be refuted and the basic issues remain unresolved as to whether patients with apparent mTBI are suffering from *"a unique scientifically definable illness"* (Ref. [27], p. 154).

2.4 MTBI – A RECURRING POST-DEPLOYMENT SYNDROME?

One characteristic is the search for explanation. In the Napoleonic Wars, a condition of cerebrospinal shock was described where individuals suffered tingling of the nerves when they returned from combat. This was attributed to wind contusions caused by a shell passing close by. It was presumed that the patient's nerves had been bruised by the force of the passing wind [29].

In the Balkans Wars of 1912 to 1913, Dr. Octave Laurent proposed the existence of a condition called "cerebromedullary shock" where the individual suffered from a variety of neurological symptoms from tingling to complete cataplexies. This condition arose when shells caused sudden changes in atmospheric pressure that affected the middle ear [29].

The outbreak of the World War I led to the unexpected emergence of considerable rates of soldiers developing a range of neurological and psychological symptoms, preventing them from fighting. Myers [42] on 15 February 1915 wrote the first known description of shell shock. He attributed the disease to "... *the concussive effects of exploding shells*". He emphasised that an important aspect of this condition was where the individual's normal personality was replaced by the "emotional personality". An enquiry into this condition at the end of the War concluded that this in fact was not due to neurological injury but an underlying psychiatric disorder [58]. The modern formulation of the potential role of concussive injury is an issue that obviously has been considered repeatedly in the course of history. Rivers [49] in his seminal paper on "*The Repression of War Experience*" used a case series, a number of who had been exposed concussive blasts. For example, he described "*the case of a young officer who was flung down by the explosion of a shell so that his face struck the distended abdomen of a German several days dead, the impact of his fall rupturing the swollen corpse*." In another case who had been concussed and buried by a previous shell explosion "*collapsed altogether after a very trying experience, in which he had gone out to seek a fellow officer and had found his body blown into pieces, with head and limbs lying separated from the trunk*". These case descriptions highlight the experiential aspects of blast exposure and the potential to be highly traumatic and cause psychopathology.

An issue that deserves conceptual comment is that these formulations about the importance of concussive injury focus on the issue of the presumed cause of the psychological symptoms. This attribution of an aetiological mechanism has often then become the subject of considerable controversy. From a diagnostic point of view, the symptoms attributed to a particular cause such as concussive injury from exploding shells are often highly non-specific and can arise from a number of other causes. The clinical challenge that is often inadequately addressed is the differentiating of the acute response, i.e., concussion, and the prolonged and delayed effects. One of the critical challenges for the clinician is to validate the acute concussion of the patient, while creating a positive expectancy about the outcome, rather than focusing on the potential that the concussion may later lead to disorder symptoms [63]. Stigma is an issue. There has been a longstanding tension about the somatic aetiology of post-traumatic morbidity that has oscillated between functional somatic syndromes and psychiatric disorder. One of the clinical limitations of the psychiatric diagnoses is that they do not capture somatic dimensions of patients' distress and preoccupation. Symptoms of skeletal pain, fatigue and headaches are very common in PTSD [52], [38], [34] which leads to particular confusion and frustration in those with physical injuries where misattribution of the cause of these symptoms. The treatment and aetiology of whiplash is a disorder which evokes similar clinical challenges and uncertainties. This debate raises the classification dilemma as to how to deal with somatization disorders and Fabrega [15] has cautioned about social and political issues about compensation distract from the scientific evidence. The debate around mTBI and the different conceptualisations is a quintessential example of how politics and compensation can impact on the conceptualisation of disease.

2.5 NEURAESTHENIC NEUROSES AND SOMATIC POST-DEPLOYMENT SYNDROMES

The somatic morbidity associated with PTSD has been more clearly established in the recent literature [37]. However, the current DSM-IV and proposed DSM-V diagnostic criteria have been lost the physical symptoms in the diagnosis of PTSD that were included in the original formulation in DSM-III. The original criteria were partly based on the observations of Kardiner who saw traumatic neurosis as a physioneurosis [30]. The failure to focus on the physical symptoms in PTSD is problematic for several reasons. Firstly it presumes the predominance of the psychosocial distress in traumatic event in contrast to the fact that the memory of the event may also encapsulate physical distress and traumatic injury that may also be present. One of the challenges in this domain is that the many factor analytic studies of the structure of PTSD based on our current computation capacity to analyse large questionnaire data sets that are systematically collected (e.g., Ref. [19]). However, the lack of somatic symptoms in these analyses in the last two decades means that the relevance of somatic symptoms and how they map on PTSD is missed [2]. For this reason some of the earlier less systematic observational studies of traumatic neurosis are worthy of examination of the insights they provide without the bias created by current formulations of the trauma response.

A valuable report on the experience of the U.S. Forces into the common presentations in World War I highlights how somatic symptoms sit at the core of traumatic neurosis and how this was conceptualised as form of neurasthenic neurosis [3]. This article not only highlighted the non-specific nature of the symptoms observed in neuropsychiatric casualties but also emphasised the role of suggestion in its aetiology. The list of symptoms focuses on somatic symptoms such as fatigue, cardiac irritability, rapid pulse, pain over the heart, and vomiting as well, there are psychological symptoms such as terrifying dreams with war content, lack of confidence and convulsions. As a matter of diagnostic parsimony, the physical and psychological symptoms were seen as being inseparable. This perspective is one that should be revisited because it does not partition somatic and psychological symptoms.

This formulation was similar to earlier accounts of post-deployment syndromes such as nostalgia [24] which was described amongst the Spanish troops fighting in the Netherlands, included:

- Melancholy;
- Insomnia;
- Weakness;
- Loss of appetite;
- Anxiety;
- Cardiac palpitations;
- Stupor; and
- Fever.

This syndrome had both neurological symptoms, those of autonomic hyperarousal and descriptive elements of the individual's mental state. A committee set up in 1865 investigated a post-deployment syndrome in the UK troops following the Crimean War which was called disordered action of the heart. This concluded that this condition was caused by the belting and tight collars which constricted the action of the heart leading to a change in uniform design. The quiet chuckle which these findings now provoke should be suppressed because the somewhat quaint conclusions highlight the risk of making aetiological attributions. This formulation and

approach inevitably was impacted upon by the American Civil War which led to the description of the Da Costa syndrome [10]. This was a constellation of symptoms of tiredness, lethargy, depression, diarrhoea, and breathlessness that was seen to be due to the malevolence of war. Nostalgia was also a syndrome used to characterise combat casualties in this setting.

In the civilian sector, the term “neuroasthenia” was simultaneously described by Beard in 1869 [4] as a “*disease of the nervous system, without organic lesion ... characterised by enfeeblement of nervous force*”. In the civilian sector it was also noted to be related to Railway Spine which was first described by Ericson as having an organic cause in 1866. However, in 1889, Oppenheim suggested that the term traumatic neurosis should be used to describe this syndrome. Hence, there was a significant overlap between the concerns and clinical challenges being faced by civilians in clinical practice and those in the military domain. The similarity of the debates in that civilian and military patients reflected the debate between psychiatry and neurology.

The continued emergence of post-deployment syndromes in the setting of recent wars such as the Gulf War, exposure to Agent Orange in the Vietnam War, and mild traumatic brain injury highlight the inseparable nature of physical and psychological symptoms and a variety of theories about the exposures which have led to these symptoms in the aftermath of conflicts.

In summary, the limitations of the current formulation of PTSD are what it does not capture, particularly somatic symptoms. The current development of DSM-V has missed this opportunity. In this revision, too much debate has focused on the fear circuitry model and cognitive constructs driven by the dominance of cognitive behaviour theorists and not enough on the general deficits of information processing. Hence PTSD as a diagnosis will continue if somatic presentations are not captured with a degree of sensitivity. Stigma is an issue. Hence, this aetiological attribution becomes a new battleground between veteran and doctor as to what is the cause of the injury. Everybody likes a physical injury rather than a psychological one.

2.6 THE CHALLENGE OF OVERLAPPING CLINICAL SYNDROMES

Neuroasthenia was a disorder where neurologists play a central role in developing the original constructs about this class of illness. Psychiatry developed as a discipline of neurology and in a number of ways, medicine has not been served well by the splitting of these disciplines particularly in the management of the dilemma as to how to advance this field. The classification and clinical management of widespread musculoskeletal pain and related non-specific somatic distress is one of the most vexed conceptual challenges facing clinicians, whether they be physicians or mental health professionals [33]. The magnitude of this clinical problem is considerable, given that approximately $\frac{1}{4}$ to $\frac{1}{2}$ of all presentations to primary and secondary care are as a consequence of somatic symptoms, not well-characterised by medical conditions [33]. One of the major difficulties in creating a uniform approach to these patients has been that somatic symptoms are often picked up by various sub-specialties of medicine, which creates idiosyncratic and overlapping approaches that lack consensus [67]. In essence, two competing systems of classification have arisen, the somatoform disorders in psychiatry and functional disorders in medicine, with little cross-reference to each other [59].

Diagnosis is ultimately a pragmatic endeavour towards a treatment plan. The importance of diagnosis is often over-weighted in the debate treatment plans for somatoform disorders as there are many commonalities in the treatment of these syndromes [54]. The cause ultimately only matters if there is a specific treatment tied to an understanding of the mechanisms of aetiology. Hence with post-deployment syndromes the obsession of some professional and veteran's groups for establishing the cause, if this remains inconclusive and controversial, is ultimately not very relevant to the need for treatment.

In the post-deployment setting, diagnosis serves the role of acknowledgment to the veteran for the sacrifice of their health for the nation and purposes of compensation. Deferring to the causal model should be understood for its distraction from the primary need for care. There are multiple agendas that impinge on this setting where there is the challenge of integrating the debates from the research literature with agreed clinical interventions that do not harm through false attributions. There are a number of examples in medicine of the importance of not to get distracted by the competing agendas in the scientific literature about aetiology such as with cancer where the cause has little impact on the treatment regime selected. This pragmatic approach works for other real diseases such as multiple sclerosis and cardiac failure.

With veterans, one critical role of diagnosis of post-deployment syndromes is to create a currency to create empathy for the sense of dysphoria and illness in the veteran. The social role of diagnosis should be acknowledged in the discussion about mTBI. Importantly, the emergence and presentation of these symptoms is as much about the sociology of illness as it is about phenomenology and aetiology. The multiple frames of reference need to be addressed between a range of different medical specialties and patient advocates. Some of the challenges and competing issues that need to be addressed will now be discussed in the fundamental issue of whether we need diagnosis anyway.

2.6.1 Illness Attributions and Beliefs

There are groups of individuals who for various reasons including the difficulties they have had in their ongoing attempt to have their condition diagnosed and managed by the medical profession, develop strongly held beliefs about the nature and cause of their condition. These individuals have strongly held beliefs about that nature and cause of their illness, often involving particular exposures, which they believe are the cause of their syndrome [56]. This group of patients present a particular challenge in clinical practice because it is difficult to engage in a free discourse about the nature of their symptoms and their possible causes. Managing this group of patients presents a burden to most clinicians because there is a significant risk of conflict over the different views about the nature of the symptoms in the consultation [51].

The problem is a greater in a military context with the clinician for a number of reasons. There is often a loss of trust with the organisation due to the lack of recognition that the veterans' health and welfare has been sacrificed. In these settings it is hard to foster rapport because there is suspicion about whether the primary allegiance of the clinician is to the patient. The occupational setting with the attendant complexities about fitness for duty favour denial by the clinician about significant association between particular symptoms and military service. This setting evokes a complex network of issues in the domains of transference and countertransference that creates a battleground between the patient and doctor if not managed in a sophisticated manner.

Media advocacy is an important factor influencing the emergence of such syndromes. Some of the dynamics include a readiness to attribute symptoms to particular exposures combined with a suspicion of denials by Government. Exposures to chemical weapons and depleted uranium in the First Gulf War were concerns that attracted particular attention in this domain as did the Agent Orange controversy create after the Vietnam War.

2.6.2 Medically Classified Syndromes / Functional Syndromes

The functional syndromes have attracted considerable attention in the practice of physicians [67]. These include:

- Irritable bowel;
- Chronic fatigue syndrome;
- Fibromyalgia;

- Myalgic encephalomyelitis;
- Non-ulcer dyspepsia; and
- Multiple chemical sensitivities.

These are syndromes where particular views about aetiology and treatment are championed by special interest clinicians [60]. The apparent validity of the diagnostic criteria for these syndromes is accepted in the published literature, despite the fact that there is a high degree of overlap between the symptoms of these syndromes. The precise diagnosis that a patient is given has as much to do with the clinician who is consulted as with the specificity of an individual's complaints. As discussed above, a diagnosis that conveys a distinct causation often does not guarantee any effective treatment.

Driving clinical practice in this domain is the important role of doctors in giving diagnoses. The emergence of special interest groups around the individual syndromes means that there is little incentive within the medical profession to address the degree of overlap of these syndromes [59]. A veteran has to try and adapt optimally in an environment where at times the media coverage of controversial research findings can foster suggestibility. Also, the willingness of some clinicians to act as advocates with special interests in aetiology of particular agents can create iatrogenesis. There is less agreement between the specialities than often presumed. Every specialty has its explanation and largely ignores the competing hypothesis [53].

2.6.3 Psychiatric Classification of Somatic and Pain Syndromes

A separate section of DSM-IV defines somatoform disorders (including somatisation disorder, pain disorder, and hypochondriasis) and is essentially based on a system of phenomenological classification [41], [57]. These syndromes have equally been criticised for a number of reasons including the variable interpretation of thresholds of severity required for these disorders and the requirement that symptoms are not better explained by some other psychiatric disorder such as depression, PTSD and anxiety [48]. Equally, there is a significant overlap between the somatoform disorders and the functional medical syndromes leading to further confusion [47]. Hence, the diagnosis which a patient receives can not only be influenced by which medical sub-specialty a patient attends but also as to whether they see a physician or a psychiatrist.

The challenge remains about how to classify the patient who does not have a physical disorder but has widespread pain and other physical symptoms [21]. The systems of assessment that are often imposed on clinical practice are practical tool with little science at that heart and are required by the insurance industry. Patients get caught in this battle for pragmatism in dealing with what are idiopathic physical symptoms, not being made aware that doctors are good at determining what is not present rather what is present [12]. The essence of the problem is how to categorise the suffering of the patient who has insufficiently explained and persistent post-deployment physical symptoms.

2.6.4 Physical Symptoms in Psychiatric Illness

A longstanding issue which has never been resolved in psychiatry is the extent to which somatic distress is a distinct but inescapable dimension of psychiatric disorder [22]. Just as anxiety and depression are highly correlated, so are somatic symptoms, in psychiatric disorders such as depression and post-traumatic stress disorder, somatic distress is almost a ubiquitous component including symptoms such as fatigue and pain [23]. A further analysis of these questions in the respective national comorbidity studies has demonstrated that back pain and joint pain have a strong relationship with the presence of psychological disorders [65]. However, this overlap has not been systematically addressed in psychiatric classification and has put to one side the significant degree of correlation between somatic distress, anxiety, and depression [22].

One of the difficulties is that different diagnostic categories depend upon symptoms being able to separate disorders. However, the specificity and sensitivity of many symptoms is relatively low and subtle clinician preferences that can influence the history taking process leads to substantial variances in diagnostic practice. However, the use of structured diagnostic interviews in epidemiological studies does provide a basis where some of this overlap can be addressed.

With the emergence of DSM-III, the prevalence of comorbidity came to be much more apparent with the later decision not to have substantial diagnostic hierarchies. Hence, current practice is confronted to a much greater degree with the breadth of symptomatology and comorbidity presented by most patients.

2.6.5 Impact of Compensation Systems

In both military and civilian life, compensation benefits and pensions depend upon clinical diagnosis and the establishment of a causal chain between deployment and the onset of a particular pattern of symptoms. To date, the extent to which this is impacted upon the description of syndromes in different countries has not been widely addressed. For example, a Purple Heart is not awarded for post-traumatic stress disorder but is awarded for mild traumatic brain injury. This fact has significant potential to confound the discussion and arguments around the aetiology of symptoms in the current conflict because of the risk of IEDs, both as a cause of physical and psychological morbidity.

Equally, in some civilian compensation systems, the standards of proof and benefits for psychological disorders are significantly more stringent and have thresholds of severity not required with physical disorders. These different approaches have the potential to influence patients and doctors alike to where possible use one classification system in contrast to another, depending upon whether they are resisting the claim or wanting to assist the patient in getting benefits. Hence the compensation and award systems impact on categorisation and the approach taken inside the specific studies to these different syndromes.

In the civilian sector, whiplash and post-concussion syndrome create similar challenges.

2.7 THE CURRENT CONTROVERSY

In summary, clinical medicine struggles for many different reasons to achieve any effective consensus about how to address the overlap of psychological and physical symptoms. There is a continuous dialogue and dynamic between the broader social acceptability of illness, the patient's beliefs, and the particular approach chosen by the clinician. There are few rules to guide broader aspects of clinical practice in this domain. History demonstrates that post-deployment distress has long been recognised and that the changes occur both along psychological and somatic axis. Furthermore, the point of transition between health and disease which is always a significant challenge is particularly apparent in this domain. The readiness of some individuals to tolerate symptoms without complaint contrasted with those where feelings of ill-health provoke particular anxiety highlights the relevance of individual illness behaviour as well. Moving forward in this field therefore is vexed from a sociological, phenomenological, and aetiological perspective.

2.7.1 Allostasis: A Shared Mechanism of Disease

An approach that has gained little currency to date but has significant promise is to examine the shared underlying aetiological processes involved in these syndromes. A review of the literature indicates that constructs such as allostasis, kindling and sensitisation are frequently quoted in explaining the progressive dysregulation and symptomatic distress of individuals [36].

Sensitisation “*refers to the observation that individuals that are repeatedly exposed to an environmental risk factor may develop progressively greater responses over time, finally resulting in a lasting change of response amplitude*” (page 220 of Ref. [8]). Furthermore, sensitisation is a construct which can explain common mechanisms linking multiple environmental effects. In other words, factors in the behavioural, physical, and neurochemical areas can all induce such changes. Therefore, the repeated presentation of a stimulus has the capacity to progressively increase the amplitude of the response of a particular physiological system.

The kindling hypothesis has been used by Post and Weiss [44] to explain the underlying pathophysiological mechanisms during the emergence of progressive limbic abnormalities and diseases such as depression and post-traumatic stress disorder.

These constructs are useful because they provide a theoretical perspective to explain the consequences of repeated exposures to major stresses prior to the onset of any disorder. Furthermore, sensitisation and kindling are also used to describe a second process related to an illness state can predict subsequent episodes. Underlying these abnormalities are changes in neurohormonal systems, such as the HPA-axis [39]. The literature of the somatic syndromes as well as psychiatric disorders such as depression and PTSD has a significant commonality of interest in these systems. Equally, chronic pain has been linked to sensitisation and kindling of the amygdala.

Hence, one approach to the post-deployment syndromes is to consider the different sub-categories and diagnostic presentations against the background over this underlying shared stress response diathesis which provides a coherent model for the impact of stress over time on an individual's health. This construct is of equal relevance to physical and psychological domains and potentially could provide a core construct that binds together this literature.

Furthermore, developments in neuroimaging highlight the shared neural systems underpinning allostasis and sensitization and that there are important dimensions of information processing abnormalities that can explain the different types of symptomatic manifestation of medically unexplained symptoms. One related literature is about the inflammatory effects of brain injury made amplify the risks and mechanisms that lead to psychiatric disorder. The role of inflammation and glial cell function is now generally accepted in a variety of disorders. Therefore the interaction between the effects of traumatic stress and head injury is an important a question as is the specificity of these aetiological mechanisms.

2.8 CONCLUSION

The current conflicts in Iraq and Afghanistan have led to particular concern about the cognitive impact of IED explosions with the related behavioural and emotional difficulties. There is significant overlap with many individuals with head injury also suffering PTSD and the diagnostic challenges are increased, as PTSD itself is associated with major deficits of attention, working memory and impaired behavioural inhibition. The risk of PTSD is greater following mTBI, raising issues similar to the possible role of head injury in the aetiology of schizophrenia and bipolar disorder.

The importance of considering the issue of mTBI in the context of the history of post-deployment syndromes is that there is evidence of a steady drift back to the importance of the psychological stress rather than the central role of the concussive wave from explosions. On the other hand, PTSD has a very strong association with a range of other somatic symptoms, which are often not dealt with in clinical settings. mTBI is at the end of a continuum of brain injury where there is no specific neurological deficit, rather manifesting as subtle information processing deficits. Cognitive capacity arising from brain injury as well as the threat of death from the IED both impact on the probability of developing PTSD. These mechanisms inextricably link PTSD and mTBI.

As several reviews have also recently highlighted, the lack of specificity of the symptoms of mTBI makes diagnosis from a phenomenological perspective very difficult as PTSD will always need to be part of the differential diagnosis. There is also the risk that some of those diagnosed with mTBI would also satisfy the diagnosis of sub-syndromal PTSD or another psychiatric disorder. This problem further compounds that lack of specificity of the symptoms of mTBI. Finally, the symptoms of poor concentration, irritability, fatigue and memory difficulties are common in those without head injury as demonstrated by studies of the post-deployment symptoms in the studies of the First Gulf War Veterans [19]. Therefore having a history of loss of consciousness and this typical symptoms cluster does not necessarily mean that the individual will have a mild traumatic brain injury. These possibilities highlight the risk of misdiagnosis in mTBI and the challenges of conducting studies of aetiology. On the other hand there is no dispute that blast wave causes neurological insults but these do need to be differentiated from those occurring in PTSD which are now characterised in neuroimaging and event-related potential research.

mTBI presents a major challenge from a diagnostic perspective as the name presumes a cause for the symptoms of memory, attentional and affect regulation difficulties. History has shown that such presumption of causation due to blast wave injury was not sustained, with the traumatic nature of the possibility of death and fear being critical factors in the majority of cases. Post-deployment syndromes are the rule rather than the exception after every conflict and the presumption of causation of the multiple symptoms that arise in veterans often disproved. This problem of presumed specificity of symptoms and aetiology is not confined to mTBI but is a shared problem of functional medical syndromes. The clinical management of these complex patients would be better served by better defining the shared aetiological mechanisms rather than presuming unique causal mechanisms in each syndrome. The concept of allostatic load, associated with the mechanisms of sensitization and kindling and its various manifestations may provide a better way of characterising the axes of dysregulation that leads to the complex range of symptoms in veterans who have experienced both psychological and physical injury. It is time for new wine in new bottles if we are to serve the veterans community with science.

2.9 REFERENCES

- [1] <http://www.purpleheart.org/HistoryOrder.aspx>.
- [2] Arguelles, L.M., Afari, N., Buchwald, D., Clauw, D., Furner, S. and Goldberg, J. (2006), A twin study of posttraumatic stress disorder symptoms and chronic widespread pain, *Pain* 124, pp. 150-157.
- [3] Bailey, P., War Neuroses, Shell Shock and Nervousness in Soldiers, *Jama*. 1918;71(26):2148-2153. doi:10.1001/jama.1918.26020520017010e.
- [4] Beard, G. (1869), "Neurasthenia, or nervous exhaustion", *The Boston Medical and Surgical Journal*: pp. 217-221.
- [5] Brenner, L.A., Ivins, B.J., Schwab, K., Warden, D., Nelson, L.A., Jaffee, M. and Terrio, H. (2010), Traumatic brain injury, posttraumatic stress disorder, and postconcussive symptom reporting among troops returning from Iraq. *J Head Trauma Rehabil*, 25(5), 307-312. doi: 10.1097/HTR.0b013e3181cada03.
- [6] Bryant, R.A., Creamer, M., O'Donnell, M., Silove, D., Clark, C.R. and McFarlane, A.C. (2009), Post-traumatic amnesia and the nature of post-traumatic stress disorder after mild traumatic brain injury, *Journal of the International Neuropsychological Society*, 15(6), pp. 862-867.

- [7] Birmes, P., Brunet, A., Carreras, D., Ducassé, J.L., Charlet, J.P., Lauque, D., Sztulman, H. and Schmitt, L., (2003), The predictive power of peritraumatic dissociation and acute stress symptoms for posttraumatic stress symptoms: A three-month prospective study, *American Journal of Psychiatry*, 160(7), pp. 1337-1339.
- [8] Collip, D., Myin-Germeys, I. and Van Os, J., (2008), Does the concept of “sensitization” provide a plausible mechanism for the putative link between the environment and schizophrenia?, *Schizophr Bull*, Mar; 34(2):220-5, Epub, January 18, Review.
- [9] Committee on Gulf War and Health: Physiologic, Psychologic, and Psychosocial Effects of Deployment-Related Stress (2007) *Gulf War and Health: Volume 6, Physiologic, Psychologic, and Psychosocial Effects of Deployment-Related Stress* <http://www.nap.edu/catalog/11922.html>.
- [10] Da Costa, J.M. (1871). “On irritable heart; a clinical study of a form of functional cardiac disorder and its consequences”. *The American Journal of the Medical Sciences* (61):18-52.
- [11] Davenport, N.D., Lim, K.O., Armstrong, M.T. and Sponheim, S.R. (2011), Diffuse and spatially variable white matter disruptions are associated with mild traumatic brain injury, *Neuroimage* 10.1016/j.neuroimage.2011.10.050.
- [12] Engel, C.C. (2006), Explanatory and Pragmatic Perspectives Regarding Indopathic Physical Symptoms and Related Syndromes, *CNS Spectrum* 11:225-232.
- [13] Engel, C.C. and Katon, W.J. (1999), Population and Need-Based Prevention of Unexplained Physical Symptoms, Appendix A IOM Report.
- [14] Engelhard, I.M., van den Hout, M.A., Weerts, J., Arntz, A., Hox, J.J. and McNally, R.J. (2007), Deployment-related stress and trauma in Dutch soldiers returning from Iraq, Prospective study. *British Journal of Psychiatry*, 191, pp. 140-145.
- [15] Fabrega, H. (1990), The concept of somatization as a cultural and historical product of Western Medicine, *Psychosomatic Medicine* 52:653-672.
- [16] Fear, N.T., Jones, E., Groom, M., Greenberg, N., Hull, L., Hodgetts, T.J. and Wessely, S. (2009), Symptoms of post-concussional syndrome are non-specifically related to mild traumatic brain injury in UK Armed Forces personnel on return from deployment in Iraq: an analysis of self-reported data, *Psychological Medicine*, 39(8), pp. 1379-1387.
- [17] Fischer, H., Klarman, K. and Oboroceanu, M.-J., *American War and Military Operations Casualties: Lists and Statistics*, Washington, DC, USA: Congressional Research Service, June 2007.
- [18] Forbes, A.B., McKenzie, D.P., Mackinnon, A.J., Kelsall, H.L., McFarlane, A.C., Ikin, J.F., Glass, D.C. and Sim, M.R., The health of Australian veterans of the 1991 Gulf War: Factor analysis of self-reported symptoms, *Occup Environ Med* 2004; 61(12):1014-20.
- [19] Forbes, D., Parslow, R., Creamer, M., O'Donnell, M., Bryant, R., McFarlane, A., Silove, D. and Shalev, A., A longitudinal analysis of posttraumatic stress disorder symptoms and their relationship with Fear and Anxious-Misery disorders: Implications for DSM-V, *J Affect Disord* 2010; 127(1-3):147-52.
- [20] Glass, A.J., Mental health programs in the armed forces, In: Arieti S (ed.). *American handbook of psychiatry*, New York: Basic Books, 1974; 800-9.

- [21] Gillespie, N., Kirk, K.M., Heath, A.C., Martin, N.G. and Hickie, I., Somatic distress as a distinct psychological dimension, *Soc Psychiatry Psychiatr Epidemiol* 1999; 34:451-8.
- [22] Goldberg, D., A dimensional model for common mental disorders, *Br J Psychiatry Suppl*: 44-9, 1996.
- [23] Henningsen, P., Zimmermann, T. and Sattel, H., Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review, *Psychosom Med* 65:528-33, 2003.
- [24] Hofer, J. (1688), *Medical Dissertation on Nostalgia* The Institute of the History of Medicine, 1934, pp. 376-391.
- [25] Hoge, C.W., Goldberg, H.M. and Castro, C.A. (2009), Care of war veterans with mild traumatic brain injury--flawed perspectives, *New England Journal of Medicine*, 360(16), pp. 1588-1591.
- [26] Hoge, C.W., McGurk, D., Thomas, J.L., Cox, A.L., Engel, C.C. and Castro, C.A. (2008). Mild traumatic brain injury in U.S. Soldiers returning from Iraq. *N Engl J Med*, 358(5), 453-463. doi: 10.1056/NEJMoA072972.
- [27] Hyams, K.C. (1998), Developing Case Definitions for Symptom-based Conditions: The problem of specificity, *Epidemiological Reviews* 20, pp. 148-156.
- [28] Jones, E., Fear, N.T. and Wessely, S. (2007). Shell shock and mild traumatic brain injury: a historical review. *Am J Psychiatry*, 164(11), 1641-1645. doi: 10.1176/appi.ajp.2007.07071180.
- [29] Jones, E. and Wessely, S., *Shell Shock to PTSD: Military Psychiatry from 1900 to the Gulf War*, Maudsley Monograph 47, Hove: Psychology Press, 2005.
- [30] Kardiner, A. (1941), *The Traumatic Neurosis of War*, New York: P. Hoeber.
- [31] Kardiner, A. and Spiegel, H. (1947), *War stress and Neurotic Illness*, New York: Hoeber.
- [32] Kelsall, H., McKenzie, D., Sim, M., Leder, K., Forbes, A. and Dwyer, T. (2009), Physical, Psychological and Functional Comorbidities of Multisymptom Illness in Australian Male Veterans of the 1991 Gulf War, *American Journal of Epidemiology* 170.
- [33] Kroenke, K. and Price, R.K., Symptoms in the community: prevalence, classification, and psychiatric comorbidity, *Arch Intern Med* 1993; 153:2474-2480.
- [34] Lee Peterlin, B., Rosso, A.L., Sheftell, F.D., Libon, D.J., Mossey, J.M. and Merikangas, K.R. (2011), Post-traumatic stress disorder, drug abuse and migraine: New findings from the National Comorbidity Survey Replication (NCS-R), *Cephalalgia*, 31(2), pp. 235-244.
- [35] Loeser, J.D. and Sullivan, M. (1997), Doctors, Diagnosis and Disability: A disastrous Division, *Clinical Orthopaedics and Related Research* 336, pp. 61-66.
- [36] McEwen, B.S., The neurobiology of stress: from serendipity to clinical relevance, *Brain Res* 2000 Dec 15; 886(1-2):172-89.
- [37] McFarlane, A.C., The delayed and cumulative consequences of traumatic stress: Challenges and issues in compensation settings, *Psychology, Injury and Law* 2010; 3(2): 100-110.

-
- [38] McFarlane, A.C., Atchison, M., Rafalowicz, E. and Papay, P., Physical symptoms in post-traumatic stress disorder, *J Psychosom Res* 38:715-726, 1994.
 - [39] McLean, S.A., Clauw, D.J., Abelson, J.L. and Liberzon, I., The Development of Persistent Pain and psychological Morbidity After Motor Vehicle Collision: Integrating the Potential Role of Stress Response Systems Into a Biopsychosocial Model, *Psychosom Med* 2005; 67:783-90.
 - [40] Marmar, C.R., Weiss, D.S., Schlenger, W.E., Fairbank, J.A., Jordan, B.K., Kulka, R.A. and Hough, R.L. (1994), Peritraumatic dissociation and posttraumatic stress in male Vietnam theater veterans, *American Journal of Psychiatry*, 151(6), pp. 902-907.
 - [41] Mayou, R., Kirmayer, L.J., Simon, G., Kroenke, K. and Sharpe, M., Somatoform disorders: time for a new approach in DSM-V, *Am J Psychiatry* 2005; 162:847-55.
 - [42] Myers, C.H. (1915), Contributions to the study of shell shock: Being an account of certain disorders of cutaneous sensibility, *Lancet* March 18, pp. 608-613.
 - [43] Okie, S. (2005), Traumatic brain injury in the war zone. *N Engl J Med*, 352(20), 2043-2047. doi: 10.1056/NEJMp058102.
 - [44] Pietrzak, R.H., Johnson, D.C., Goldstein, M.B., Malley, J.C. and Southwick, S.M. (2009), Posttraumatic stress disorder mediates the relationship between mild traumatic brain injury and health and psychosocial functioning in veterans of Operations Enduring Freedom and Iraqi Freedom. *J Nerv Ment Dis*, 197(10), 748-753. doi: 10.1097/NMD.0b013e3181b97a75.
 - [45] Polusny, M.A., Kehle, S.M., Nelson, N.W., Erbes, C.R., Arbisi, P.A. and Thuras, P. (2011), Longitudinal effects of mild traumatic brain injury and posttraumatic stress disorder comorbidity on postdeployment outcomes in national guard soldiers deployed to Iraq. *Arch Gen Psychiatry*, 68(1), 79-89. doi: 10.1001/archgenpsychiatry.2010.172.
 - [46] Post, R.M. and Weiss, S.R., Sensitization and kindling phenomena in mood, anxiety, and obsessive-compulsive disorders: the role of serotonergic mechanisms in illness progression, *Biol Psychiatry* 1998; 44:193-206.
 - [47] Richardson, R. and Engel, C. (2004), Evaluation and the Management of Medically Unexplained Symptoms, *Neurologist* 10:18-30.
 - [48] Rief, W. and Isaac, M., Are somatoform disorders 'mental disorders'? A contribution to the current debate, *Curr Opin Psychiatry* 2007 Mar; 20(2):143-6.
 - [49] Rivers, W.H.R. (1918), An Address on the Repression of War Experience, *Lancet* February 2.
 - [50] Rona, R.J., Jones, M., Fear, N.T., Hull, L., Murphy, D., Machell, L. and Wessely, S. (2012). Mild traumatic brain injury in UK military personnel returning from Afghanistan and Iraq: cohort and cross-sectional analyses. *J Head Trauma Rehabil*, 27(1), 33-44. doi: 10.1097/HTR.0b013e318212f814.
 - [51] Sayar, K., Barsky, A.J. and Gulec, H., Does somatosensory amplification decrease with antidepressant treatment? *Psychosomatics* 2005 Jul-Aug; 46(4):340-4.

- [52] Schneiderman, A.I., Braver, E.R. and Kang, H.K. (2008), Understanding sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: persistent postconcussive symptoms and posttraumatic stress disorder. *Am J Epidemiol*, 167(12), 1446-1452. doi: 10.1093/aje/kwn068.
- [53] Schur, M., Afari, N., Furber, H., Olart, M., Goldberg, J., Sullivan, P. and Buchwald, D. (2007), Feeling bad in more ways the one: Comorbidity patterns of medically unexplained and psychiatric conditions, *Journal of General Internal Medicine* 22:818-821.
- [54] Shalev, A., Bleich, A. and Ursano, R.J., Posttraumatic stress disorder: somatic comorbidity and effort tolerance, *Psychosomatics* 31:197-203, 1990.
- [55] Sharpe, M. and Mayou, R., Somatoform disorders: a help or hindrance to good patient care? *Br J Psychiatry*; 2004;184:465-467.
- [56] Showalter, E., *Hystories: Hysterical epidemics and modern culture*, New York, Columbia University, 1997.
- [57] Smith, R.C., Gardiner, J.C., Lyles, J.S., Sirbu, C., Dwamena, F.C., Hodges, A., Collins, C., Lein, C., Given, C.W., Given, B. and Goddeeri, J., Exploration of DSM-IV criteria in primary care patients with medically unexplained symptoms, *Psychosom Med* 67:123-9, 2005.
- [58] Southborough, Lord: Report of the War Office Committee of Enquiry into "Shell-Shock", London, UK, His Majesty's Stationery Office, 1922.
- [59] Strassnig, M. and Stowell, K.R., First, M.B. and Pincus, H.A., General medical and psychiatric perspectives on somatoform disorders: separated by an uncommon language, *Curr Opin Psychiatry* 2006; 19:194-200.
- [60] Talley, N.J. and Spiller, R., Irritable bowel syndrome: a little understood organic bowel disease?, *Lancet* 2002; 360:555-564.
- [61] Tanielian, T. and Jaycox, L.H. (Eds.) (2008), *Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery*, Santa Monica, CA, USA: RAND Corporation.
- [62] Terrio, H., Brenner, L.A., Ivins, B.J., Cho, J.M., Helmick, K., Schwab, K. and Warden, D. (2009), Traumatic brain injury screening: preliminary findings in a US Army Brigade Combat Team. *J Head Trauma Rehabil*, 24(1), 14-23. doi: 10.1097/HTR.0b013e31819581d8.
- [63] Trimble, M.R. (1982), Functional diseases. *Br Med J (Clin Res Ed)*, 285(6357), pp. 1768-1770.
- [64] Ursano, R.J., Fullerton, C.S., Epstein, R.S., Crowley, B., Vance, K., Kao, T-C. and Baum, A. (1999), Peritraumatic Dissociation and Posttraumatic Stress Disorder Following Motor Vehicle Accidents, *American Journal of Psychiatry*, 156(11), pp. 1808-1810.
- [65] Von Korff, M., Crane, P., Lane, M. *et al.* (2005), Chronic spinal pain and physical-mental comorbidity in the United States: results from the national comorbidity survey replication, *Pain* 113:331-9.
- [66] Vasterling, J.J., Verfaellie, M. and Sullivan, K.D. (2009), Mild traumatic brain injury and posttraumatic stress disorder in returning veterans: perspectives from cognitive neuroscience, *Clinical Psychology Review*, 29(8), pp. 674-684.

- [67] Wessely, S. (2006), Introduction. The health of Gulf War veterans, *Philos Transactions of Royal Society London Biological Science*, 361:531-2.
- [68] Wessely, S., Nimnuan, C. and Sharpe, M. (1999), Functional somatic syndromes: one or many, *Lancet*: 354, pp. '936-939.
- [69] Zamorski, M., Darch, A. and Jung, H.W. (2009), Preliminary report on the self-reported incidences of mild traumatic brain injury/concussion in CF members deployed in support of the mission in Afghanistan, Ottawa, Canada: Canadian Forces Health Services, Directorate of Mental Health/Deployment Health.



Chapter 3 – ALLOSTATIC LOAD REVIEW

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3.1 INTRODUCTION

The allostatic load model has been used to refocus the stress disease literature, emphasising that their multiple biological systems are vulnerable to a temporal cascade of dysregulation [30]. These progressive dysregulations lead to the emergence of a range of disease trajectories that arise from this common pathway to disease. This approach provides a broader construct than traditional detection methods used in biomedical practice for understanding how repeated challenges from the environment lead to increasingly maladaptive disruptions of homeostatic mechanisms. The essence of the allostatic load model is that the body is subject to wear and tear with repeated activation during stressful situations [44]. These stresses and threats, dysregulate homeostasis by initiating sympathetic adrenal medullary axis release of catecholamines and activation of the HPA-axis. They also mobilise energy through the flight or fight response. These processes are essentially coordinated through the hippocampal, amygdaloid, and prefrontal cortical regulatory systems [43]. Diseases in a range of organ systems are underpinned by these common mechanisms of dysregulation.

Allostatic load originated from the concept of homeostasis, the belief that biological systems work towards maintaining a stable internal environment. Homeostasis has however been criticised for two reasons. First, it fails to take account of the individuals changing physical and psychological circumstances overtime and second, how these changing circumstances in turn, make different demands on various parts of the physiological systems. The alternate concept of allostasis was introduced in 1988 to overcome such criticisms [39]. Unlike homeostasis, allostasis recognises that there is no single ideal internal physiological environment, and both physical and psychological stressors elicit various physiological systems in order to maintain a steady state over time [11].

Overtime, however, the cost of continually attempting to maintain this steady state may result in allostatic load [29]. Allostatic load refers to the consequences of sustained or repeated action by physiological systems in order to deal with either or both physical and/or psychological stress [11]. In turn, continuous wear and tear across these multiple physiological systems contributes to overall health risk [38]. By measuring an individual's allostatic load, it is possible to estimate not only their current health status, but also the probability of future morbidity or mortality.

3.2 RELATED CONSTRUCTS OF SENSITIZATION AND KINDLING

The literature indicates that allostasis is frequently discussed in association with the related mechanisms of kindling and sensitisation in explaining the progressive dysregulation and symptomatic distress of individuals [27]. Hence these related constructs require definition. Sensitisation “*refers to the observation that individuals that are repeatedly exposed to an environmental risk factor may develop progressively greater responses over time, finally resulting in a lasting change of response amplitude*” (Ref. [42], p. 220). Furthermore, sensitisation is a construct which can explain common mechanisms linking multiple environmental effects. In other words, factors in the behavioural, physical, and neurochemical areas can all induce such changes. Therefore, the repeated presentation of a stimulus has the capacity to progressively increase the amplitude of the response of a particular physiological system.

The kindling hypothesis has been used by Post and Weiss [46] to explain the underlying pathophysiological mechanisms during the emergence of progressive limbic abnormalities and diseases such as depression and post-traumatic stress disorder.

These constructs are useful because they provide a theoretical perspective to explain the consequences of repeated exposures to major stresses prior to the onset of any disorder. Furthermore, sensitisation and kindling are also used to describe a second process related to an illness state can predict subsequent episodes. Underlying these abnormalities are changes in neurohormonal systems, such as the HPA-axis [45]. The literature of the somatic syndromes as well as psychiatric disorders such as depression and PTSD has a significant commonality of interest in these systems. Equally, chronic pain has been linked to sensitisation and kindling of the amygdala.

Hence, one approach to the post-deployment syndromes and disease that are common in veterans is to consider the different sub-categories and diagnostic presentations against the background over this underlying shared stress response diathesis which provides a coherent model for the impact of stress over time on an individual's health. This construct is of equal relevance to physical and psychological domains and potentially could provide a core construct that binds together this literature.

Furthermore, developments in neuroimaging highlight the shared neural systems [15] underpinning allostasis and sensitization and that there are important dimensions of information processing abnormalities that can explain the different types of symptomatic manifestation of medically unexplained symptoms. One related literature is about the inflammatory effects of brain injury made amplify the risks and mechanisms that lead to psychiatric disorder [41]. The role of inflammation and glial cell function is now generally accepted in a variety of disorders [40]. Therefore the interaction between the effects of traumatic stress and head injury is an important a question as is the specificity of these aetiological mechanisms.

3.3 STRESS AND POTENTIAL RISK FACTORS

Two types of stressors which potentially lead to an increase in allostatic load have been identified. The first is physical exertion such as dealing with radical changes in temperature or responding to an infectious disease and the second being psychological stressors including fear and anxiety, both of which challenge the physiological systems [29]. Despite the fact that intense physical activity may challenge the physiological system, many allostatic load studies to date have focused on psychological stress.

Daily life challenges, whether they be physical and/or psychological temporarily activate a physiological system response without any long-term side effects. However, inappropriate responses to daily challenges may increase allostatic loads. Examples of inappropriate responses result from frequent acute challenges, a failure to either adapt to or shut off after the challenge has abated, or the physiological systems do not respond appropriately [26], [28].

Macro, exo micro and individual challenges together impact on the individual [18] and the ability of the individual to meet these challenges is impacted by a number of factors [28] including previous life challenges such as early childhood experiences, genetic load, individual behaviours and habits such as smoking, drinking as well as social and environmental factors including the types of relationships and degree of support available to the individual [15].

Individuals with a low socio economic status are particularly vulnerable to physical and psychological challenges. Allostatic load, for example, has been shown to increase as composite measures of socio economic status decline [14]. A study of over 300 American school children also found that an increased total allostatic

load score was significantly associated to socio economic status including factors such as poverty, single parent families and exposure to violence [7].

Age has also been shown to be associated with increases in age, one large population study finding that allostatic loads increase with age up to about 60 [5]. Seeman [35] has also found that ethnicity plays a mediating role on the development of allostatic load. In a study of 782 black and white men and women both poor and non-poor African American participants were found to have a significantly higher allostatic load than other ethnic groups. While not as yet tested, personality traits are also believed to impact on allostatic load scores with high aggression thought to result in the development of allostatic load measures such as hypertension, atypical depression and even chronic fatigue [23].

Work stress, particularly where personnel are dealing with a combination of psychological as well as physical stressors are of particular concern [29]. A study [33] involving 332 industrial workers in Germany found that high job demands, poor social support and low decision latitude were all associated with individual measures of allostatic load. The association between scores associated with exhaustion and low job demand, and allostatic load was investigated in a sample of German teachers. Participants high on the exhaustion scale also showed significantly higher allostatic load scores in comparison to those who reported low levels of exhaustion. Juster [19] found that as the frequency and severity of burnout symptoms increased, so did their allostatic load. Finally, Gustafsson [12] in a study of general life stressors and allostatic load, found that allostatic load was most notably associated with the domains of work, finances and caregiving.

Single factors are however unlikely to have a significant impact. Instead, individuals may be ‘primed’ for a delayed impact of stress whereby, the gradual build-up of repeated traumatic stressful events can gradually lead to increases in allostatic load over a longer period [30]. How, these factors which are both internal and external to the individual are accounted for in an allostatic load model is still being investigated. Further studies investigating associations between increased allostatic load and work stress, may benefit from considering how roles which are highly stressful over long periods of time such as military, police and firefighters, impact on allostatic load.

3.4 MEASURING ALLOSTATIC LOAD

The MacArthur Successful Aging Study was the first to calculate an allostatic load. Based to some extent on measures that were available, the allostatic load index included measures of systolic and diastolic blood pressure, waist to hip ratio, serum high density lipid, total cholesterol, glycosylated haemoglobin, serum dihydroepiandrosterone sulphate, cortisol, as well as norepinephrine and epinephrine [28]. In order to make comparisons with McEwen *et al.*’s work, many studies have continued to base their allostatic indexes on these or similar measures [21], [33], [4].

Additional measures have also been included in a number of studies. Crimmins *et al.* [5] included peak flow as a measure of lung function, albumin, c reactive protein and fibrinogen as a measure of inflammation and triglycerides as a measure of the metabolic system. Bellingrath *et al.* [1] extended the measures used in the MacArthur Successful Aging Study by including CRP, TNF-alpha, fibrinogen, D-dimer percent body fat, triglycerides and fasting glucose levels to account for immunological, blood coagulation and metabolic processes. BMI [10] and waist circumference [25] have also been substituted for waist to hip ratio. Treatments for conditions such as hypertension or inflammation have also been included to account for any distortion in the measurements [31].

What is included in the measurement of allostatic load is still controversial [12]. There are, however, two generally agreed principles. First, a combined index which includes multiple system measurements is better at predicting morbidity and mortality than single physiological components [21]. Second, calculations of allostatic load index should include measures from all of the primary physiological systems involved the mediation of physical and or psychological stress [27], [28] – hypothalamic-pituitary-adrenal and sympathetic nervous systems as well as the cardiovascular system and metabolic processes.

Another way of considering what should be included is to divide the measures into primary mediators which lead to primary effects and then to secondary outcomes which may then lead to tertiary outcomes [27]. Cortisol, adrenalin and norepinephrine are examples of primary mediators. Primary effects such as cellular events like enzymes, receptors, ion channels Systolic and diastolic blood pressure, waist to hip ratio and total cholesterol are defined as secondary outcomes because they are an effect of one or more of the primary mediators. Finally, tertiary or disease outcomes such as cardiovascular disease are realised. The suggestion being that measure of primary mediators and outcomes and secondary outcomes should be included in any allostatic load index in order to predict tertiary outcomes [36].

3.5 DEVELOPING AN ALLOSTATIC LOAD SCORE

In order to develop an allostatic load score the MacArthur Successful Aging Study classified each of their measures into quartiles based on the distribution. One point was given for each time an individual fell into the highest risk quartile. These scores were summed in order to identify the individual's cumulative allostatic load score [29]. As ten measures were used in this study, the highest allostatic load score was ten and the lowest was zero. Once again, many subsequent studies have followed a similar scoring system [31], [10], [13], [6].

Several limitations in this cumulative scoring system have been identified [9]. First, the assignment of high risk quartiles is arbitrary and may not reflect an appropriate cut-off. Nor should it be assumed that the same cut-off should be used for each population. Second, there is no opportunity to weight the measures according to their ability to predict tertiary outcomes.

Seeman [35] extend previous research by investigating alternative models of calculating an allostatic load score. A meta-factor allostatic load model was devised with core domains of inflammation and metabolism. This provided a much better fit than the cumulative scoring mode, representing 84% of the pattern of association.

Several studies have also used z-scores with mixed results. This method is based on averaging the normal scores (z scores) for each of the parameters. Seeman *et al.* [37] compared this method to the traditional cumulative scoring system and found that both yielded essentially the same result although the later showed a stronger effect. Hawkey *et al.* [14] successfully used z-scores to show the association between socio economic status and allostatic load. In comparison, Mair [24] also used z-score, however in this case the results did not differ significantly from the traditional cumulative scoring system.

Using a principal component factor analysis Buckwalter *et al.* [2] identified a seven-factor model:

- 1) Stress hormones;
- 2) Metabolic syndrome;
- 3) Pre-inflammatory elements;

- 4) Cholesterol;
- 5) Blood sugars;
- 6) Blood pressure; and a combination of DHEA; and
- 7) Peak flow and IGF.

This model was also found to predict more of the variance in measures of depression, anxiety and medical outcomes than the cumulative allostatic load score. Further work to identify the most appropriate way of calculating the allostatic load index is therefore warranted. In addition to those mentioned above, latent cluster analysis which is used to identify underlying clusters of individuals who share common factors may be useful in identifying measures of allostatic load.

3.6 ASSOCIATIONS OF INTEREST

Studies that have utilised allostatic load have found a plethora of associations. In the first follow up from the MacArthur Study of Aging, higher baseline allostatic loads were associated with significantly greater risk for mortality and was also marginally associated with cardiovascular disease at 2.5 years [36].

Psychological disorders such as Post-Traumatic Stress Disorder (PTSD) and depression have also found to be associated with increased allostatic load scores, primarily though to be due to dysregulation in the amygdale which is involved in the expectations of stress and adversity [34]. A study involving mothers of cancer sufferers, with (n = 10) and without (n = 10) PTSD and a control group (n = 8) demonstrated that being in the PTSD group was significantly associated with high allostatic load scores, and that this was a dose response relationship, in that the lowest allostatic load scores were found in the control group, middle range allostatic load scores were found in the group of mothers without PTSD and the highest allostatic load scores were found in the group of mothers with PTSD. Juster *et al.* [17] conducted a longitudinal study looking at the association between allostatic load scores and depression. They found that higher allostatic load scores were significantly associated with increased acute depressive symptoms at baseline and each of the two follow-ups respectively. However, baseline allostatic load scores were not significantly associated with the onset of depression at either of the two follow-ups.

Cognitive functioning has also been found to be associated with increased allostatic load scores. In the first follow-up of the MacArthur Study of Aging, poorer cognitive functioning including decreased spatial ability, abstract reasoning and cognitive performance together with a decline in working memory were all associated with higher allostatic load scores [37]. Decreased working memory has also been found to be significantly associated with higher cumulative allostatic load scores in a large U.S. population study [22]. However, further studies which consider how a wide range of cognitive domains is associated with physiological decline are required, in order to better understand the link between specific cognitive functioning and allostatic load.

Associations between self-report health and allostatic load are even less clear. Using factor analysis, Hasson [13]) found that the association between self-report health and allostatic load was stronger than associations between self-reported health and any single physiological measure. Their final model, however, indicated that working within a female-dominated health care sector, being older, having a lower education as well as poorer self-reported health was associated with a higher allostatic load. In comparison, Carolsson *et al.* [3] found no correlation between self-reported health and allostatic load in a study of diabetes patients.

3.7 RESILIENCE

The concept of allostasis and allostatic load can inform the understanding of resilience as much as identify factors which predict long-term decline. Allostasis is itself a system of resilience whereby physiological responses occur in order to maintain stability. It is only as these responses are dysregulated that physical and/or psychological health is impacted in the long term [20]. Therefore it may be possible to identify an allostatic score which identifies protective factors. For example, a study of military personnel identified that those participants with high neuropeptide Y levels tolerated stress experiences better than those with lower levels [32]. In addition, high levels of social support and social integration are significantly associated with a number of allostatic load measures [21]. By identifying measure associated with lower allostatic load scores, an index of allostatic support, in addition to allostatic load could be measured [8].

3.8 REFERENCES

- [1] Bellingrath, S., Weigl, T. and Kudiella, B.M. (2009), Chronic work stress and exhaustion is associated with higher allostasis load in female school teachers, *Stress*, 12, pp. 37-48.
- [2] Buckwalter, J.G., Rizzo, A., John, B.S., Finlay, L., Wong, A., Chin, E., Wellman, J., Smolinski, S. and Seeman, T., Analyzing the impact of stress: a comparison between a factor analytic and a composite measurement of allostatic load, In: *Interservice/Industry Training, Simulation, and Education Conference*, 2011.
- [3] Carolsson, A.C., Andreasson, A.N. and Wandell, P.E. (2011), Poor self-related health is not associated with high total allostatic load in type 2 diabetic patients - But high blood pressure is, *Diabetes & Metabolism*, 37, pp. 446-451.
- [4] Clark, M.S., Bond, M.J. and Hecker, J.R. (2007), Environmental stress, psychological stress and allostatic load, *Psychology, Health & Medicine*, 12, pp. 18-30.
- [5] Crimmins, E.M., Johnston, M., Hayward, M. and Seeman, T. (2003), Age differences in allostatic load: an index of physiological dysregulation, *Experimental Gerontology*, 38, pp. 731-734.
- [6] Deuster, P.A., Kim-Dorner, S.J., Remaley, A.T. and Poth, M. (2011), Allostatic load and health status of African Americans and whites, *American Journal of Health Behavior*, 35, pp. 641-653.
- [7] Evans, G.W. (2003), A multimethodological analysis of cumulative risk and allostatic load among rural children, *Developmental Psychology* 39, pp. 924-933.
- [8] Friedman, E.M. (2001), Allostatic versus empirical perspectives on pharmacotherapy for PTSD, In: Wilson, J.P., Friedman, M.J. and Lindy, J.D. (eds.) *Psychological trauma & PTSD*, New York: The Guilford Press.
- [9] Gleib, D.A., Goldman, N., Chuang, Y-L. and Weinstein, M. (2007), Do chronic stressors lead to physiological dysregulation? Testing the theory of allostatic load. *Psychosomatic Medicine*, 69, pp. 769-776.
- [10] Glover, D.A., Stuber, M. and Poland, R.E. (2006), Allostatic load in women with and without PTSD symptoms, *Psychiatry*, 69, pp. 191-203.

- [11] Goldstein, D.S. and McEwen, B.S. (2002), Allostasis, homeostats, and the nature of stress, *Stress*, 5, pp. 55-58.
- [12] Gustafsson, P.E., Janlert, U., Theorell, T., Westerlund, H. and Hammarstrom, A. (2011), Social and material adversity from adolescence to adulthood and allostatic load in middle-aged women and men: results from the Northern Swedish cohort, *Annals Behavior Medicine* [Online].
- [13] Hasson, D., Von Thiele Schwarz, U. and Lindfors, P. (2009), Self-rated health and allostatic load in women working in two occupational sectors. *J Health Psychol*, 14(4), 568-577. doi: 10.1177/1359105309103576.
- [14] Hawkey, L.C., Lavelle, L.A., Berntson, G.G. and Cacioppo, J.T. (2011), Mediators of the relationship between socioeconomic status and allostatic load in the Chicago Health, Aging, and Social Relations Study (CHASRS), *Psychophysiology*, 48, pp. 1134-1145.
- [15] Jaggi, A.S. and Singh, N. (2010), Differential effect of spironolactone in chronic constriction injury and vincristine-induced neuropathic pain in rats. *Eur J Pharmacol*, 648(1-3), 102-109. doi: 10.1016/j.ejphar.2010.08.050
- [16] Juster, R-P., Bizik, G., Picard, M., Arsenault-Lapierre, G., Sindi, S., Trepanier, L., Marin, M-F., Wan, N., Sekerovic, Z., Lord, C., Fiocco, A., Plusquellec, P., McEwen, B.S. and Lupien, S.J. (2011a), A transdisciplinary perspective of chronic stress in relation to psychopathology throughout life span development, *Development and Psychopathology*, 23, pp. 725-776.
- [17] Juster, R.P., Marin, M.F., Sindi, S., Nair, N.P., Ng, Y.K., Pruessner, J.C. and Lupien, S.J. (2011), Allostatic load associations to acute, 3-year and 6-year prospective depressive symptoms in healthy older adults. *Physiol Behav*, 104(2), 360-364. doi: 10.1016/j.physbeh.2011.02.027.
- [18] Juster, R-P., McEwen, B.S. and Lupien, S.J. (2010), Allostatic load biomarkers of chronic stress and impact on health and cognition, *Neuroscience and biobehavioral Reviews* [Online].
- [19] Juster, R-P., Sindi, S., Marin, M-F., Perna, A., Hashemi, A., Pruessner, J.C. and Lupien, S.J. (2011c), A clinical allostatic load index is associated with burnout symptoms and hypocortisolemic profiles in health workers, *Psychoneuroendocrinology*, 36, pp. 797-805.
- [20] Karatsoreos, I.N. and McEwen, B.S. (2011), Psychobiological allostasis: resistance, resilience and vulnerability, *Trends in Cognitive Science*, 15, pp. 576-584.
- [21] Karlamangla, A.S., Singer, B.H., McEwen, B.S., Rowe, J.W. and Seeman, T. (2002), Allostatic load as a predictor of functional decline, MacArthur studies of successful aging. *Journal of Clinical Epidemiology*, 55, pp. 696-710.
- [22] Kobrosly, R.W., Seplaki, C.L., Jones, C.M. and Van Wiungaarden, E. (2012), Physiological dysfunction scores and cognitive function test performance in US adults, *Psychosomatic Medicine*, 74, pp. 81-88.
- [23] Korte, S.M., Koolhaas, J.M., Wingfield, J.C. and McEwen, B.S. (2005), The Darwinian concept of stress: benefits of allostasis and costs of allostatic load and the trade-offs in health and disease, *Neuroscience and Biobehavioral Reviews*, 29, pp. 3-38.
- [24] Mair, C.A., Cutchin, M.P. and Peek, K.M. (2011), Allostatic load in an environmental riskscape: the role of stressors and gender, *Health & Place*, 17, pp. 978-987.

- [25] Mattei, J., Noel, S.E. and Tucker, K. L. (2011), A meat, processed meat, and French fries dietary pattern is associated with high allostatic load in Puerto Rican older adults. *J Am Diet Assoc*, 111(10), 1498-1506. doi: 10.1016/j.jada.2011.07.006.
- [26] McEwen, B.S. (1998), Stress, adaptation, and disease, *Allostasis and Allostatic Load*, Annals New York Academy of Sciences [Online], 840, Available: DOI: 10.1111/j.1749-6632.1998.tb09546.x [Accessed January 20, 2012].
- [27] McEwen, B.S. (2000), *Allostasis and allostatic load: Implications for neuropsychopharmacology*, Neuropsychopharmacology, 22, pp. 108-124.
- [28] McEwen, B.S. and Seeman, T. (1999), Protective and damaging effects of mediators of stress, Elaborating and testing the concepts of allostasis and allostatic load, Annals New York Academy of Sciences [Online], 896, Available: DOI: 10.1111/j.1749-6632.1999.tb08103.x [Accessed January 25, 2012].
- [29] McEwen, B.S. and Stellar, E. (1993), Stress and the individual, *Arch Intern Med*, 153, pp. 2093-2101.
- [30] McFarlane, A.C. (2010), The long-term costs of traumatic stress: intertwined physical and psychological consequences, *World Psychiatry*, 9, pp. 3-10.
- [31] Mellner, C., Krantz, G. and Lundberg, U. (2005), Medically unexplained symptoms in women as related to physiological stress responses, *Stress and Health*, 21, pp. 45-52.
- [32] Morgan, C.A., Wang, S., Southwick, S.M., Rasmusson, A., Hazlett, G., Hauger, R.L. and Charney, D.S. (2000), Plasma neuropeptide-y concentrations in humans exposed to military survival training, *Biological Psychiatry*, 47, pp. 902-909.
- [33] Schnorpfeil, P., Noll, A., Schulze, R., Ehlert, U., Frey, K. and Fishcher, J.E. (2003), Allostatic load and work conditions, *Social Science and Medicine*, 57, pp. 647-656.
- [34] Schulkin, J., McEwen, B.S. and Gold, P.W. (1994), Allostasis, amygdala and anticipatory angst, *Neuroscience and Biobehavioral Reviews*, 18, pp. 385-396.
- [35] Seeman, T., Gruenewald, T.L., Karlamangla, A.S., Sidney, S., Liu, K., McEwen, B.S. and Schwartz, J. (2010), Modeling multisystem biological risk in young adults: the coronary artery risk development in young adults study, *American Journal of Human Biology*, 22, pp. 463-472.
- [36] Seeman, T., McEwen, B.S., Rowe, J.W. and Singer, B.H. (2001), Allostatic load as a marker of cumulative biological risk: MacArthur studies of successful aging, *Proceedings of the National Academy of Science*, 98, pp. 4770-4775.
- [37] Seeman, T., Singer, B.H., Rowe, J.W., Horwitz, R.I. and McEwen, B.S. (1997), Price of adaptation - allostatic load and its health consequences, *Arch Intern Med*, 157.
- [38] Seeman, T., Singer, B.H., Ryff, C.D., Love, G.D. and Levy-Stroms, L. (2002), Social relationships, gender, and allostatic load across two age cohorts, *Psychosomatic Medicine*, 64, pp. 395-406.
- [39] Sterling, P. and Eyer, J. (1988), Allostasis: a new paradigm to explain arousal pathology, In: Fisher, S. and Reason, J. (eds.) *Handbook of life stress, cognition, and health*, New York: John Wiley and Sons Inc.

- [40] Anisman, H., Merali, Z., Poulter, M.O. and Hayley, S., Cytokines as a precipitant of depressive illness: animal and human studies, *Curr Pharm Des.* 2005; 11(8):963-72.
- [41] Brydon, L., Walker, C., Wawrzyniak, A., Whitehead, D., Okamura, H., Yajima, J., Tsuda, A. and Steptoe, A., Synergistic effects of psychological and immune stressors on inflammatory cytokine and sickness responses in humans, *Brain Behav Immun.* 2009; 23(2):217-24.
- [42] Collip, D., Myin-Germeys, I. and Van O.J. (2008), Does the concept of “sensitization” provide a plausible mechanism for the putative link between the environment and schizophrenia?, *Schizophr Bull*, Mar; 34(2):220-5.
- [43] McEwen, B.S., Physiology and neurobiology of stress and adaptation: central role of the brain, *Physiol Rev.* 2007 Jul; 87(3):873-904.
- [44] McEwen, B.S. and Wingfield, J.C. (2003), The concept of allostasis in biology and biomedicine, *Horm Behav*, 43(1):2-15.
- [45] McLean, S.A., Clauw, D.J., Abelson, J.L. and Liberzon, I., The Development of Persistent Pain and psychological Morbidity after Motor Vehicle Collision: Integrating the Potential Role of Stress Response Systems into a Biopsychosocial Model, *Psychosom Med* 2005; 67:783-90.
- [46] Post, R.M. and Weiss, S.R., Sensitization and kindling phenomena in mood, anxiety, and obsessive-compulsive disorders: the role of serotonergic mechanisms in illness progression, *Biol Psychiatry* 1998; 44:193-206.



Chapter 4 – THE LONG-TERM COSTS OF TRAUMATIC STRESS: INTERTWINED PHYSICAL AND PSYCHOLOGICAL CONSEQUENCES

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ABSTRACT

The gradual emergence of symptoms following exposure to traumatic events has presented a major conceptual challenge to psychiatry. The mechanism that leads to the progressive escalation of symptoms with the passage of time leading to delayed onset Post-Traumatic Stress Disorder (PTSD) involves the process of sensitisation and kindling. The development of traumatic memories at the time of stress exposure represents a major vulnerability through repeated environmental triggering of the increasing dysregulation of an individual's neurobiology. An increasing body of evidence demonstrates how the increased allostatic load associated with PTSD is associated with a significant body of physical morbidity in the form of chronic musculoskeletal pain, hypertension, hyperlipidaemia, obesity and cardiovascular disease. This increasing body of literature suggests that the effects of traumatic stress need to be considered as a major environmental challenge that places individual's physical and psychological health equally at risk. This broader perspective has important implications for developing treatments that address the underlying dysregulation of cortical arousal and neurohormonal abnormalities following exposure to traumatic stress.

4.1 INTRODUCTION

One of the greatest challenges to the field of traumatic stress has been the observation that many individuals who coped at the time of their traumatic exposure became unwell at a later date.

This observation was particularly challenging in the context of World War I and World War II because the prevailing psychopathological theories at the time did not have a clear rationale for this phenomenon and led to considerable stigmatization of disabled veterans [1]. The later emergence of disability in veterans was attributed to compensation neurosis, pre-existing personality disorder, and suggestibility [2]. Furthermore, with the blossoming of the general life events stress literature, this pattern of morbidity was not consistent with the prevailing views about high levels of acute distress that progressively ameliorated with time [3], [4]. The life events literature which reached its zenith in the 1960s and 1970s focused on notions such as brought-forward time, and emphasized that there was generally a window of approximately six months following which a life event stress could lead to the onset of disorder [5]. Delayed onset Post-Traumatic Stress Disorder (PTSD) was seen as inconsistent with this conclusion about the window of effect of stressful life events [6].

A primary question has been about how a model of psychopathology could account for this lingering and delayed impact of extreme adversity. Prevailing psychoanalytic constructs and later learning theory did not readily provide an answer to this question. Many significant observations in the context of the depression literature have not been readily adapted by the field of traumatic stress until recent links through the research concerning the relevance of child abuse to depression [7].

This chapter explores the evidence about the delayed effects of traumatic stress and their cumulative burden on psychological and physical health. An underlying psychopathological model is summarized and its potential implications for treatment are discussed.

4.2 THE RELATIONSHIP BETWEEN ACUTE STRESS DISORDER AND PTSD

The relation between acute post-traumatic symptoms and the emergence of PTSD is an issue of considerable theoretical and clinical importance. There is now a significant body of research documenting that the majority of people who develop PTSD do not initially meet the diagnostic criteria for an acute stress disorder [8]. In contrast, the majority of those who have an acute stress disorder are likely to display subsequent PTSD.

A number of longitudinal studies of accident victims have demonstrated that it is only with the passage of time that the level of symptoms crosses a threshold sufficient to warrant a clinical diagnosis [9]-[13]. A similar phenomenon was found in a study of severely injured U.S. troops who were assessed at one month, 4 month and 7 months. This study demonstrated that 78.8% who had a disorder at 7 months did not attract a diagnosis at one month [14]. Further support for the delayed emergence is the finding from the screening of military populations that symptoms increase in the first six months following deployment [15], [16]. Additional adversity, conflict or stress plays a role in the later emergence of psychopathology [17]. Hence, in a significant number of individuals, PTSD is a disorder that is not initially manifest in the aftermath of the trauma. Rather, there is a progressive escalation of distress or a later emergence of symptoms, particularly in military and emergency service personnel. A related construct is delayed onset PTSD.

4.3 DELAYED ONSET PTSD

Delayed/late onset PTSD is defined in the DSM-IV [18] as a disorder meeting the diagnostic criteria for PTSD which is present after a post-trauma adjustment period of at least 6 months during which diagnostic criteria were absent or sub-threshold [19]. From a theoretical point of view, these are likely to be individuals who have managed to contain their individual distress by adaptive means, but subsequent stresses and/or the natural progression of neurobiology have led to the manifestation of the symptoms. A recent review about delayed onset PTSD emphasized how much of the confusion has arisen from different definitions of delayed onset PTSD [20]. For example, different interpretations of the concept include an individual who has had sub-syndromal symptoms that have subsequently crossed a threshold of clinical severity as well as an individual who has been asymptomatic and then at some later point developed the disorder.

The existence of this delayed form of PTSD emphasizes how a traumatic experience can apparently lie relatively dormant with an individual only to become manifest at some future point. Many unanswered questions remain about when and how this sub-clinical state is triggered into a full-blown syndrome of PTSD. However, increasingly the evidence would suggest that sub-clinical symptoms leave the individual at risk of progressive activation with further environmental stress or trauma exposure.

A related construct in the depression literature is how individuals who have had partial remission following treatment for an episode of a major depressive disorder are at significantly greater risk of a further recurrence [21]. This vulnerability relates to the sensitivity of individuals with residual depressive symptoms to environmental triggers. The underlying neural structures that are sensitive to activation are the same that have been identified as being relevant to the aetiology of PTSD. For example, Ramel *et al.* [22] highlighted that amygdala reactivity is an important issue in people with a history of depression in contrast to those without such a history. These results indicated that the amygdala plays an essential role in modulating mood congruent memory, particularly during the induction of sad states of mind in individuals who are vulnerable to depression.

In such individuals, the cognitive and neural processing of emotional information potentially contributes to the vulnerability for negative emotions and the onset of depressive episodes [23]. Hence, there is a significant body of literature documenting that individuals who are primed in emotionally labile and sensitive states are at risk for the progressive intensification of further symptoms, particularly when these resonate with the environment. Hence, the presentation of delayed onset of PTSD is not a unique construct in mental health.

Furthermore, Hedtke *et al.* [24] demonstrated that there is a cumulative effect of exposure to interpersonal violence in terms of PTSD, depression and substance abuse problems. The cumulative risk model highlights the ongoing interaction between prior stress exposure and subsequent life events. The severity of stresses that are experienced prior to and following a traumatic exposure have a significant impact on the incidence and severity of the condition [25]. Hence, delayed onset PTSD is intimately involved with the fact that individuals live in a dynamic environment in which traumatic events and other life stresses interact, with the progressive accumulation of risk.

A related question is whether a longer duration of repeated exposures to trauma in defined time periods carries a greater risk of PTSD, a question relevant to the military and police. The recent UK study of Rona *et al.* [26] provides the first reliable data from the military addressing this question and suggests that the risk of PTSD is greater in those units that have had longer durations of deployment with less time to recuperate between deployments. This study highlights that PTSD is an emerging disorder where multiple traumatic events progressively increase the risk of occurrence.

4.4 THE ENDURING IMPACT OF TRAUMATIC MEMORY

The repeated recollection of traumatic memories is a central component of the phenomenological response to traumatic events. Freud highlighted the importance of traumatic memories in his first lecture with Breuer, suggesting that these were the “agent still at work” playing a central role in symptom onset and maintenance [27]. Subsequently, modelling in epidemiological samples has highlighted how traumatic memories account for the relationship between exposure to traumatic events and the symptoms of hyperarousal and avoidance [28].

The triggering of these memories is also a consequence of fear conditioning mechanisms [29], and these serve to sustain and kindle the increased arousal that is central to the symptoms of PTSD [30]. The disorder arises because some individuals are unable to progressively shut off the acute stress response, which is ubiquitous at times of exposure to such events. From a learning theory perspective, this process is seen as a failure of extinction or new learning in the aftermath of the fear conditioning. Rather, there is a progressive augmentation of the amplitude of the response to reminders.

4.5 TRIGGERING AND SENSITIZATION

A primary component of the symptomatology of PTSD is the re-experiencing or reliving of the traumatic memory that has both elements of psychophysiological reactivation and psychological distress. A unique part of this condition is the repeated reactivation of the traumatic memory and the associated stress response with the attendant risk of the progressive augmentation of the reactivity of the individual [31]. In fact, the suggestion has been made that in PTSD there is a failure of the retention and extinction of conditioned fear and that this is an acquired deficit in the condition [32].

On reviewing the available evidence, Rauch *et al.* [33] have suggested that in PTSD there is an exaggerated amygdala response which underpins the excessive acquisition of fear associations and the expression of fear

responses. A corresponding deficit of frontal cortical functioning plays a central role in mediating extinction. There is also a deficit in the appreciation of the context of safety, which is related to hippocampal function.

The central mechanism is the process of sensitization to the subtle reminders of traumatic memories as well as exposure to prior and future traumatic events. This process of reactivity to minor cues, which very frequently go unrecognised, serves to progressively increase and exacerbate the reactivity of the dysfunctional individual [34]. This leads to an interaction between the individual's distress, psychophysiological reactivity, and the neurohormonal response at the time of the traumatic event. In discussing this question, it is important to recognize that some traumas in combat and policing are not the equivalent of a single traumatic event such as being in a motor vehicle accident. Combat and emergency service work involves repeated activations of the fear and stress systems that are then prone to present as future dysregulation over time.

Individuals who develop PTSD have been found to have a progressive evolution of dysfunction as described above [30]. Progressively, they react to the presence of potential threat with greater amplitude or intensity and ultimately develop a generalized over-reactivity to a range of stimuli in their civilian and military environments that remind them of the traumatic event. This cycle of increasing reactivity to a widening range of cues in their environment serves to further reinforce the distress response. This pattern is not unique to PTSD and has been highlighted in depression as having a critical role in early episodes [35].

Elzinga and Bremner [36] have further characterized the role of the noradrenergic system in the enhanced encoding of the emotional memories and fear-conditioning in individuals who develop PTSD. The failure of the normal neurotransmitter inhibitory mechanisms that quell the stress response appears to be important in the progression of the individual's distress into a full blown post-event or post-traumatic stress disorder. According to Miller [37], childhood trauma increases the risk of adult psychopathology because of the same process of sensitization [7]. Shalev [38] has highlighted that this process is also intimately integrated into the person's social and cultural setting. He states that traumatic events are followed by "*a critical period of increased brain plasticity, during which irreversible neuronal changes may occur in those who develop PTSD*". He also emphasizes the importance of group cohesion, marital discord, and leadership skills as mediating factors.

Fear conditioning, kindling, and sensitization contribute to the manner in which repeated activation of the fear memories, in PTSD, leads to the emergence of spontaneous intrusive memories [39]. In depression, a similar process predisposes an individual to negative affective appraisal and increasingly depressed mood. There is an emerging medical scientific literature indicating that pharmacological agents may be able to modify these responses [40].

The measurement of the startle response can objectively characterize the sensitization that occurs in the fear and alarm response in PTSD. Increased heart rate in response to sudden loud tones is an abnormality that emerges following traumatic exposure [41], [42]. This increased reactivity suggests the role of fear conditioning and the impact the environment following the event. The acquisition of an increased startle response was not related to the severity of the event or the initial intensity of the symptoms. These observations are consistent with the model of progressive neuronal sensitization and increasing heart rate reactivity over the subsequent six months to trauma exposure. This pattern of increased reactivity is also observed in relationship to innocuous and aversive stimuli in a conditioning experiment where increased autonomic reactivity was demonstrated to both types of stimuli [43]. Once conditioned, those with PTSD had reduced extinction to conditioned responses.

PTSD is only one of the outcomes that have been associated with trauma exposure. The emergence of multiple physical symptoms also has a strong association, and the consensus opinion is that these syndromes are indicative of a general reflection of distress. The underlying mechanisms of these disorders have been related to

similar mechanisms of sensitization noted in those with PTSD [44]. In parallel, multiple traumas have an accumulative effect on physical health which appears to be independent of the development of PTSD [45].

4.6 PHYSICAL MORBIDITY ASSOCIATED WITH TRAUMATIC STRESS

There is longstanding interest in the effects of stress on health, due to the strain that it places on the adaptive capacity of individuals, which thereby leads to an increased risk of disease.

The effects of stress on the Hypothalamic Pituitary Adrenal (HPA)-axis and the autonomic nervous system have long been studied and the regulation of these systems has been referred to as “allostatic load”. This refers to the wear and tear on the body in response to repeated cycles of stress. This phenomenon has the potential to be manifest in various ways, influenced by the interaction with other personal and environmental risk factors for disease. Hence, the physiological dysregulation that underpins allostasis represents a final common pathway to disease that can be manifest in various ways.

Particularly in the context of post-deployment syndromes, the link to musculoskeletal symptoms has become a focus of increasing interest. Equally, the role of allostatic load has come to be seen as an important risk for coronary arterial disease and its antecedent risk factors. However, the intermediary role of PTSD has not been the focus of particular interest in explaining these relationships until recently. The emerging body of evidence, which coincides with the real prevalence of PTSD in studies such as the National Comorbidity Survey Replication [46], suggests that physiological dysregulation associated with PTSD may play a central mediating role in a range of conditions.

4.7 PTSD AND PSYCHOSOMATIC SYNDROMES

Andreski *et al.* [47] reported that, of all the psychiatric disorders, PTSD is the one with the strongest relationship with somatization and particularly medically unexplained pain. Although there is substantial literature relating somatization to PTSD, this body of knowledge is seldom referred to in the broader literature about somatization, which has largely focused on the role of depression and anxiety [48]-[52]. Particularly in the light of more recent epidemiological studies which suggest the previous underestimation of the prevalence of traumatic events and PTSD in many settings, there is a greater need to focus on the possible role of trauma in populations with medically unexplained symptoms [53].

There has been an increasing recognition of a shared pattern of symptoms and aetiology between whiplash, fibromyalgia, irritable bowel, chronic fatigue and PTSD. In particular, disorders of the HPA-axis have been identified in all these disorders [54], [55], where the shared dysfunction appears to be an enhanced negative feedback of the axis. Such stress-induced changes have been associated with major impacts on neurogenesis and brain functioning [56], [57]. A recent prospective study has suggested that this dysfunction of the HPA-axis plays an important role in the onset of chronic widespread musculoskeletal pain in a general population sample [58]. McEwen’s model of allostasis has focused on the temporal lobe and the changes induced by cortisol at the times of stress exposure [56]. Whilst focusing on the importance of this process in PTSD, persistent pain has also been associated with stress-like induced alterations of hippocampal neurogenesis and gene expression [59].

Sensitization is a critical process in the onset of pain syndromes and also in PTSD, as outlined above. The exposure to environmental triggers to the traumatic memory structure plays a critical role in the emergence and progressive escalation of an individual’s distress across time, which includes somatic dimensions. This complex biological process emerges in the weeks and months following the event, involving the interaction between the individual’s distress and the neurohormonal response at the time of the traumatic event [34].

The central role of the amygdala in the kindling in PTSD has much in common with the phenomena of windup of C fibre evoked pain [60]. The centrality of this process has been suggested in both fibromyalgia and chronic fatigue [61], [62].

Similar patterns of sensitization and modified pain sensitivity have been characterized in irritable bowel syndrome [63], [64]. The shared neurobiological abnormalities in these conditions are a further argument in favour of a generalized stress response syndrome underpinning multiple complaints. Furthermore, this has been associated with a modified autonomic function, that is also thought to play an important role in the pain response in fibromyalgia patients, individuals with neck and shoulder pain, and irritable bowel disorder [65], and has been found to be present also in individuals absent from work with stress-related illness [66].

4.8 THE RELATIONSHIP BETWEEN HYPERTENSION AND PTSD

A number of studies have suggested that PTSD has a direct relationship with the risk of developing hypertension. A study of a probability sample from the U.S. National Comorbidity Survey examined the interaction between PTSD and major depression as determinants of hypertension. It concluded that PTSD was related to hypertension, independent of depression, and that this finding could possibly explain the elevated rates of cardiovascular disease associated with PTSD [67]. This specific relationship explains the high prevalence rate of hypertension identified amongst refugee psychiatric patients [68].

O'Toole and Catts [69] examined an epidemiological sample of Australian Vietnam veterans, aiming to explore the relationship between the physical health consequences of combat trauma exposure and PTSD. Hypertension was one of the conditions that was found to be associated with PTSD, both before and after controlling for potential confounds. In PTSD, it has been recognized that exposure to traumatic triggers leads to increased blood pressure, heart rate, and sympathetic activation of sweating in the hands [70]. This abnormality has a significant degree of specificity for PTSD [71]. This is consistent with the observation that in PTSD there is an increased activity of the sympathetic nervous system, and in particular a hyperfunction of the central noradrenergic system [72].

A U.S. population study of hypertensive individuals looked at the impact of the September 11, 2001 attacks. Whilst these patients did not have a particularly high level of exposure, in the two months following the terroristic attacks they had an increase between 1.7 and 3.3 mm of mercury of systolic blood pressure compared with a similar period in 2000. Hence, at a population level, individuals who are suffering from hypertension are at risk of increases in blood pressure as a consequence of exposure to stressful events [73].

This body of evidence indicates that there is a link between PTSD and the risk of hypertension. This is an important development, as it indicates that the failure to specifically look at the relationship between PTSD and hypertension in earlier studies has led to confusion about the link between stress and coronary heart disease. For example, the Australian National Heart Foundation in 2003 suggested that there was no strong or consistent evidence for a causal association between chronic life events, work stress, patterns of hostility/anxiety disorders or panic disorder and coronary heart disease. The intermediary role of PTSD in this relationship is an important link [74].

4.9 HYPERLIPIDAEMIA

Lipid metabolism is an area of importance to the risk of vascular disease. A study of Brazilian police officers demonstrated that officers with PTSD had significantly higher levels of total cholesterol and triglycerides [75].

A study from Croatia compared patients with combat-related PTSD and a control group consisting of patients with major depressive disorder [76]. In this study, lipid profiles consisting of cholesterol, LDL, HDL, and triglycerides were assessed. The groups were matched for age and Body Mass Index (BMI). The individuals with PTSD had higher mean levels of cholesterol, LDL-C, and triglycerides and lower HDL-C than the control group. The arteriosclerotic index was higher in the PTSD than the control group. These results were taken to conclude that patients with combat-related PTSD had a higher risk of arteriosclerosis [76]-[78]. It is probable these findings will generalize to other populations.

4.10 THE RELATIONSHIP BETWEEN OBESITY AND PTSD

Obesity is associated with an increased risk for several diseases, including cardiovascular disease. Vieweg *et al.* [79], using a national database, documented a significantly increased BMI in individuals with PTSD, not affected by the decade of life. It was concluded that PTSD may be a risk factor for being overweight. This relationship has also been found in clinical samples [80].

A population study of young adults in Germany [81] examined the relationship between a PTSD diagnosis and having a BMI greater than 30. In the 10-year follow-up of this sample from childhood, obesity was predicted by an antecedent sub-threshold or full blown PTSD, with an odds ratio of 3, amongst men but not women. This relationship has not been universally identified, and a series of complexities influencing it should be acknowledged. However, a further population sample in New Zealand did find an association between PTSD and obesity (odds ratio 2.64) [82].

In a study of police officers, the relationship between PTSD symptoms and metabolic syndrome was examined. Metabolic syndrome was deemed to be present if an individual had 3 of more components (obesity, elevated blood pressure, reduced high density lipoprotein (HDL cholesterol), elevated triglycerides and abnormal glucose). The officers with severe PTSD had 3 times the rate of metabolic syndrome of the lowest PTSD severity category [83].

4.11 THE RELATIONSHIP BETWEEN PTSD SYMPTOMS AND CORONARY HEART DISEASE

The U.S. Department of Veterans' Affairs has conducted a normative aging study [84]. The sample, including men who had completed two scales for PTSD, was recruited in 1990. The men were followed up and the incidence of coronary heart disease occurring up to May 2001 was assessed. For each standard deviation increase in the level of post-traumatic symptoms, the men had an attributed relative risk of 1.26 for non-fatal myocardial infarction and fatal coronary heart disease combined and 1.21 for all coronary heart disease outcomes. The importance of this study is that it indicated that the level of post-traumatic symptoms, rather than the PTSD diagnosis of itself, is associated with an increased risk of coronary heart disease. These results were maintained after controlling for depressive symptoms.

While hypertension, hyperlipidaemia and obesity are risk factor associations that could link PTSD to heart disease, this could also relate to the exaggerated catecholamine response to trauma-related triggers. It has been demonstrated in a variety of settings that catecholamines may lead to injury of the lining intimal endothelium of the coronary arteries, leading to the development of atherosclerosis [85], [86]. Kubzansky *et al.* [84] concluded that “*exposure to trauma and prolonged stress not only may increase the risk of serious mental health problems but also be cardiotoxic*”.

Boscarino [87] studied a national random sample of 4,328 Vietnam veterans who did not have heart disease at baseline in 1985. The mortality due to heart disease from having PTSD had a hazard ratio of 2.25. When the effects of depression were controlled for, the degree of combat exposure made little difference to the results. The author concluded that “*early age heart disease may be an outcome after military service among PTSD positive veterans*”. Again, this study emphasized that there is a specific risk for heart disease mortality associated with PTSD, but there is also a risk simply associated with increasing level of post-traumatic symptoms in individuals who do not reach the diagnostic threshold.

Another study carried out in former World War II prisoners of war found that prisoners with PTSD had a significantly increased risk of cardiovascular diseases, including hypertension and chronic ischemic heart disease, compared with individuals who had been prisoners of war but had not developed PTSD as well as non-prisoners [88].

In summary, the evidence from prospective studies is suggestive of a link between heart disease and PTSD.

4.12 CLINICAL IMPLICATIONS

The association between PTSD and a number of physical conditions emphasizes that the effects of traumatic stress are far reaching. There is the potential for a pervasive disruption of an individual’s neurobiology and psychophysiology following exposure, and PTSD is only one end point. The association with cardiovascular risk factors and inflammatory markers indicates that exposure to traumatic stress leads to a general disruption of an individual’s underlying homeostasis [89], [90].

In essence, the internal physiological environment of an individual adapts to external demands. This dynamic regulatory process involves a continuous adaptation of physiology in response to environmental demand. When the body is repeatedly stressed, the consequent allostatic state has the capacity to disrupt an individual’s health [91]. For example, Karlamangla *et al.* [92] looked at the longitudinal impact of allostatic load in the MacArthur studies of successful aging, and found that those individuals whose allostatic load dropped over a 5-year period had a significant lower risk of mortality.

Hence, the underlying acclimatization of an individual to an environment and the costs that this exerts on the body is critical to the maintenance of health from a psychological and physical perspective [93]. Traumatic stress leads to a disruption of the glucocorticoid system, in concert with a range of other neuropeptides such as Corticotrophin-Releasing Factor (CRF), beta endorphin, neuropeptide Y and the catecholamines. The impact of glucocorticoids on the amygdala and hippocampus as part of contextual fear conditioning is an essential component of allostatic adaptation [94].

4.13 TREATMENT IMPLICATIONS

At the present time, the treatment of PTSD focuses on cognitive behavioural therapy and the use of selective serotonin reuptake inhibitors [95]. However, recommended treatments do not take into account the need to address the underlying instability of psychophysiology, particularly in the earlier periods following exposure. In this light, it is interesting that prazosin, an alpha-adrenergic antagonist, has been found to have a beneficial role in the treatment of PTSD [96], and that cortisol has been found in intensive care populations to have a protective effect against PTSD [97].

One treatment that may be of particular significance and requires systematic investigation is neurofeedback [98], [99]. There is now an established literature about abnormalities of quantitative EEG which suggest a

significant disruption of cortical arousal in PTSD [100]. Neurofeedback has been used in other disorders where there are demonstrated abnormalities of cortical activity. Particularly in populations at a significant risk for PTSD, such as military and emergency service groups, the use of this technique may be beneficial. Equally, the development of methods to modify the progressive augmentation of startle could help individuals to re-establish their psychophysiology to its baseline state. Recalibration may be easier prior to the development of a full-blown clinical disorder.

4.14 CONCLUSION

The progressive emergence of symptoms following traumatic stress exposure is a challenging concept and delayed onset PTSD has long been a controversial notion. However, there is an increasing body of literature demonstrating that a significant proportion of trauma victims do not have their maximal stressor response in the immediate aftermath of the event, but rather this progressively increases with time. In some individuals, the apparent adverse consequences of the stress exposure lie dormant for a long period of time before some intercurrent adversity leads to its manifestation.

Thus, it would appear that trauma exposure initiates a process of disruption of an individual's internal psychophysiology that is then progressively sensitized and kindled with the repeated exposures to triggers. This pattern of increasing sensitivity to environmental load can also manifest as hypertension, hyperlipidaemia, and obesity. There is now an established association between cardiovascular disease and PTSD.

Ultimately, major treatment advances in PTSD may arise from considering the broader disruption of these neurobiological systems by their repeated activation. This emphasizes that PTSD is not simply a psychosocial disorder, but one underpinned by a major neurobiological disruption.

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4.16 REFERENCES

- [1] Shephard, B., *A war of nerves: soldiers and psychiatrists in the twentieth century*, Cambridge: Harvard University Press, 2001.
- [2] Glass, A.J., *Mental health programs in the armed forces*, In: Arieti, S. (ed). *American handbook of psychiatry*, New York: Basic Books, 1974.
- [3] Brown, G.W., Harris, T.O. and Peto, J., *Life events and psychiatric disorders*, 2. Nature of causal link. *Psychol Med* 1973; 3:159-76.
- [4] Paykel, E.S., *Contribution of life events to causation of psychiatric illness*, *Psychol Med* 1978; 8:245-53.
- [5] McFarlane, A.C., *The effects of stressful life events and disasters: research and theoretical issues*, *Aust N Z J Psychiatry* 1985; 19:409-21.

- [6] Solomon, Z., The impact of posttraumatic stress disorder in military situations, *J Clin Psychiatry* 2001; 62 (Suppl. 17):11-5.
- [7] Heim, C. and Nemeroff, C.B., The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies, *Biol Psychiatry* 2001; 49:1023-39.
- [8] Bryant, R.A., Creamer, M., O'Donnell, M.L. *et al.*, A multisite study of the capacity of acute stress disorder diagnosis to predict posttraumatic stress disorder, *J Clin Psychiatry* 2008; 69:923-9.
- [9] McFarlane, A.C., Atchison, M. and Yehuda, R., The acute stress response following motor vehicle accidents and its relation to PTSD, *Ann N Y Acad Sci* 1997; 821:437-41.
- [10] Carty, J., O'Donnell, M.L. and Creamer, M., Delayed-onset PTSD: a prospective study of injury survivors, *J Affect Disord* 2006; 90:257-61.
- [11] Orcutt, H.K., Erickson, D.J. and Wolfe, J., The course of PTSD symptoms among Gulf War veterans: a growth mixture modeling approach, *J Trauma Stress* 2004; 17:195-202.
- [12] Solomon, Z. and Mikulincer, M., Trajectories of PTSD: a 20-year longitudinal study, *Am J Psychiatry* 2006; 163:659-66.
- [13] Southwick, S.M., Morgan, C.A., Darnell, A. *et al.*, Trauma-related symptoms in veterans of Operation Desert Storm: a 2-year follow-up, *Am J Psychiatry* 1995; 152:1150-5.
- [14] Grieger, T.A., Cozza, S.J., Ursano, R.J. *et al.*, Posttraumatic stress disorder and depression in battle-injured soldiers, *Am J Psychiatry* 2006; 163:1777-83.
- [15] Bliese, P., White, K., Adler, A. *et al.*, Post-Deployment Psychological Screening: Interpreting and Scoring DD Form 2900, Research Report 2005-003. Heidelberg: US Army Medical Research Unit – Europe, 2005.
- [16] Milliken, C.S., Auchterlonie, J.L. and Hoge, C.W., Longitudinal assessment of mental health problems among active and reserve component soldiers returning from the Iraq war, *JAMA* 2007; 298:2141-8.
- [17] Benyamini, Y. and Solomon, Z., Combat stress reactions, posttraumatic stress disorder, cumulative life stress, and physical health among Israeli veterans twenty years after exposure to combat, *Soc Sci Med* 2005; 61:1267-77.
- [18] American Psychiatric Association, Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC, USA: American Psychiatric Association, 1994.
- [19] Buckley, T.C., Blanchard, E.B. and Hickling, E.J., A prospective examination of delayed onset PTSD secondary to motor vehicle accidents, *J Abnorm Psychol* 1996; 105:617-25.
- [20] Andrews, B., Brewin, C.R., Philpott, R. *et al.*, Delayed-onset posttraumatic stress disorder: a systematic review of the evidence, *Am J Psychiatry* 2007; 164:1319-26.
- [21] Pintor, L., Gasto, C., Navarro, V. *et al.*, Relapse of major depression after complete and partial remission during a 2-year follow-up, *J Affect Disord* 2003; 73:237-44.

- [22] Ramel, W., Goldin, P.R., Eyler, L.T. *et al.*, Amygdala reactivity and mood-congruent memory in individuals at risk for depressive relapse, *Biol Psychiatry* 2007; 61:231-9.
- [23] Leppanen, J.M., Emotional information processing in mood disorders: a review of behavioral and neuroimaging findings, *Curr Opin Psychiatry* 2006; 19:34-9.
- [24] Hedtke, K.A., Ruggiero, K.J., Fitzgerald, M.M. *et al.*, A longitudinal investigation of interpersonal violence in relation to mental health and substance use, *J Consult Clin Psychol* 2008;76:633-47.
- [25] Maes, M., Mylle, J., Delmeire, L. *et al.*, Pre- and post-disaster negative life events in relation to the incidence and severity of post-traumatic stress disorder, *Psychiatry Res* 2001;105:1-12.
- [26] Rona, R.J., Fear, N.T., Hull, L. *et al.*, Mental health consequences of overstretch in the UK armed forces: first phase of a cohort study, *BMJ* 2007; 335:603.
- [27] Freud, S., The aetiology of hysteria, In: Strachey J (ed). The standard edition of the complete psychological works of Sigmund Freud, Vol. 3, London, UK: Vintage, 1962.
- [28] McFarlane, A.C., Avoidance and intrusion in posttraumatic stress disorder, *J Nerv Ment Dis* 1992; 180:439-45.
- [29] Wessa, M. and Flor, H., Failure of extinction of fear responses in posttraumatic stress disorder: evidence from second-order conditioning, *Am J Psychiatry* 2007; 164:1684-92.
- [30] Post, R.M., Weiss, S.R., Smith, M. *et al.*, Kindling versus quenching. Implications for the evolution and treatment of posttraumatic stress disorder, *Ann N Y Acad Sci* 1997; 821:285-95.
- [31] McFarlane, A.C., Yehuda, R. and Clark, C.R., Biologic models of traumatic memories and post-traumatic stress disorder. The role of neural networks, *Psychiatr Clin North Am* 2002; 25:253-70.
- [32] Milad, M.R., Orr, S.P., Lasko, N.B. *et al.*, Presence and acquired origin of reduced recall for fear extinction in PTSD: results of a twin study, *J Psychiatr Res* 2008; 42:515-20.
- [33] Rauch, S.L., Shin, L.M. and Phelps, E.A., Neurocircuitry models of posttraumatic stress disorder and extinction: human neuroimaging research – past, present, and future, *Biol Psychiatry* 2006; 60:376-82.
- [34] Marshall, R.D. and Garakani, A., Psychobiology of the acute stress response and its relationship to the psychobiology of post-traumatic stress disorder, *Psychiatr Clin North Am* 2002; 25:385-95.
- [35] Kendler, K.S., Thornton, L.M. and Gardner, C.O., Stressful life events and previous episodes in the etiology of major depression in women: an evaluation of the “kindling” hypothesis, *Am J Psychiatry* 2000; 157:1243-51.
- [36] Elzinga, B.M. and Bremner, J.D., Are the neural substrates of memory the final common pathway in posttraumatic stress disorder (PTSD)?, *J Affect Disord* 2002; 70:1-17.
- [37] Miller, L., Neurosensitization: a model for persistent disability in chronic pain, depression, and posttraumatic stress disorder following injury, *NeuroRehabilitation* 2000; 14:25-32.

- [38] Shalev, A.Y., Biological responses to disasters, *Psychiatr Q* 2000; 71:277-88.
- [39] Grillon, C., Southwick, S.M. and Charney, D.S., The psychobiological basis of posttraumatic stress disorder, *Mol Psychiatry* 1996; 1:278-97.
- [40] Bonne, O., Grillon, C., Vythilingam, M. *et al.*, Adaptive and maladaptive psychobiological responses to severe psychological stress: implications for the discovery of novel pharmacotherapy, *Neurosci Biobehav Rev* 2004; 28:65-94.
- [41] Morgan, C.A, III, Grillon, C., Southwick, S.M. *et al.*, Exaggerated acoustic startle reflex in Gulf War veterans with posttraumatic stress disorder, *Am J Psychiatry* 1996;153:64-8.
- [42] Shalev, A.Y., Peri, T., Brandes, D. *et al.*, Auditory startle response in trauma survivors with posttraumatic stress disorder: a prospective study, *Am J Psychiatry* 2000; 157:255-61.
- [43] Peri, T., Ben-Shakhar, G., Orr, S.P. *et al.*, Psychophysiology assessment of aversive conditioning in posttraumatic stress disorder, *Biol Psychiatry* 2000; 47:512-9.
- [44] McFarlane, A.C., Stress-related musculoskeletal pain, *Best Pract Res Clin Rheumatol* 2007; 21:549-65.
- [45] Sledjeski, E.M., Speisman, B. and Dierker, L.C., Does number of lifetime traumas explain the relationship between PTSD and chronic medical conditions? Answers from the National Comorbidity Survey-Replication (NCS-R), *J Behav Med* 2008; 31:341-9.
- [46] Kessler, R.C., Berglund, P., Demler, O. *et al.*, Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication, *Arch Gen Psychiatry* 2005; 62:593-602.
- [47] Andreski, P., Chilcoat, H. and Breslau, N., Post-traumatic stress disorder and somatization symptoms: a prospective study, *Psychiatry Res* 1998; 79:131-8.
- [48] O'Malley, P.G., Jackson, J.L., Kroenke, K. *et al.*, The value of screening for psychiatric disorders in rheumatology referrals, *Arch Intern Med* 1998; 158:2357-62.
- [49] Patten, S.B., Williams, J.V. and Wang, J., Mental disorders in a population sample with musculoskeletal disorders, *BMC Musculoskelet Disord* 2006; 7:37.
- [50] Simon, G.E. and Von Korff, M., Somatization and psychiatric disorder in the NIMH Epidemiologic Catchment Area study, *Am J Psychiatry* 1991; 148:1494-500.
- [51] Stang, P.E., Brandenburg, N.A., Lane, M.C. *et al.*, Mental and physical comorbid conditions and days in role among persons with arthritis, *Psychosom Med* 2006;68:152-8.
- [52] Von Korff, M., Crane, P., Lane, M. *et al.*, Chronic spinal pain and physical-mental comorbidity in the United States: results from the national comorbidity survey replication, *Pain* 2005; 113:331-9.
- [53] Zautra, A.J. and Smith, B.W., Depression and reactivity to stress in older women with rheumatoid arthritis and osteoarthritis, *Psychosom Med* 2001; 63:687-96.
- [54] Pillemer, S.R., Bradley, L.A., Crofford, L.J. *et al.*, The neuroscience and endocrinology of fibromyalgia, *Arthritis Rheum* 1997; 40:1928-39.

- [55] Yehuda, R., Post-traumatic stress disorder, *N Engl J Med* 2002; 346:108-14.
- [56] McEwen, B.S., The neurobiology of stress: from serendipity to clinical relevance, *Brain Res* 2000; 886:172-189.
- [57] Korte, S.M., Koolhaas, J.M., Wingfield, J.C. *et al.*, The Darwinian concept of stress: benefits of allostasis and costs of allostatic load and the trade-offs in health and disease, *Neurosci Biobehav Rev* 2005; 29:3-38.
- [58] McBeth, J., Silman, A.J., Gupta, A. *et al.*, Moderation of psychosocial risk factors through dysfunction of the hypothalamic-pituitary-adrenal stress axis in the onset of chronic widespread musculoskeletal pain: findings of a population-based prospective cohort study, *Arthritis Rheum* 2007; 56:360-71.
- [59] Duric, V. and McCarron, K.E., Persistent pain produces stress-like alterations in hippocampal neurogenesis and gene expression, *J Pain* 2006; 7:544-55.
- [60] Staud, R., Craggs, J.G., Robinson, M.E. *et al.*, Brain activity related to temporal summation of C-fiber evoked pain, *Pain* 2007; 129:130-42.
- [61] Meeus, M. and Nijs, J., Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome, *Clin Rheumatol* 2007; 26:465-73.
- [62] McLean, S.A., Clauw, D.J., Abelson, J.L. *et al.*, The development of persistent pain and psychological morbidity after motor vehicle collision: integrating the potential role of stress response systems into a biopsychosocial model, *Psychosom Med* 2005; 67:783-90.
- [63] Talley, N.J. and Spiller, R., Irritable bowel syndrome: a little understood organic bowel disease?, *Lancet* 2002; 360:555-64.
- [64] Verne, G.N., Himes, N.C., Robinson, M.E. *et al.*, Central representation of visceral and cutaneous hypersensitivity in the irritable bowel syndrome, *Pain* 2003; 103:99-110.
- [65] Nilsen, K.B., Sand, T., Westgaard, R.H. *et al.*, Autonomic activation and pain in response to low-grade mental stress in fibromyalgia and shoulder/neck pain patients, *Eur J Pain* 2007; 11:743-55.
- [66] Heiden, M., Barnekow-Bergkvist, M., Nakata, M. *et al.*, Autonomic activity, pain, and perceived health in patients on sick leave due to stress-related illnesses, *Integr Physiol Behav Sci* 2005; 40:3-16.
- [67] Kibler, J.L., Joshi, K. and Ma, M., Hypertension in relation to posttraumatic stress disorder and depression in the US National Comorbidity Survey, *Behav Med* 2009; 34:125-32.
- [68] Kinzie, J.D., Riley, C., McFarland, B. *et al.*, High prevalence rates of diabetes and hypertension among refugee psychiatric patients, *J Nerv Ment Dis* 2008; 196:108-12.
- [69] O'Toole, B.I. and Catts, S.V., Trauma, PTSD, and physical health: an epidemiological study of Australian Vietnam veterans, *J Psychosom Res* 2008; 64:33-40.
- [70] Orr, S.P., Metzger, L.J. and Pitman, R.K., Psychophysiology of post-traumatic stress disorder, *Psychiatr Clin North Am* 2002; 25:271-93.

- [71] Keane, T.M., Kolb, L.C., Kaloupek, D.G. *et al.*, Utility of psychophysiological measurement in the diagnosis of posttraumatic stress disorder: results from a Department of Veterans Affairs Cooperative Study, *J Consult Clin Psychol* 1998; 66:914-23.
- [72] Bedi, U.S. and Arora, R., Cardiovascular manifestations of posttraumatic stress disorder, *J Natl Med Assoc* 2007; 99:642-9.
- [73] Gerin, W., Chaplin, W., Schwartz, J.E. *et al.*, Sustained blood pressure increase after an acute stressor: the effects of the 11 September 2001 attack on the New York City World Trade Center, *J Hypertens* 2005; 23:279-84.
- [74] Bunker, S.J., Colquhoun, D.M., Esler, M.D. *et al.*, "Stress" and coronary heart disease: psychosocial risk factors, *Med J Aust* 2003; 178:272-6.
- [75] Maia, D.B., Marmar, C.R., Mendlowicz, M.V. *et al.*, Abnormal serum lipid profile in Brazilian police officers with post-traumatic stress disorder, *J Affect Disord* 2008; 107:259-63.
- [76] Karlovic, D., Buljan, D., Martinac, M. *et al.*, Serum lipid concentrations in Croatian veterans with post-traumatic stress disorder, post-traumatic stress disorder comorbid with major depressive disorder, or major depressive disorder, *J Korean Med Sci* 2004; 19:431-6.
- [77] Solter, V., Thaller, V., Karlovic, D. *et al.*, Elevated serum lipids in veterans with combat-related chronic posttraumatic stress disorder, *Croat Med J* 2002; 43:685-9.
- [78] Kagan, B.L., Leskin, G., Haas, B. *et al.*, Elevated lipid levels in Vietnam veterans with chronic posttraumatic stress disorder, *Biol Psychiatry* 1999; 45:374-7.
- [79] Vieweg, W.V., Julius, D.A., Bates, J. *et al.*, Posttraumatic stress disorder as a risk factor for obesity among male military veterans, *Acta Psychiatr Scand* 2007; 116:483-7.
- [80] David, D., Woodward, C., Esquenazi, J. *et al.*, Comparison of comorbid physical illnesses among veterans with PTSD and veterans with alcohol dependence, *Psychiatr Serv* 2004; 55:82-5.
- [81] Perkonig, A., Owashi, T., Stein, M.B. *et al.*, Posttraumatic stress disorder and obesity: evidence for a risk association, *Am J Prev Med* 2009; 36:1-8.
- [82] Scott, K.M., McGee, M.A., Wells, J.E. *et al.*, Obesity and mental disorders in the adult general population, *J Psychosom Res* 2008; 64:97-105.
- [83] Violanti, J.M., Fekedulegn, D., Hartley, T.A. *et al.*, Police trauma and cardiovascular disease: association between PTSD symptoms and metabolic syndrome, *Int J Emerg Ment Health* 2006; 8:227-37.
- [84] Kubzansky, L.D., Koenen, K.C., Spiro, A., III *et al.*, Prospective study of posttraumatic stress disorder symptoms and coronary heart disease in the Normative Aging Study, *Arch Gen Psychiatry* 2007; 64:109-16.
- [85] Schneiderman, N., Psychophysiologic factors in atherogenesis and coronary artery disease, *Circulation* 1987; 76:141-7.

- [86] Vanitallie, T.B., Stress: a risk factor for serious illness, *Metabolism* 2002; 51:40-5.
- [87] Boscarino, J.A., A prospective study of PTSD and early-age heart disease mortality among Vietnam veterans: implications for surveillance and prevention, *Psychosom Med* 2008; 70:668-76.
- [88] Kang, H.K., Bullman, T.A. and Taylor, J.W., Risk of selected cardiovascular diseases and posttraumatic stress disorder among former World War II prisoners of war, *Ann Epidemiol* 2006; 16:381-6.
- [89] von Kanel, R., Hepp, U., Kraemer, B. *et al.*, Evidence for low-grade systemic proinflammatory activity in patients with posttraumatic stress disorder, *J Psychiatr Res* 2007; 41:744-52.
- [90] von Kanel, R., Hepp, U., Traber, R. *et al.*, Measures of endothelial dysfunction in plasma of patients with posttraumatic stress disorder, *Psychiatry Res* 2008; 158:363-73.
- [91] McEwen, B.S. and Stellar, E., Stress and the individual. Mechanisms leading to disease, *Arch Intern Med* 1993; 153:2093-101.
- [92] Karlamangla, A.S., Singer, B.H. and Seeman, T.E., Reduction in allostatic load in older adults is associated with lower all-cause mortality risk: MacArthur studies of successful aging, *Psychosom Med* 2006; 68:500-7.
- [93] McEwen, B.S. and Wingfield, J.C., The concept of allostasis in biology and biomedicine, *Horm Behav* 2003; 43:2-15.
- [94] McEwen, B.S., Mood disorders and allostatic load, *Biol Psychiatry* 2003; 54:200-7.
- [95] Australian Centre for Posttraumatic Mental Health, Australian Guidelines for the Treatment of Adults with Acute Stress Disorder and Posttraumatic Stress Disorder, Melbourne: Australian Centre for Posttraumatic Mental Health, 2007.
- [96] Raskind, M.A., Peskind, E.R., Kanter, E.D. *et al.*, Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study, *Am J Psychiatry* 2003; 160:371-3.
- [97] de Quervain, D.J. and Margraf, J., Glucocorticoids for the treatment of post-traumatic stress disorder and phobias: a novel therapeutic approach, *Eur J Pharmacol* 2008; 583:365-71.
- [98] Arns, M., de Ridder, S., Streh, U. *et al.*, Efficacy of neurofeedback treatment in ADHD: the effects on inattention, impulsivity and hyperactivity: a meta-analysis, *Clin EEG Neurosci* 2009; 40:180-9.
- [99] Linden, D.E., Brain imaging and psychotherapy: methodological considerations and practical implications, *Eur Arch Psychiatry Clin Neurosci* 2008; 258 (Suppl. 5):71-5.
- [100] Clark, C.R., Galletly, C.A., Ash, D.J. *et al.*, Evidence-based medicine evaluation of electrophysiological studies of the anxiety disorders, *Clin EEG Neurosci* 2009; 40:84-112.



Chapter 5 – ISSUES AND CHALLENGES IN DIAGNOSIS OF MILD TRAUMATIC BRAIN INJURY IN MILITARY SETTINGS: IMPLICATIONS FOR CLINICAL PRACTICE

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ABSTRACT

This review outlines a number of considerations for researchers and clinicians alike when assessing suspected concussion/mTBI in military personnel.

The measurement and identification of concussion/mTBI is fraught with difficulty because its symptom profile lacks specificity and overlaps with psychiatric disorders. It can be difficult to disentangle the relative influence of physical versus psychological factors on a range of symptoms reported by individuals who have been in combative and/or traumatic environments.

Areas to be considered include:

- *Potential for explanations other than concussion to exist for reported loss of awareness and/or memory, particularly when an injury occurs in the context of life threatening trauma;*
- *Poor specificity and major overlap of the symptoms that define residual complaints of concussion with psychiatric conditions (particularly Post-Traumatic Stress Disorder; PTSD); and*
- *Overlap in areas of the brain implicated in concussion and psychiatric comorbidities as evidenced using neuroimaging and neuropsychological assessments.*

The issues discussed in this review are highly relevant to Australian health care professionals working with individuals returning from deployment. Considerations for clinical management of those presenting with concerns related to concussion/mTBI are proposed.

5.1 INTRODUCTION

The prevalence of mild Traumatic Brain Injury (mTBI) in soldiers has been a particularly concerning issue in the last decade due to frequent attacks with Improvised Explosive Devices (IEDs) in Iraq and Afghanistan. The perceived impact of mTBI is such that it has been labelled the “signature injury” of the Afghanistan and Iraq wars [1]. In this context, mTBI is characterised by “brief loss of consciousness or altered mental status, as a result of deployment-related head injuries, particularly those resulting from proximity to blast explosions” (Ref. [2], p. 454).

Vast and varied literature exists on the subject of mTBI, or concussion, in military settings. This review aims to summarise the main issues in the literature identified while compiling a larger report on this matter. First and foremost, the use of the term “mTBI”, which appears regularly in the literature, is not helpful as it often inappropriately assumes aetiology of symptoms. Consequently, this review will use the term “concussion” to describe the experience of loss or alteration of consciousness that can have multiple causes including blast waves from IEDs. Specifically, this review summarises key themes and challenges identified relevant to closed head mTBI in a military setting rather than penetrating head injury and/or moderate-to-severe traumatic brain injury.

Three major areas of complexity relating to the accurate identification of concussion will be addressed. First, although concussion is often identified by loss of awareness and/or memory, other explanations for these symptoms exist, particularly when an injury occurs in the context of psychological trauma (as is common in military groups) [2], [3]. Second, symptoms that define residual complaints of concussion (often termed post-concussive symptoms) have poor specificity and major overlap with psychiatric conditions, in particular Post-Traumatic Stress Disorder (PTSD [4]). Finally, even with neuroimaging and neuropsychological assessments, a clinical profile for concussion is yet to be confirmed and there is overlap between areas of the brain implicated in concussion and psychiatric comorbidities. Australians are amongst those exposed to blasts in the current Middle East conflicts and, therefore, Australian health professionals and researchers would benefit from familiarity with the issues addressed in this review.

5.2 ISSUES RELATED TO CAUSATION OF LOSS OF AWARENESS AND MEMORY

The first impediment to consistent, accurate identification of concussion is that symptoms experienced acutely can have multiple aetiologies. For instance, recently, much research has used Carroll *et al.*'s [5] definition of mTBI which includes feeling dazed/confused, loss of consciousness (≤ 30 minutes) or post-traumatic amnesia (< 24 hours) following an injury to the head [5]. These symptoms are routinely accepted as indication of physical injury to the brain [2], [3], [6]-[8], resulting from various causes such as a blast wave. However, these symptoms may have other causes. For example, blast exposure incidents can be life threatening and can evoke feelings of extreme helplessness; these can be highly psychologically traumatic. Psychological reactions to trauma can also involve alteration of consciousness and dissociative or anterograde amnesia [4]. Reliance on retrospective recall of exposures and symptoms that can be unreliable further complicates the issue [6], [9]. Additionally, personal accounts of injury events, even in close temporal proximity, can be unreliable as what is reported as loss of consciousness could in reality be memory loss misinterpreted by the subject [10], [11]. A psychological explanation for these reactions could be considered exclusion criteria according to Carroll *et al.*'s definition [5]; however, this can be difficult to discriminate or may be overlooked. Although difficult and logistically challenging to obtain, information obtained from a witness regarding the circumstances of a potential injury event and any change in level of consciousness at the time of injury would be beneficial. Regardless, what is reported as loss or alteration of consciousness due to concussion may have another cause, yet is routinely accepted as unequivocal indication of such an injury.

5.3 ISSUES RELATING TO POST-CONCUSSIVE SYMPTOMS

The second area of controversy relates to the longer-term consequences of concussion. Symptoms that can occur and may persist following concussion include problems with memory, sleep and concentration, tinnitus, headache, fatigue and irritability [12], [13]. However, these symptoms are highly non-specific and cannot be interpreted as proof of concussion. These symptoms are common not only across psychiatric disorders such as PTSD [2], [3], [13], [14] and depression [15], [16], but also in chronic pain patients [17] and indeed in the

general population [18]. Additionally, non-specific symptoms have been reported by deployed personnel not reporting concussion [19], [20]. Zamorski *et al.* [20] found that, of Canadian military personnel reporting three or more post-concussive symptoms post-deployment, only 16% had reported mTBI/concussion. Similarly, Polusny *et al.* [6] concluded that persistent post-concussive symptoms can be entirely accounted for by PTSD, and others report they could be partially explained by PTSD [2], [21].

Thus, persistent symptoms are not definitive and therefore, cannot confirm concussion [22]. Furthermore, when symptoms do persist following injury, it is extremely difficult to prove causality. This source of diagnostic error can encourage unnecessary concern in individuals, resulting in hypochondriacal preoccupations and possibly false attributions about brain damage. In recent years, many researchers have stressed caution when interpreting the aetiology of such symptoms [10]-[13], [22]-[26] that can be influenced by many known and unknown factors.

5.4 ISSUES RELATED TO NEUROIMAGING, NEUROPSYCHOLOGICAL ASSESSMENT AND CONCUSSION

The third major challenge in identification of concussion relates to its indistinct neurological and cognitive profile. Broadly, areas of the brain most often implicated in concussion include the orbital prefrontal cortex and related circuitry (sub-cortical white matter, basal ganglia, and thalamus) and the amygdala and hippocampus in the temporal lobes, as they are especially vulnerable to biomechanical forces [10], [27]-[32]. Areas of cognitive functioning thought to decline post-concussion include executive function, processing speed, working memory and attention, and memory [33], [34]. Unfortunately, these neurological changes and cognitive abnormalities can also arise in conditions such as depression and PTSD and, therefore, do not serve a discriminative function. Hence, it is fundamentally problematic to assess the structural and functional impact of concussion when trauma co-occurs, as is likely the case in military samples.

Furthermore, the neurological and cognitive changes induced by physical and psychological trauma not only overlap, but can interact [35]. Specifically, neuropathological mechanisms of head injury may interact with the neuropsychological pathology and neurohormonal stress reactivity in PTSD. This may increase the risk of PTSD development [36] or its severity if it is pre-existing. For example, loss of inhibitory control of the limbic system caused by concussion-induced prefrontal cortex damage may exacerbate PTSD fear responses and perpetuate symptoms [34]. The impact of concussion on executive function may result in unregulated recall of trauma that could also exacerbate PTSD symptoms [34]. Additionally, concussion may increase risk of PTSD by interrupting the trauma memory encoding and affecting subsequent trauma event processing [34]. Assessing the trajectory of neuropsychological outcomes may aid in differentiating between concussion and PTSD profiles. In particular, post-blast cognitive impairments attributed to concussion reportedly diminish over time, whereas those associated with PTSD may endure [33], [37], [38].

Notwithstanding this potential overlap between concussion and PTSD, a separate issue is that unique neuropathological markers of concussion have been difficult to ascertain. Specifically, the diffuse and subtle changes in brain architecture that occur following blast exposure are difficult to detect [10], [33]. A recent review suggested that Computer Tomography (CT) scans classified mTBI in only 5 – 12 % of cases [39], while another study showed that conventional EEG was abnormal in only 10% of those with mTBI classification [40]. The time lapse between injury and neuroimaging can also be problematic as subtle injury may resolve by the time imaging takes place [41]. Recent research has shown that assessing white matter loss using Diffuse Tensor Imaging (DTI), [32], [42] at times combined with quantitative analysis of EEG recordings [31], provides promise for identification of concussion.

Similarly, aside from the overlap in areas of cognitive function implicated in concussion and PTSD, neuropsychological assessment is not yet able to consistently identify functional changes in working memory and attention that discriminate concussion from PTSD and major depressive disorders. For example, Van Boven *et al.* [32] found little association between neuropsychological and DTI findings in their review; however, these studies assumed that DTI accurately identified concussion/mTBI cases initially. Sponheim *et al.* [31] found no relationship between cognitive function and disrupted brain coordination. A separate issue is that neuropsychological testing may not provide the sensitivity to detect subtle changes in brain architecture. For example, an individual may expend more effort to achieve the same outcome on a particular cognitive task [43], [44]; effort that may not be observable. Alternatively, in the case of mild injury, alternative neural pathways may be utilised to accurately complete a cognitive task such that existing deficit is not recognised [31].

Comparison of pre- and post-concussion cognitive functioning would provide optimal assessment. Although this does not negate the potential impact of psychological trauma in military environments, comparison of specific changes across time within individuals may nonetheless prove beneficial. Sports literature has demonstrated the usefulness of pre- and post-injury cognitive assessment [45] to identify concussion and monitor recovery.

5.5 MULTI-FACETED OVERLAP WITH PTSD

PTSD is a prominent complicating factor common to each of the three aforementioned issues. There is significant overlap between PTSD symptoms and both acute symptoms experienced during concussion and post-concussive symptoms, and overlap in neurological changes and cognitive abnormalities associated with both PTSD and concussion. Importantly, there is also aetiological overlap in that deployment-related concussion often coincides with a psychologically traumatic event [2], [3], [46]. This can increase the likelihood of a “false-positive” concussion/mTBI screen. Much research has been conducted on the relationship between these two conditions (Vasterling, Verfaellie and Sullivan [34] provide a comprehensive review). However, research findings must be considered with the important caveat that “mTBI” diagnoses are based on non-specific criteria that have significant overlap with PTSD.

Thus, the overlap between concussion and PTSD, particularly in this military context, is multi-faceted. Indeed, this is not a new dilemma. Debate about the origin of *Shell Shock* (i.e., neurological/physical vs. psychological) began during World War I and has never really been resolved [47]. In fact, Jones *et al.* [47] propose that a straightforward answer to this extremely complex problem is unlikely due to the inherent coexistence of the two disorders in this context. The substantial overlap between post-concussive symptoms and symptoms of other psychiatric morbidities such as depressive disorders further complicates the issue. Despite the lack of clarity in the relevant literature, it is clear that psychiatric comorbidity must be considered when an individual presents with suspected concussion/mTBI.

5.6 IMPLICATIONS FOR RESEARCH AND POLICY

In spite of the aforementioned challenges, significant literature on deployment-related mTBI and associated post-deployment functioning in Afghanistan and Iraq veterans exists. To date, the majority of these studies have been conducted by American researchers, [2], [3], [6], [7], [21], [48] with smaller contributions from English, [13], [49] Canadian [20] and Dutch [50], [51] research groups. Until several recent publications [20], [49], the vast bulk of publications about mTBI have come from the United States (USA). The high profile of mTBI in the U.S. has influenced health care provision and compensation policies for American military personnel [52] and deployment-related mTBI is now recognised as an injury for which the Purple Heart military decoration may be awarded.

However, without the ability to accurately and consistently identify concussion, research in this area is inherently problematic. In addition to the issues already discussed, researchers have used different criteria to classify concussion/mTBI. Thus, a broad understanding of findings across studies, for example, the determination of prevalence rates, has been difficult to obtain. For instance, some researchers classify “mTBI” based on either loss or alteration of consciousness [2], [3], [6], [53]; others include loss of consciousness only [54], others require the additional criterion of *current* symptoms for classification [21].

Furthermore, Carroll *et al.*'s [5] regularly cited mTBI definition does not explicitly specify minimal symptomatology required for classification. Their definition states clearly that, in an injury event, loss or alteration of consciousness lasting 30 minutes would be classified as mTBI, and if these problems persist beyond this time, the injury would be classed as moderate or severe. However, there are no explicit guidelines as to the classification of injury (if any) identified by 10 seconds of confusion or disorientation. The lack of specificity in this area provides additional potential for inconsistency and requires resolution.

5.7 PREVALENCE ESTIMATES FOR CONCUSSION/MTBI AND POST-CONCUSSIVE SYMPTOMS

In light of the issues already discussed, accurate prevalence rates are difficult to ascertain. Notably, there are no distinctive, consensus diagnostic criteria and commonly used screening measures are not diagnostic tools [52]. At present, prevalence estimates of deployment-related concussion/mTBI appear higher in American samples (approximately 9 – 22 % [2], [3], [6], [8], [55]) compared with the few Canadian and British samples that exist (approximately 4 – 10 % [20], [49]). Higher prevalence in American samples could be attributable to factors such as the greater focus on mTBI in the U.S.; it may be more likely for personnel or clinicians to attribute highly non-specific symptoms to such an injury. Additionally, greater combat exposure has been linked with increased reports of concussion/mTBI [20], [49] and U.S. prevalence estimates are often calculated using combat-deployed samples [2], [7], [8].

Prevalence estimates for reports of persistent post-concussive symptoms have also varied. Although estimates have been as high as 20%, comprehensive, general mTBI reviews report 5% is likely more accurate [30], [41]. In this instance, prevalence is difficult to establish as these highly non-specific symptoms are prone to causal attribution errors, particularly in the absence of simultaneous psychiatric assessment. The reliance on retrospective recall of symptoms and events compounds this problem. Additionally, the point at which symptoms become “persistent” is not systematically and consistently defined. The sports literature, where assessment of concussion is more straightforward, has shown post-concussive symptoms usually resolve within 15 minutes to 2 weeks of injury [56]-[58]. Findings are more varied in other populations in which complicating factors such as psychological trauma or compensation can impact symptom reporting [23]. One recent review [23] concluded that, by and large, 2 – 3 months is an appropriate period in which to expect symptom resolution. Authors of both general and military-specific reviews agree that symptoms persisting beyond this period are likely to be due to factors beyond physical injury [23], [24].

5.8 IMPLICATIONS FOR TREATMENT

Problems with identifying concussion highlighted thus far have implications for treatment. When an individual presents with suspected concussion/mTBI, first and foremost, thorough and comprehensive assessment is required due to the complex and multi-faceted overlap of mTBI with other conditions. A key issue is not inappropriately attributing symptoms of unknown aetiology to “brain injury” with its implied consequences and loss of neuronal function. It is clear that individuals experiencing depression, PTSD, chronic pain or other

psychiatric disorders during or after deployment could misattribute their symptoms to concussion/mTBI. Consequences of this misattribution include inappropriate treatment procedures and failure to address underlying conditions [52]. Symptoms that persist (i.e., beyond the usual days-to-weeks recovery period) are likely indicative of factors other than concussion.

If concussion is confirmed, patient education interventions that emphasise hopeful expectancy of recovery are best practice [52], [59], [60]. Negative expectations of recovery have been associated with persistent symptom reporting [61] (see Ref. [24] for a review), as have external incentives such as financial compensation for injuries [62]. Compensation has also been linked with poorer cognitive performance [63]. Importantly, confirmation of concussion does not negate the need to address potential psychiatric comorbidity.

Consistent with the suggestion of communicating hopeful expectancy, some researchers have recommended the term “concussion” be used over “mTBI” or “brain injury” to enhance patients’ expectations of recovery [52], [55]. McKinlay *et al.* [64] provide evidence that there is some public confusion about the meaning and connotation of such terms.

5.9 RECOMMENDATIONS

Key recommendations specific to military environments based on the current review are outlined in Table 5-1. Although these recommendations are focused on Defence Force health care, they are also relevant to research and broader health care communities that may encounter symptomatic veterans (e.g., general practitioners, or medical specialists such as neuropsychiatrists, neurologists, psychiatrists, rehabilitation physicians).

Table 5-1: General Recommendations for Identification of Concussion/mTBI in Military Settings.

<i>Key Recommendations</i>
• Pre- and post-deployment neurocognitive assessment to facilitate intra-individual comparison of symptoms in the event of suspected injury.
• Documentation of the nature of injury as soon as practicable after the event whilst deployed (e.g., proximity to a blast, symptoms reported by self and accounts from other personnel).
• Development and provision of psychoeducation about the expected course of recovery for those who have had concussion (ideally provided in close temporal proximity to the injury).
• Concussion screening questions to be included in immediate post-deployment military assessments.
• Clinicians and researchers to adopt the use of the term “concussion” rather than “brain injury” or “mTBI”.

On the basis of this review, we strongly suggest consensus guidelines be developed for the routine assessment of individuals with suspected concussion/mTBI. Ideally, this would include a combination of self-report and structured diagnostic measures as well as standard neuropsychological/electrophysiological and neuroimaging investigations. A consensus protocol could reduce errors related to interrater reliability of diagnoses and identification of psychiatric comorbidity when present. Such a protocol would also assist in research, as comparative datasets would be available. A proposed assessment protocol for military personnel with suspected concussion/mTBI is included in Table 5-2.

Table 5-2: Proposed Assessment Protocol for Concussion/mTBI in Military Personnel.

<i>Proposed Assessment Protocol</i>
In the event that an individual reports concussion and/or post-concussive symptoms, a thorough assessment would ideally include: • A full assessment of non-specific symptoms and health-related matters following deployment; • Contemporaneous records regarding the alleged injury including the nature and mechanics of the injury; • A full history of traumatic exposures during and prior to deployment; • A full history of other physical injuries that may exacerbate head injury during and prior to deployment; • A full neurological examination; • MRI or other suitable neuroimaging procedures; • A complex battery of neuropsychological and neurocognitive assessments, including electrophysiological measures; • Thorough, systematic neuropsychiatric assessment with particular attention to PTSD and depression; and • A full history of substance use that may contribute to cognitive dysfunction.

5.10 CONCLUSION

In summary, mTBI is a vexed and complicated matter due to its indistinct clinical profile and multi-faceted overlap with psychiatric disorders, particularly PTSD. Australian health care providers and researchers should be mindful of the issues outlined in this review in order to provide appropriate care for military personnel experiencing non-specific symptoms attributable to concussion/mTBI. Evidently, post-deployment syndromes are not new phenomena, the roots of which date back almost a century when physicians and psychologists began debating explanations for Shell Shock [47]. Jones *et al.* [47] aptly advise “*disorders that cross any divide between physical and psychological require a nuanced view of their interpretation and treatment*” (p. 1641).

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5.12 REFERENCES

- [1] Okie, S., Traumatic brain injury in the war zone, *N Engl J Med* 2005; 352:2043-2047.
- [2] Hoge, C.W., McGurk, D., Thomas, J.L. *et al.*, Mild traumatic brain injury in U.S. Soldiers returning from Iraq, *N Engl J Med* 2008; 358:453-463.

- [3] Schneiderman, A.I., Braver, E.R. and Kang, H.K., Understanding sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: persistent postconcussive symptoms and posttraumatic stress disorder, *Am J Epidemiol* 2008; 167:1446-1452.
- [4] American Psychiatric Association, Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC, USA: American Psychiatric Association, 1994.
- [5] Carroll, L.J., Cassidy, J.D., Holm, L. *et al.*, Methodological issues and research recommendations for mild traumatic brain injury: The WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury, *J Rehabil Med* 2004; 43 (Suppl):113-125.
- [6] Polusny, M.A., Kehle, S.M., Nelson, N.W. *et al.*, Longitudinal effects of mild traumatic brain injury and posttraumatic stress disorder comorbidity on postdeployment outcomes in national guard soldiers deployed to Iraq, *Arch Gen Psychiatry* 2011; 68:79-89.
- [7] Terrio, H., Brenner, L.A., Ivins, B.J. *et al.*, Traumatic brain injury screening: Preliminary findings in a US army brigade combat team, *J Head Trauma Rehabil* 2009; 24:14-23.
- [8] Wilk, J.E., Thomas, J.L., McGurk, D.M. *et al.*, Mild traumatic brain injury (concussion) during combat: Lack of association of blast mechanism with persistent postconcussive symptoms, *J Head Trauma Rehabil* 2010; 25:9-14.
- [9] Wessely, S., Unwin, C., Hotopf, M. *et al.*, Stability of recall of military hazards over time: Evidence from the Persian Gulf War of 1991, *Br J Psychiatry* 2003; 183:314-322.
- [10] Arciniegas, D.B., Anderson, C.A., Topkoff, J. *et al.*, Mild traumatic brain injury: a neuropsychiatric approach to diagnosis, evaluation, and treatment, *Neuropsychiatr Dis Treat* 2005; 1:311-327.
- [11] Belanger, H.G., Uomoto, J.M. and Vanderploeg, R.D., The veterans health administration system of care for mild traumatic brain injury: Costs, benefits, and controversies, *J Head Trauma Rehabil* 2009; 24:4-13.
- [12] Bryant, R.A., Disentangling mild traumatic brain injury and stress reactions, *N Engl J Med* 2008; 358:525-527.
- [13] Fear, N.T., Jones, E., Groom, M. *et al.*, Symptoms of post-concussional syndrome are non-specifically related to mild traumatic brain injury in UK Armed Forces personnel on return from deployment in Iraq: an analysis of self-reported data, *Psychol Med* 2009; 39:1379-1387.
- [14] Cooper, D.B., Kennedy, J.E., Cullen, M.A. *et al.*, Association between combat stress and post-concussive symptom reporting in OEF/OIF service members with mild traumatic brain injuries, *Brain Inj* 2011; 25:1-7.
- [15] Carlson, K.F., Nelson, D., Orazem, R.J. *et al.*, Psychiatric diagnoses among Iraq and Afghanistan war veterans screened for deployment-related traumatic brain injury, *J Trauma Stress* 2010; 23:17-24.
- [16] Iverson, G.L., Misdiagnosis of the persistent postconcussion syndrome in patients with depression, *Arch Clin Neuropsychol* 2006; 21:303-310.
- [17] Smith-Seemiller, L., Fow, N.R., Kant, R. *et al.*, Presence of post-concussion syndrome symptoms in patients with chronic pain vs mild traumatic brain injury, *Brain Inj* 2003; 17:199-206.

- [18] Iverson, G.L., Lange, R.T., Brooks, B.L. *et al.*, “good old days” bias following mild traumatic brain injury, *Clin Neuropsychol* 2010; 24:17-37.
- [19] Schwab, K.A., Ivins, B., Cramer, G. *et al.*, Screening for traumatic brain injury in troops returning from deployment in Afghanistan and Iraq: initial investigation of the usefulness of a short screening tool for traumatic brain injury, *J Head Trauma Rehabil* 2007; 22:377-389.
- [20] Zamorski, M., Darch, A. and Jung, H.W., Preliminary report on the self-reported incidences of mild traumatic brain injury/concussion in CF members deployed in support of the mission in Afghanistan, Ottawa, Ontario, Canada: Canadian Forces Health Services, Directorate of Mental Health/Deployment Health, 2009.
- [21] Pietrzak, R.H., Johnson, D.C., Goldstein, M.B. *et al.*, Posttraumatic stress disorder mediates the relationship between mild traumatic brain injury and health and psychosocial functioning in veterans of Operations Enduring Freedom and Iraqi Freedom, *J Nerv Ment Dis* 2009; 197:748-753.
- [22] Iverson, G.L., Langlois, J.A., McCrea, M.A. *et al.*, Challenges associated with post-deployment screening for mild traumatic brain injury in military personnel, *Clin Neuropsychol* 2009; 23:1299-1314.
- [23] Carroll, L.J., Cassidy, J.D., Peloso, P.M. *et al.*, Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury, *J Rehabil Med* 2004; 43 (Suppl): 84-105.
- [24] Howe, L.L., Giving context to post-deployment post-concussive-like symptoms: blast-related potential mild traumatic brain injury and comorbidities, *Clin Neuropsychol* 2009; 23:1315-1337.
- [25] Powell, G.E., Mild traumatic brain injury and postconcussion syndrome: the importance of base rates in diagnosis and clinical formulation, *J Neurol Neurosurg Psychiatry* 2008; 79:237.
- [26] Stein, M.B. and McAllister, T.W., Exploring the convergence of posttraumatic stress disorder and mild traumatic brain injury, *Am J Psychiatry* 2009; 166:768-776.
- [27] Bigler, E.D., Neuropsychology and clinical neuroscience of persistent post-concussive syndrome, *J Int Neuropsychol Soc* 2008; 14:1-22.
- [28] Elder, G.A., Mitsis, E.M., Ahlers, S.T. *et al.*, Blast-induced mild traumatic brain injury, *Psychiatr Clin North Am* 2010; 33:757-781.
- [29] Jaffee, M.S. and Meyer, K.S., A brief overview of traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) within the Department of Defense, *Clin Neuropsychol* 2009; 23:1291-1298.
- [30] McCrea, M., Iverson, G.L., McAllister, T.W. *et al.*, An integrated review of recovery after mild traumatic brain injury (MTBI): implications for clinical management, *Clin Neuropsychol* 2009; 23:1368-1390.
- [31] Sponheim, S.R., McGuire, K.A., Kang, S.S. *et al.*, Evidence of disrupted functional connectivity in the brain after combat-related blast injury, *Neuroimage* 2011; 54:S21-S29.
- [32] Van Boven, R.W., Harrington, G.S., Hackney, D.B. *et al.*, Advances in neuroimaging of traumatic brain injury and posttraumatic stress disorder, *J Rehabil Res Dev* 2009; 46:717-757.

- [33] Brenner, L.A., Vanderploeg, R.D. and Terrio, H., Assessment and diagnosis of mild traumatic brain injury, posttraumatic stress disorder, and other polytrauma conditions: burden of adversity hypothesis, *Rehabil Psychol* 2009; 54:239-246.
- [34] Vasterling, J.J., Verfaellie, M. and Sullivan, K.D., Mild traumatic brain injury and posttraumatic stress disorder in returning veterans: perspectives from cognitive neuroscience, *Clin Psychol Rev* 2009; 29:674-684.
- [35] Rosenfeld, J.V. and Ford, N.L., Bomb blast, mild traumatic brain injury and psychiatric morbidity: a review, *Injury* 2010; 41:437-443.
- [36] Bryant, R.A., Creamer, M., O'Donnell, M. *et al.*, Post-traumatic amnesia and the nature of post-traumatic stress disorder after mild traumatic brain injury, *J Int Neuropsychol Soc* 2009; 15:862-867.
- [37] Sutker, P.B., Vasterling, J.J., Brailey, K. *et al.*, Memory, attention, and executive deficits in POW survivors: Contributing biological and psychological factors, *Neuropsychology* 1995; 9:118-125.
- [38] Yehuda, R., Tischler, L., Golier, J.A. *et al.*, Longitudinal assessment of cognitive performance in Holocaust survivors with and without PTSD, *Biol Psychiatry* 2006; 60:714-721.
- [39] Mayer, A.R., Mannell, M.V., Ling, J. *et al.*, Auditory orienting and inhibition of return in mild traumatic brain injury: a fMRI study, *Hum Brain Mapp* 2009; 30:4152-4166.
- [40] Arciniegas, D.B. and Topkoff, J.L., Applications of the P50 evoked response to the evaluation of cognitive impairments after traumatic brain injury, *Phys Med Rehabil Clin N Am* 2004; 15:177-203.
- [41] Iverson, G.L., Outcome from mild traumatic brain injury, *Curr Opin Psychiatry* 2005; 18:301-317.
- [42] MacDonald, C.L., Johnson, A.M., Cooper, D. *et al.*, Detection of blast-related traumatic brain injury in U.S. military personnel, *N Engl J Med* 2011; 364:2091-2100.
- [43] McAllister, T.W., Saykin, A.J., Flashman, L.A. *et al.*, Brain activation during working memory 1 month after mild traumatic brain injury: a functional MRI study, *Neurology* 1999; 53:1300-1308.
- [44] McAllister, T.W., Sparling, M.B., Flashman, L.A. *et al.*, Differential working memory load effects after mild traumatic brain injury, *Neuroimage* 2001; 14:1004-1012.
- [45] Erlanger, D., Saliba, E., Barth, J. *et al.*, Monitoring resolution of postconcussion symptoms in athletes: Preliminary results of a web-based neuropsychological test protocol, *J Athl Train* 2001; 36:280-287.
- [46] Vanderploeg, R.D., Belanger, H.G. and Curtiss, G., Mild traumatic brain injury and posttraumatic stress disorder and their associations with health symptoms, *Arch Phys Med Rehabil* 2009; 90:1084-1093.
- [47] Jones, E., Fear, N.T. and Wessely, S., Shell shock and mild traumatic brain injury: a historical review, *Am J Psychiatry* 2007; 164:1641-1645.
- [48] Brenner, L.A., Ivins, B.J., Schwab, K. *et al.*, Traumatic brain injury, posttraumatic stress disorder, and postconcussive symptom reporting among troops returning from Iraq, *J Head Trauma Rehabil* 2010; 25:307-312.

- [49] Jones, N., Fear, N.T., Rona, R., Fertout, M., Thandi, G., Wessely, S. and Greenberg, N. (2014), Mild traumatic brain injury (mTBI) among UK military personnel whilst deployed in Afghanistan in 2011. *Brain Inj*, 28(7), 896-899. doi: 10.3109/02699052.2014.888479.
- [50] Engelhard, I.M., Huijding, J., van den Hout, M.A. *et al.*, Vulnerability associations and symptoms of post-traumatic stress disorder in soldiers deployed to Iraq, *Behav Res Ther* 2007; 45:2317-2325.
- [51] Engelhard, I.M., van den Hout, M.A., Weerts, J. *et al.*, Deployment-related stress and trauma in Dutch soldiers returning from Iraq, Prospective study. *Br J Psychiatry* 2007; 191:140-145.
- [52] Hoge, C.W., Goldberg, H.M. and Castro, C.A., Care of war veterans with mild traumatic brain injury--flawed perspectives, *N Engl J Med* 2009; 360:1588-1591.
- [53] Meares, S., Shores, E.A., Taylor, A.J. *et al.*, Mild traumatic brain injury does not predict acute postconcussion syndrome, *J Neurol Neurosurg Psychiatry* 2008; 79:300-306.
- [54] Norrie, J., Heitger, M., Leatham, J. *et al.*, Mild traumatic brain injury and fatigue: A prospective longitudinal study, *Brain Inj* 2010; 24:1528-1538.
- [55] Thompson, J.M., Persistent symptoms following mild traumatic brain injury (mTBI) - A resource for clinicians and staff. Charlottetown, Canada: Veterans Affairs Canada, 2008. www.vac-acc.gc.ca/pdf/pro_research/mtbi-report-sep08.pdf (Accessed September 2011).
- [56] Riemann, B.L. and Guskiewicz, K.M., Effects of mild head injury on postural stability as measured through clinical balance testing, *J Athl Train* 2000; 35:19-25.
- [57] McCrory, P.R., Ariens, T. and Berkovic, S.F., The nature and duration of acute concussive symptoms in Australian football, *Clin J Sport Med* 2000; 10:235-238.
- [58] Macciocchi, S.N., Barth, J.T., Alves, W. *et al.*, Neuropsychological functioning and recovery after mild head injury in collegiate athletes, *Neurosurgery* 1996; 39:510-514.
- [59] Comper, P., Bisschop, S.M., Carnide, N. *et al.*, A systematic review of treatments for mild traumatic brain injury, *Brain Inj* 2005; 19:863-880.
- [60] Mittenberg, W., Canyock, E.M., Condit, D. *et al.*, Treatment of post-concussion syndrome following mild head injury, *J Clin Exp Neuropsychol* 2001; 23:829-836.
- [61] Whittaker, R., Kemp, S. and House, A., Illness perceptions and outcome in mild head injury: A longitudinal study, *J Neurol Neurosurg Psychiatry* 2007; 78:644-646.
- [62] Kashluba, S., Paniak, C. and Casey, J.E., Persistent symptoms associated with factors identified by the WHO task force on mild traumatic brain injury, *Clin Neuropsychol* 2008; 22:195-208.
- [63] Belanger, H.G., Curtiss, G., Demery, J.A. *et al.*, Factors moderating neuropsychological outcomes following mild traumatic brain injury: A meta-analysis, *J Int Neuropsychol Soc* 2005; 11:215-227.
- [64] McKinlay, A., Bishop, A. and McLellan, T., Public knowledge of 'concussion' and the different terminology used to communicate about mild traumatic brain injury (MTBI), *Brain Inj* 2011; 25:761-766.



Chapter 6 – STRESS-RELATED MUSCULOSKELETAL PAIN

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ABSTRACT

While stress is often considered by patients and clinicians alike as an important factor in the onset and maintenance of widespread musculoskeletal pain, the relationship is more complex than appears on initial consideration. The type of events that lead to stress need description and the role of traumatic events are particularly important because of the shared association with post-traumatic stress disorder. The substantial overlap with psychiatric disorders and the role of stress in their aetiology must be assessed in patients. The lack of specificity of the symptoms of the different disorders used to describe widespread musculoskeletal pain may be explained by their shared aetiology, including neural sensitisation and alterations of the HPA-axis due to stress. Fear avoidance is a central stress, related perceptual characteristic and behavioural dimension in these disorders. Treatment depends on thorough assessment, including psychiatric diagnosis, avoiding simplistic attributions and implementing evidence-based treatments that are well-documented.

6.1 INTRODUCTION

The relationship between stress and widespread musculoskeletal pain is one of the most vexed questions facing clinicians, whether they be physicians or mental health professionals. Patients are often reluctant to accept any link between stress and their pain experience, as they perceive this relationship as a way of the physician telling them that their distress and suffering is all in their mind and hence imaginary. Chapter 5 has highlighted the prevalence of these complaints in the community and their public health importance. However, this clinical problem has not been readily resolved by systematic research and clinical observation. This chapter will address this challenging domain of clinical practice, first, by exploring the nature of stress. Stress is a word that is often used in contradictory ways and requires careful conceptual clarification.

This chapter will also highlight how one of the main problems for clinicians is the multiple and competing frames of references that exist for the diagnosis and understanding of such patients. The general lack of recognition of this overlap has only further added to the confusion and, at times, stigmatisation of these patient groups. The involvement of some of these patients in compensation proceedings, in particular, those with chronic musculoskeletal pain such as whiplash after motor vehicle accidents and low back pain after industrial accidents, further taints them with the suspicion that surrounds compensable injury [1].

Against this background, the possible mechanisms and nature of the relationship between stress and chronic musculoskeletal pain will highlight that there is a potential multiplicity of pathways to explain this relationship. This relationship will be discussed against the perennial dilemma as to whether stress does have an independent effect above and beyond the well-established relationship between psychiatric disorders and pain.

Stress can contribute to pain via a variety of mechanisms. It is important that the psychological and physiological processes be clearly articulated because the nature of the treatment that is likely to be effective is probably more influenced by understanding the basic mechanisms than the muddled diagnoses which plague this field. Whilst many pain clinics have set up well-structured, multi-disciplinary programmes, the treatment literature which

allows an evidence-based approach to this domain has not been as well-researched as the prevalence of these disorders would warrant.

6.2 THE NATURE OF STRESS

The seminal work of Hans Selye [2] introduced the concept of stress and the related importance of homeostasis which was the process central to the stability of physiological systems to maintain life. Selye is reputed to have later stated that his choice of the word ‘stress’ was a consequence of English being his second language, and that in fact the word ‘strain’ would have been a better characterisation of the nature of the challenges of adaptation and destabilisation of homeostasis, which he saw as being central to understanding health and disease.

Much of the seminal work looking at the role of stress and illness was conducted in the 1960s and 1970s. Many researchers began looking at the impact of particular life events that could be developed into lists and their impact on physical and psychological health [3]. However, the complexity of the relationship between life events and illness was often not addressed by the initial work in this field and a number of researchers became highly critical of the earlier studies [4]-[6]. Dohrenwend and Dohrenwend [7] even went as far as to suggest that the idea that life stress caused illness was supported more by faith than scientific evidence. The complexity of these relationships and the contribution of stress to illness have been established for a range of disorders [8].

A number of difficulties exist when trying to define stressful events. Particularly if they are being recorded at the same time as illness is being assessed, there is the potential for the distressed individual to be biased by the search for attributions. This need for explanation can lower the threshold of reporting of adversity and strain when compared to individuals who are not ill. In fact, the reliability of reporting life events both in terms of the inter-rater and retest reliability has been found to range from being very low to moderate [9]. Furthermore, a critical issue is that events can be a consequence of illness as well as the cause [10]. Such a relationship can clearly confound any exploration of this subject. Furthermore, personality also influences that the experience of life event stress and the quality of interpersonal relationships [11], highlighting that these are not independent phenomena. One way of attempting to address this potential source of error has been to develop the concept of ‘independent event’, that is an event that could not be as a result of the person’s illness [12] and their role in the onset of illness to avoid these confounds.

Furthermore, longitudinal research designs have been used to explore this complex relationship between illness and stress. In a recent editorial about this issue, Paykel [8] suggested that the evidence was as much that illness causes stress as stress caused illness, on the basis of data collected from longitudinal studies with multiple data points [10]. Clinically this makes sense. An individual whose resources are depleted as a consequence of illness will struggle to maintain their occupational and social relationships and will report significantly greater demand in maintaining the same level of activity. This load extends the strain on the individual’s limited resources. Furthermore, conflict may arise over their limitations and impairments which when manifested in the work place and at home, can lead to misunderstandings and underperformance in a variety of roles. Stress can cause fatigue and irritability if an individual’s resources are depleted.

Conversely, events that involve loss, conflict, or threat deplete an individual’s resources, thereby placing major physiological and psychological strains on the individual. The activation of the many stress systems in the body, such as the HPA-axis, autonomic nervous system, the immunological reactivity of the individual, and a cascade of neurotransmitter systems, are an integral part of the challenges to an individual’s homeostasis. These systems form a central role in modulating an individual’s sense of health and well-being by determining their adaptive capacity. Dysregulation of these systems can play a central role in the onset of disease or make an individual more prone to external pathogens. The transformation of regulatory systems can lead to the onset of the gene

expression of possible genotypic vulnerability at this time. In so doing, many illnesses, which involve pain as a predominant symptom can be triggered. In musculoskeletal disorders, particularly those of an inflammatory nature, these patterns of dysregulation can play an important role in determining disease activity and progression.

6.3 STRESS AND ADAPTATION TO LIFE EVENTS

Quite apart from the objective evidence as to the bi-directional relationship between stress and illness, patients have their own complex set of attributions and illness beliefs. Often these will dominate the consultation environment as patients struggle to make sense of their suffering, debility and pain. It is important that clinicians do not simply accept these attributions because often there are multiple recall biases and inferences of causal direction that do not stand up to closer scrutiny. There is some suggestion that the reinforcement of these beliefs is associated with a poorer outcome [13].

Stress can also be used incorrectly as a diagnosis. Stress is an environmental occurrence that demands adaptation. The specific reaction, adaptation or disorder that emerges in the individual must be clearly classified and described. What is of particular importance is that any underlying psychiatric disorder, such as anxiety or depression is diagnosed. There is a tendency to presume that psychiatric disorders are an automatic consequence of particularly more severe life stressors. The important finding of epidemiological research is that even following the most extreme types of stress, such as being tortured or placed in a concentration camp, there are very few studies which have demonstrated prevalence rates of greater than 50% [14]. After severe events such as motor vehicle accidents involving substantial injury and bereavement such as the death of a spouse, the rates of disorder are generally between 15% and 25%. In these situations, the failure to diagnose a condition can do the individual a considerable disservice. Whilst the occurrence of the event may not be able to be modified, with appropriate treatment, the individual's reaction can be specifically addressed.

Stress has become a 'catch all' word that can confuse rather than clarify. A central principle is that stress is not seen as an illness. Rather, it describes those external events that can contribute to the onset of disorder and pain. It is important that the events separated into those that are the day to day life events, such as divorce, loss of job, or illness to a family member, in contrast to day to day hassles. Day to day hassles are stresses such as inadequate resources in the workplace to perform on a person's duties effectively, difficulty balancing a domestic budget, or having an unreliable motor vehicle. Hassles are more enduring events rather than specific occurrences that are described by life events. In chronic fatigue syndrome, stressful life events and difficulties characterised as dilemmas appear to be a role in the onset [15]. Childhood adversity has found to be a risk factor for chronic fatigue syndrome indicating that stress can contribute to the onset of these conditions and also have a long tail of effect [16]. In chronic fatigue syndrome, the events in the three months immediately preceding the presentation appear to be particularly important [17].

It is also important to distinguish those events that are chance occurrences over which the individual has little or no control, mainly independent life events. These are the type of life events, such as the death of a family member, where the individual has no determining role as to the occurrence of the event. In contrast, dependent life events are those that have the potential to be influenced by the individual's behaviour, such as divorce or loss of a job, which may follow upon poor performance. Finally, these general categories of life events need to be distinguished from traumatic life events that are a distinguishable class. The importance of traumatic events to the understanding of stress is outlined below.

6.4 TRAUMATIC EVENTS AND MUSCULOSKELETAL PAIN

It is against this matrix that the role of stress in chronic musculoskeletal disorder needs to be considered. These are events that inflict both an external and internal reality that disrupts people's ideas and beliefs about safety, control and freedom from pain. The external reality is of danger and events that cannot be controlled and have a capacity to kill, maim, brutalise and injure. These are events such as wars, rape, assault, motor vehicle accidents and predatory violence, events which the victim has little or no control over as they unfold. These are events that can bring the internal reality of fear, horror and lack of control. Often the individual is left trapped more by the memory of his or her own perceptions and feelings of helplessness than the experience of what has happened. These are events that as a consequence, can lead to a sense of fragmentation as well as a constant re-traumatisation by memories, which are often triggered by subtle reminders of the event. These are events that previous life knowledge does little to equip people for. Using the definition of DSM-IV [18], the stressor criteria states that:

- 1) The person has experienced, witnessed or been confronted with an event or events that involve actual or threatened death or serious injury or threat to the physical integrity to the self or others.
- 2) The person's response involves intense fear, helplessness or horror (in children, disorganised or agitated behaviour).

Individuals may or may not be injured in their exposure to such events. This difference is important to distinguish, as the impact on an individual's physical health and pain experience can be affected substantially differently. If an individual has sustained a physical injury in the course of a traumatic event, one of the profound memories of the experience will be the pain and the fear of the consequence of the injury. The events of the rescue and the experience of treatment will form integral components of this memory. The memories of traumatic events are often unserialised and composed of experiences from various sensory domains such as sight, sound, proprioceptive and smell. These sensory memories are often poorly differentiated in terms of an individual's awareness of time [19].

As a consequence, in the aftermath when the underlying physical injuries such as a fracture has healed, the patient may continue to be intensely preoccupied with the traumatic experience which can include a memory of the pain. However, they may not be aware of the temporal dislocation of the pain memory, believing that there is still some ongoing organic pathology associated with their injury. Similarly, these memories can evoke a substantial behavioural avoidance. The avoidance can also extend to attempts to shut out the thoughts and feelings associated with the event. In this way, an ongoing escalating cycle of avoidance behaviour designed to limit the pain experience can lead to inappropriate attributions as to the nature and significance of the pain and disrupt the individual's rehabilitation.

In individuals who have not been injured in any substantial way, the kinaesthetic or proprioceptive experiences of the traumatic event can become the source of the traumatic memory that are readily cued by any similar movements that trigger these memories. Again, individuals frequently have little conscious awareness of these links. Particularly with rear-end motor vehicle collisions, any movement of the head in a rapid manner can provide a trigger to the memory of the accident. A series of reflexive and protective muscular activity can emerge escalating into a cycle of neck pain and headaches. Again, little conscious link is made to the underlying event. Victimization, abuse and neglect are also an important class of traumatic events in chronic fatigue syndrome and fibromyalgia [20].

Traumatic events such as war can also be linked to a range of other health-related concerns [21]. Particularly in the age of chemical, nuclear and biological warfare, soldiers in battle become intensely preoccupied about minor changes in somatic symptomatology as these symptoms can be indicative of exposure to a toxic agent which is

otherwise invisible. This increased vigilance of a range of somatic sensations can create a pathological hypersensitivity to the normal physiological shifts that occur within an individual on a day-to-day basis, such as minor aches and pains that would otherwise be dismissed as inconsequential. This process can lead to an increasing hypersensitivity to somatic sensations that would otherwise be of no relevance to an individual's day to day health and functioning. A fear of disease and illness can follow anxieties in the media about the effects of multiple vaccinations or the ingestion of chemoprophylactic agents to be used as pre-treatment for nerve gas attacks.

Furthermore, these events are associated with a significant increase in a range of psychopathology. Post-traumatic stress disorder is the condition most typically associated with an exposure to these events. There is now a substantial body of epidemiology that has looked at specific traumatic events such as disasters and motor vehicle accidents, special occupational groups such as emergency service workers and veterans, and population-based stratified epidemiological samples [14]. A number of these studies have now been prospective investigations. The exposure to traumatic events in civilian communities is in fact far higher than was previously anticipated. The National Comorbidity Study in the U.S. [22] identified that 41% of women and 61% of men had been exposed to such events in their lifetime. Similar rates were found in replication of this study in Australia [23] with 49.5% of women and 64% of males having been exposed.

Traumatic events also are commonly associated with major depressive disorder [24], [25], substance abuse [26] and somatoform disorders [27]-[29]. Quite apart from this independent relationship with traumatic events, these disorders also are frequently comorbid with post-traumatic stress disorder.

Evidence from a variety of clinical populations indicates that these conditions are frequently undiagnosed and, as a consequence, their contribution to the individual's presentation behaviour is poorly documented and recognised [30].

6.5 EPIDEMIOLOGICAL EVIDENCE

Epidemiological studies can assist the clinicians approach to managing the relationship between stress and pain in their patients. First the co-occurrence of reported stress in an individual's life and the occurrence of psychiatric disorders have been extensively examined. The recent replication of the National Comorbidity Study looking at the prevalence of psychiatric disorders in the U.S. community highlights this conundrum. This found that at some point in their life, 46.4% of the U.S. population will have a psychiatric disorder based upon the careful stratified epidemiological design used in this study [31]. Of particular note was the prevalence of anxiety disorders (28.85%) and mood disorders (20.8%). The onset of mood disorders was significantly later with the mean age of onset of 30 years compared to that of 11 years for anxiety disorders. The implications of these findings are that on the bias of simple probability, at least one in two patients, consulting medical practitioners with a pain complaint, are likely to have had a psychiatric disorder at some point in their life, with the probability in fact being higher because of the over representation of psychiatric disorders in patients who seek medical help.

Even if one looks at the 12 month prevalence data from this study [32], the 12 month prevalence was 26.2%, with 9.5% having a mood disorder and 18.1% having an anxiety disorder. Of these conditions, 37.3% were rated as being severe. Post-traumatic stress disorder had a 12 month prevalence of 3.5% and a lifetime prevalence of 8.7%. This emphasises that there is still a substantial probability that patients seeking assistance are likely to have a psychiatric disorder. The range of severity means that particularly in the less dramatic forms, patients are not as likely to complain of their symptoms or be diagnosed. Conversely, it is recognised that particularly mood disorders and anxiety disorders frequently present with pain as the presenting symptom of a psychiatric

diagnosis. For example, in the epidemiological catchment area survey, 50% of individuals who had five or more current functional somatic symptoms had a psychiatric diagnosis, most typically an anxiety or depressive disorder [33].

In general practice settings and emergency settings, it is equally well-recognised that pain is the frequent presentation of psychiatric disorders. [34]-[37].

Looking at specific conditions, the study of von Korff *et al.*, [37] looking at chronic spinal pain in the United States population, found that 68.6% of these individuals had some other pain condition and 35% had a mental disorder, in particular anxiety disorder. The complexity of these relationships is further highlighted by the studies such as Zautra and Smith [38], where depressive symptoms in people with rheumatoid arthritis predicted elevated pain ratings, negative affect, the reporting of negative life events, perceived stress and decreased positive event ratings. Furthermore, patients with osteoarthritis who were also depressed were found to have higher levels of arthritis pain and negative affect. These studies suggest an aggregation around psychiatric symptoms and perceived stress and pain. Also, in longitudinal patient populations, emotional distress is a significant predictor of low back pain disability. Brage *et al.*, [39] found that the chronic back pain was associated with a prior history of back pain, emotional distress, less education and high physical job stress. Therefore, even in longitudinal studies, emotional distress is a significant predictor of long-term poor outcomes in terms of back pain and is associated with a variety of indicators of psychosocial disadvantage, which are linked to indicators of chronic stress.

These findings emphasise the importance of determining the prevalence of independent life events, namely those that could not have been caused by the individual and their role as predictors of chronic pain. Post-traumatic stress disorder is a major consequence of exposure to such events but the relationship is complicated by the fact that the victims can be physically injured during these events. The prevalence of chronic pain following lower extremity trauma are substantial even when the individuals are followed up long after supposed healing would have occurred [40]. The strong association between post-traumatic stress disorder and musculoskeletal pain [28], even in a population that did not sustain musculoskeletal trauma at the time of their traumatic events, highlights the importance of post-traumatic stress disorder as an independent determinant of chronic somatic symptoms.

This strong association with psychiatric disorders however should not lead clinicians to make presumptions that pain is simply an indication of the associated psychiatric disorder [41]. Kronke *et al.*, [42] have suggested the psychiatric diagnosis has been too readily accepted as a way of understanding such patients, a criticism that has been further supported by other reviews [41], [43]. A psychiatric diagnosis fails to address the fact that inevitably such symptoms have some biological underpinnings and should not simply be seen as psychogenic. The challenge is therefore to conceptualise how stress may or may not lead to psychiatric disorder, and can also modify an individual's somatic self-perception.

6.6 DIAGNOSTIC OVERLAP WITH CHRONIC PAIN DISORDERS

A further issue to confuse clinicians is the number of diagnoses has proliferated to explain a variety of medically unexplained symptoms that are frequently associated with pain. The sense of frustration of these patients and their demand for explanation has been a substantial driver to the creation of schools of illness such as:

- Chronic fatigue syndrome;
- Fibromyalgia;
- Temporomandibular joint dysfunction;

- Whiplash;
- Multiple chemical sensitivity;
- Irritable bowel syndrome; and
- Post-concussion syndrome.

The certainty of a diagnosis implies and creates a valued currency for labels. In clinical practice, the overlap of these syndromes [44] is infrequently acknowledged by the clinicians who see themselves as specialists in any one of these “conditions”.

A recent literature has attempted to unpack the substantial overlap between these conditions. Aaron *et al.*, [45] specifically examined the overlap between ten conditions and noted particularly high lifetime rates amongst these patients (chronic fatigue syndrome 92%, fibromyalgia 77%, temporomandibular joint disorder 64% compared with controls 18%). The prevalence of chronic back pain was also noted amongst these populations. The findings of this study highlighted how this group of patients have many shared symptoms such as:

- Generalised pain sensitivity;
- Sleep and concentration difficulties; and
- Bowel complaints.

The longitudinal relationship between these conditions becomes a matter of critical clinical importance.

A similar study by the same group [46] looked at a twin population and identified one proband who had chronic fatigue syndrome. Whilst a weakness of this study was the method of evaluation of the disorder, very high rates of overlap of ten disorders including low back pain, tension headache, fibrositis, fibromyalgia, etc., within the probands who had chronic fatigue which were not similarly represented in the non-fatigue co-twin, they suggested that the complex clinical picture in chronic fatigue emphasised the importance of establishing comorbid clinical conditions.

The issue of comorbidity, whether of other physical disorders or of a psychiatric disorder, presents a major problem in the majority of clinical settings. The laws of diagnostic parsimony mean that most clinicians fail to adequately assess comorbidities, rather presuming the centrality of the initially presented condition of the patient. The patient’s initial presentation can be subject to many factors including their social situations and beliefs. For example, the role of compensation on pain and the presentation of whiplash is well-recognised [1].

The risk to the patient from the clinicians’ failure to recognise these patterns of comorbidity are highlighted by the aftermath of motor vehicle accidents. Depending upon the diagnostic bent and interest of the physician first consulted, a variety of disorders may be diagnosed including whiplash, fibromyalgia, post-concussion syndrome if there has been a minor head injury, temporomandibular joint disorder, and post-traumatic stress disorder [47]. The lack of specificity of the diagnostic criteria of post-concussion syndrome and whiplash is obvious with an examination of the specific symptoms [48], [49]. For example, these conditions can also involve headache or facial pain. A recent study of individuals, who had not sustained a deceleration injury, found that headache was experienced by 64% of individuals with post-traumatic stress disorder, and 10% also had jaw pain [50].

McLean and Clauw [51] further highlighted how there are many shared aetiological factors among whiplash, with post-infectious illness fatigue and post-deployment syndromes in veterans of combat. They highlighted that whilst the stressor can be central to the onset, other factors such as worry or expectation of chronicity are

particularly important in symptomatic outcomes. One of the challenges for medical practice is that there is a continuing propensity to change the diagnostic labels in order to try and provide a socially acceptable and non-stigmatising diagnosis for patients. The instability of these diagnoses [52] further highlights that the shift in the predominant presentation of a patient's distress across time can erroneously lead to a transition between diagnostic groups rather than establishing the core nature of the individual's underlying condition.

In summary, the problem facing a clinician is that stress is not an independent axis directly related to pain. Stress can cause psychiatric disorder and psychiatric disorder can cause stress. It also appears that individuals in substantial pain are generally more reactive to stress and hence, potentially biased to increase reporting of stress.

6.7 SHARED NEUROBIOLOGY

Psychiatric disorders share a common neurobiology with the underlying pathophysiology of chronic pain and have a shared mechanism of symptom manifestation. One domain that has been extensively explored is the relationship between Gulf War veterans and unexplained pain and fatigue. The Presidential Advisory Committee exploring this question acknowledged the centrality of stress as a factor for consideration [53]. There are many studies of both veterans and non-veterans that have demonstrated that life stressors such as divorce are associated with multiple adverse health outcomes including somatic symptoms such as pain. Fiedler *et al.*, [54] further explored these relationships. Again, they found a similar aggregation where personality, negative coping strategies, life events, stress after the war, and the environmental exposures during the war were significant predictors of the veteran's current physical outcomes.

The challenge demanded in interpreting such research is that all of these factors are measured post-hoc and may, in part, be accounted for by a bias to over-reporting. This is akin to the finding from Gulf War veterans with post-traumatic stress disorder who progressively report greater exposures from the same conflict with the passage of time [55]. Studies of the role of psychosocial factors in primary care patients who complain of musculoskeletal pain highlights a constellation of psychosocial factors such as being female, older divorced, foreign born and under financial strain. These individuals report greater levels of depression, burnout and job strain than comparable individuals free of such pain, attending the same primary care setting. Such studies highlight the issues that patients presenting with chronic pain are likely to speak to their doctors about their need to have explained the onset and nature of their symptoms. The problem is that while these are associated links, the causal role remains to be clearly established.

An individual's social circumstances will be substantially reflected in marital functioning and the impact that this may have on illness outcomes is another stress worthy of consideration. One study examining these matters found that physical disability, pain severity, and negative spouse response to pain were particularly important in depression in contrast to anxiety symptoms [56]. However, such a study emphasises the complexity of the dynamic interrelationship between these factors.

6.8 THE INTERACTIVE RELATIONSHIP

Psychosocial factors, such as stress, have perhaps been most explored with back pain in longitudinal designs. The South Manchester Back Pain Study found that work dissatisfaction was higher amongst people with low back pain but treatment seeking was associated with low social status and perceived inadequacy of income [57]. Gatchel *et al.*, [58] examined return to work after back injury and demonstrated that combined with compensation factors, self-reported pain and disability and associated with emotional vulnerability strongly predicted poor return to work, although psychiatric disorders either prior or concurrent, did not have an

effect [59]. A twin study [59], found that poor overall physical function and depressive symptomatology were associated with low back pain.

A prospective cohort study [60] followed a group of nurses during a three year training period. They found that either a prior history of low back pain and pre-existing psychological distress were the only factors to influence the occurrence of new episodes of low back pain. In general, the psychological distress preceded the occurrence of new episodes of pain by only short periods, implying the importance of acute distress in the onset of back pain. This was similar to a study which found that psychological distress in individuals without back pain, predicted the subsequent onset of later episodes of low back pain and that psychological factors would account for approximately 16% of the occurrence of new episodes [61]. One of the problems of the general psychosocial risk factors defined in such studies is the lack of specificity of the findings.

However, an important development has been the identification of fear avoidance beliefs as being a critical determinant of poor outcome in response to pain and psychosocial stressors. A prospective study of back pain found that kidney-injured individuals had a rapid decrease in their fear avoidance whereas chronic low back pain sufferers had more fear-avoidance beliefs than those with acute back pain [62]. These papers highlight the importance of developing more specific aetiological models that take account of the multiplicity of factors that should be assessed in patients presenting with stress-related pain disorders.

6.8.1 How Does Stress Lead to Pain – Research Agenda

- There is a need to develop a system of classification that accounts for the overlap of widespread musculoskeletal pain syndromes.
- The ... and mechanisms of neural sensitisation and stress-related changes of the HPA-axis to physical and psychological outcomes of stress require exploration and characterisation.
- The role of early intervention in managing fear avoidance reactions is an urgent priority.

Prospective studies have provided a valuable insight into a better understanding of the complex interaction between stress, psychosocial vulnerability factors, and physical injury as determinants of chronic pain. McLean *et al.*, [63] have highlighted the importance of a model for explaining the transition from acute injury to chronic pain and the role of fear avoidance. While they focus particularly on a multi-variate model of chronic pain pathogenesis [64], [65], pain-related fear and avoidance has a central factor creating a trajectory to chronic pain. This coping style that shapes a pattern of behavioural adaptation, leads to the amplification of peripheral sensations. This model further links this psychological process to an underlying complex cascade of the neurohormonal stress systems of the central nervous system. A substantial body of research has been now conducted in post-traumatic stress disorder that has documented a series of domains of the changes in the stress response systems [66], [67].

There has been an increasing recognition of a shared pattern of aetiology between whiplash, fibromyalgia, chronic fatigue and post-traumatic stress disorder. In particular, the disorders of the HPA-axis have been identified in these disorders [68], [69]. The dysfunction of the HPA-axis in these disorders appears to be a shared abnormality of enhanced negative feedback of the HPA-axis. Such stress-induced changes have been associated with major impacts on neurogenesis and brain functioning [70], [71]. A recent prospective study has suggested

that this dysfunction of the HPA-axis plays an important role in the onset of chronic widespread musculoskeletal pain in a general population sample [72]. McEwen's model of allostasis has focused on the temporal lobe and the changes induced by cortisol at the times of stress exposure. While focusing on the importance of this process in post-traumatic stress disorder, persistent pain has also been associated with stress-like induced alterations of hippocampal neurogenesis and gene expression [73].

Elsewhere this volume addresses the question of the role of sensitisation as a critical process in the onset of pain syndromes. This process has been of central interest also in post-traumatic stress disorder. In post-traumatic stress disorder, the exposure to environmental triggers to the traumatic memory structure plays the critical role in the emergence and progressive escalation of an individual's distress across time. Post-traumatic stress disorder is not a condition that immediately develops at the time of the trauma; rather it is a complex biological process which emerges in the weeks and months following the event that involves the interaction between the individual's distress and the neurohormonal response at the time of the traumatic event [74].

Elzinger and Bremner [75] have further characterised the role of the neurogenesis in the enhanced and coding of emotional memories and the fear conditioning individuals who develop post-traumatic stress disorder experience. The further failure of the normal inhibitory mechanisms to quell the stress response appears to be important in the progression of the individual's distress and the development of the full-blown condition. While a full exploration of these matters is beyond the scope of this chapter, the amygdala plays a central role in the kindling of the fear response in post-traumatic stress disorder. There is significant similarity between the neural networks involved in post-traumatic stress disorders and those associated with the phenomena of windup of C fibre evoked pain [76]. The centrality of this process has been suggested to both fibromyalgia and chronic fatigue [77], [78]. The interaction between fear avoidance and sensitisation has broad relevance to understanding individual's reporting of subjective health complaints [79].

Similar patterns of sensitisation and modified pain sensitivity have been characterised in irritable bowel syndrome [80], [81]. The shared neurobiological abnormalities in these conditions are a further argument for considering the possibility that there is a generalised stress response syndrome underpinning multiple complaints. Furthermore, this has been associated with modified autonomic function that is also thought to play an important role in the pain response in fibromyalgia patients, individuals with neck and shoulder pain, and irritable bowel disorder [82] and has been found to be present also in individuals absent from work with stress-related illness [83].

6.8.2 Practice Points

- Comprehensive psychosocial assessment, including life events and possible psychiatric disorders is the role of every clinician.
- Establish the pattern of fear-avoidance behaviours and reinforcing maladaptive reactions to stress.
- Use evidence-based approaches to manage specific aspects of the patient's physical and psychiatric disorders.

Given that stress does impact in a major way on people's health, the mechanisms and pathways to the somatic manifestations of its effect are of particular importance. Stress of itself can modify people's perception and capacity to deal with pain in chronic illness simply because it depletes an individual's resources and capacity to

cope. The variability of individual coping styles as well as his or her general social resources are important determinants of an individual's pattern of reactivity. However, chronic diseases such as rheumatoid arthritis indicate that even in chronic disease, depression is not simply a consequence of an individual's symptoms [84]. For this reason, stress should not be presumed to automatically lead to a psychiatric diagnosis and that there are a variety of risk factors that contribute to these outcomes. An area that is of particular importance in understanding widespread musculoskeletal pain is traumatic events described above.

The dimensions of stress reactivity underpin post-traumatic stress disorder such as abnormalities of the HPA-axis and sensitisation have independently been identified as central to the pathophysiology of various syndromes associated with chronic musculoskeletal pain. These findings as reviewed above highlight the importance of assessing these outcomes as a dimensional aspect of a patient's adaptation. Above all else, clinicians need to take account of the complex dynamic that is involved in patients' awareness of their symptoms and the development of their attributions [85]. It is frequently this aspect of a patient's presentation and their preoccupation with ill health which is central to the development of any effective intervention. Strongly held views about causation, which ultimately may have relatively little support in scientific evidence, present one of the greatest challenges in clinical practice.

What patients want to know is whether they can be helped and their pain can be treated. In particular, they are interested in whether their suffering is a permanent or reversible complaint. Whilst it is beyond the scope of this chapter, there are a variety of evidence-based treatments that are now well-established both for the psychological and physical aspects of patient's adaptations. Major depressive disorder, post-traumatic stress disorder and panic disorder all have extensively developed evidence-based treatment guidelines documented such as in the Cochrane library. Similarly, the National Institute of Clinical Excellence in the United Kingdom has systematically examined the question of treatment for these conditions. A variety of interventions, both calling upon psychotherapeutic and pharmacological approaches have significant benefit in clinical settings. In patients with chronic widespread musculoskeletal pain, these interventions by themselves are likely to have significant clinical gains. However, focussing on the psychiatric diagnosis alone potentially dismisses the core of the patient's presentation and difficulties.

It is therefore central that the patient's physical condition is focussed upon and addressed in the treatment setting. These interventions have been addressed in other parts of this Volume. However, it is critical that the process of fear-avoidance, which is central to much of the behavioural response of these patients, interlinks the psychological and physical interventions. Fear-avoidance is a central aspect of the response of individuals to traumatic events. They attempt to control and manage their distress by avoiding sensory, environmental and behavioural triggers of their symptoms. Given that somatic self-registration is a central element of human consciousness [86] often in an unconscious way, a variety of somatic states will remind the patients of their primary traumatic exposure. For example, pain is often the critical element of a life threatening accident or assault. The continued experience of pain long after the fracture or injury has healed can arise because pain remains a central element of the undigested memory of the traumatic event. However, the fact that this somatic preoccupation arises from memory rather than current tissue pathology is often very confusing and difficult for patients to understand. This is in part because the underlying attentional processes, the influence and the filtering of bodily sensations are disrupted in traumatic reactions [19], [87].

The neurohormonal consequences of the exposure to stress play a critical role in the disruption of working memory mechanisms that modify somatic self-representation. Clinicians must therefore not fall into the typical Cartesian trap of presuming that an experience is either mind or body. All experience, even of a psychological nature, depends upon psychobiology and this underpins emotional and somatic reactions to adversity are the essence of the human condition.

It is therefore critical that the patient comes to grapple with the fact that a symptom of itself cannot be treated alone but rather their perception and affective appraisal of a symptom as critical to mastery. Ultimately, the behavioural response, the consequent disability and handicap are the critical factors in the outcome, namely the improvement of function and quality of life.

Stress of itself has much to do with the randomness of chance and how it impinges on individuals. Particularly independent life events are ones that individuals cannot control. However, the hassles and strains of day to day life [88] are potentially very much of the making of an individual through their conscious choices. This element of stress is a matter that can be managed. However, patients with chronic widespread musculoskeletal pain become almost phobic of demand because of the associated symptoms of fatigue and perception of worsening of their condition when they place themselves in challenging environments. In contrast to the athlete who views their stiffness and tiredness after exertion as being indicative of effort and benefit, these sensations trigger fear and apprehension about exacerbation and worsening ill health. Therefore, a critical aspect of any intervention involves both a regulation of an individual's life but not in such a way as simply to create a very constricted range of involvements supposedly to limit stress. Stress of itself is not damaging, in fact it is critical to growth and a sense of personal reward. The aim in many patients with chronic musculoskeletal pain is to increase their hardiness and sense of resilience in the face of demand, which comes to be perceived as damaging.

6.9 SUMMARY

The examination of the question as to whether stress can precipitate widespread musculoskeletal pain indicates that stress impacts on pain via a variety of mechanisms. However, many uncertainties remain as to the exact relationship between stress, psychiatric disorder and chronic musculoskeletal pain. If anything, it appears that many of the assumptions that underpin current diagnostic formulations of this question have done more to confuse rather than clarify the issue. It is erroneous to presume that a psychiatric disorder and stress simply explain the presence of musculoskeletal pain. Rather, this needs to be seen as a separate axis of presentation of psychological distress [41]. The diagnostic categories that have been used to explain these presentations such as chronic fatigue, fibromyalgia, etc., have a great deal of overlap and the lack of specificity of their diagnostic criteria means that patients are potentially at risk of being provided with a certainty of diagnosis determined more by the practitioner that they happen to consult and his or her particular views of these conditions rather than the reality of their illness.

This domain of medicine has probably been historically one of the most challenging [89] for the last two centuries. The new insights from neuroscience and stress physiology are beginning to further emphasise the Cartesian split as a matter that medicine must shy away from. Premature explanations and diagnosis of patients is probably the most damaging approach rather than the clinician confronting individuals with the reality that there are no simple answers to the nature of these conditions.

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6.11 REFERENCES

- [1] Cassidy, J.D., Carrol, L.J., Côté, P. *et al.*, Effect of Eliminating Compensation for Pain and Suffering on the Outcome of Insurance Claims for Whiplash Injury, *N Engl J Med* 2000 April 20; 342(16):1179-86.

- [2] McEwen, B.S., Protection and Damage from Acute and Chronic Stress: Allostasis and Allostatic Overload and their Relevance to the Pathophysiology of Psychiatric Disorders, *Ann N Y Acad Sci* 2004; 1032:1-7.
- [3] McFarlane, A.C., The Effects of Stressful Life Events and Disasters: Research and Theoretical Issues, *Aust N Z J Psychiatry* 1985; 19:409-21.
- [4] Paykel, E.S., Contribution of life events to causation of psychiatric illness, *Psychol Med* 1978; 8(2):245-53.
- [5] Rabkin, J.G. and Struening, E.L., Life Events Stress and Illness, *Science* 1976; 194:1013-20.
- [6] Andrews, G. and Tennant, C., Being upset and becoming ill: an appraisal of the relation between life events and physical illness, *Med J Aust* 1978 March 25; 1(6):324-7.
- [7] Dohrenwend, B.S. and Dohrenwend, B.P., Some issues in research on stressful life events, *J Nerv Ment Dis* 1978; 166:7-15.
- [8] Paykel, E., Life events: effects and genesis, *Psychol Med* 2003; 33:1145-8.
- [9] Paykel, E.S., Methodological aspects of life events research, *J Psychosom Res* 1983; 27(5):341-52.
- [10] Patton, G.C., Coffey, C., Posterino, M. *et al.*, Life events and early onset depression: cause or consequence?, *Psychol Med* 2003; 33:1203-10.
- [11] Kendler, K.S., Gardner, C.O. and Prescott, C.A., Personality and the experience of environmental adversity, *Psychol Med* 2003; 33:1193-202.
- [12] Brown, G.W. and Harris, T., *The Social Origins of Depression: A Study of Psychiatric Disorder in Women*, London, UK: Tavistock; 1978.
- [13] Bentler, S.E., Hartz, A.J. and Kuhn, E.M., Prospective observational study of treatments for unexplained chronic fatigue, *J Clin Psychiatry* 2005; 66(5):625-32.
- [14] McFarlane, A.C., The contribution of epidemiology to the study of traumatic stress, *Soc Psychiatry Psychiatr Epidemiol* 2004; 39(11):874-82.
- [15] Hatcher, S. and House, A., Life events, difficulties and dilemmas in the onset of chronic fatigue syndrome: a case-control study, *Psychol Med* 2003; 33(7):1185-92.
- [16] Heim, C., Wagner, D., Maloney, E. *et al.*, Early adverse experience and risk for chronic fatigue syndrome: results from a population-based study, *Arch Gen Psychiatry* 2006; 63(11):1258-66.
- [17] Theorell, T., Blomkvist, V., Lindh, G. and Evengard, B., Critical life events, infections, and symptoms during the year preceding chronic fatigue syndrome (CFS): an examination of CFS patients and subjects with a nonspecific life crisis, *Psychosom Med* 1999; 61(3):304-10.
- [18] American Psychiatric Association, *Diagnostic criteria from DSM-IV*, Washington, DC, USA: American Psychiatric Association; 1994.
- [19] Van der Kolk, B.A., Pelcovitz, D., Roth, S. *et al.*, Dissociation, somatization, and affect dysregulation: the complexity of adaptation of trauma, *Am J Psychiatry* 1996; 153(7 (Suppl)):83-93.

- [20] van Houdenhove, B., Neerinx, E., Lysens, R. *et al.*, Victimization in chronic fatigue syndrome and fibromyalgia in tertiary care: a controlled study on prevalence and characteristics, *Psychosomatics* 2001 Jan-Feb; 42(1):21-8.
- [21] Forbes, A.B., McKenzie, D.P., Mackinnon, A.J. *et al.*, The health of Australian veterans of the 1991 Gulf War: factor analysis of self-reported symptoms, *Occup Environ Med* 2004 Dec; 61(12):1014-20.
- [22] Kessler, R.C., Sonnega, A., Bromet, E. *et al.*, Posttraumatic stress disorder in the National Comorbidity Survey, *Arch Gen Psychiatry* 1995; 52(12):1048-60.
- [23] Creamer, M., Burgess, P. and McFarlane, A.C., Post-traumatic stress disorder: findings from the Australian National Survey of Mental Health and Well-being, *Psychol Med* 2001 Oct; 31(7):1237-47.
- [24] Fullerton, C.S., Ursano, R.J. and Wang, L., Acute Stress Disorder, Posttraumatic Stress Disorder, and Depression in Disaster or Rescue Workers, *Am J Psychiatry* 2004; 161:1370-6.
- [25] Shalev, A.Y., Freedman, S., Peri, T. *et al.*, Prospective study of posttraumatic stress disorder and depression following trauma, *Am J Psychiatry* 1998 May; 155(5):630-7.
- [26] Jacobsen, L.K., Southwick, S.M. and Kosten, T.R., Substance use disorders in patients with posttraumatic stress disorder: a review of the literature, *Am J Psychiatry* 2001 Aug; 158(8):1184-90.
- [27] Andreski, P., Chilcoat, H. and Breslau, N., Post-traumatic stress disorder and somatization symptoms: a prospective study, *Psychiatry Res* 1998; 79:131-8.
- [28] McFarlane, A.C., Atchison, M., Rafalowicz, E. and Papay, P., Physical symptoms in post-traumatic stress disorder, *J Psychosom Res* 1994; 38(7):715-26.
- [29] Zatzick, D.F., Russo, J.E. and Katon, W., Somatic, posttraumatic stress, and depressive symptoms among injured patients treated in trauma surgery, *Psychosomatics* 2003; 44(6):479-84.
- [30] Zimmerman, M. and Mattia, J.I., Is posttraumatic stress disorder underdiagnosed in routine clinical settings?, *J Nerv Ment Dis* 1999; 187(7):420-8.
- [31] Kessler, R.C., Berglund, P., Demler, O. *et al.*, Lifetime Prevalence and Age-of-Onset Distributions of *DSM-IV* Disorders in the National Comorbidity Survey Replication, *Arch Gen Psychiatry* 2005 June; 62:593-602.
- [32] Kessler, R.C., Chiu, W.T., Demler, O. and Walters, E.E., Prevalence, Severity, and Comorbidity of 12-Month *DSM-IV* Disorders in the National Comorbidity Survey Replication, *Arch Gen Psychiatry* 2005 June; 62:617-27.
- [33] Simon, G.E. and Von Korff, M., Somatization and psychiatric disorder in the NIMH Epidemiologic Catchment Area study, *J Psychiatr* 1991; 148:1494-500.
- [34] O'Malley, P.G., Jackson, J.L., Kroenke, K. *et al.*, The Value of Screening for Psychiatric Disorders in Rheumatology Referrals, *Arch Intern Med* 1998 Nov 23; 158:2357-62.
- [35] Patten, S.B., Williams, J.V.A. and Wang, J., Mental disorders in a population sample with musculoskeletal disorders, *BMC Musculoskelet Disord* 2006; 7:37.

- [36] Stang, P., Brandenberg, N.A., Lane, M.C. *et al.*, Mental and Physical Comorbid Conditions and Days in Role among Persons with Arthritis, *Psychosom Med* 2006; 8:152-8.
- [37] Von Korff, M., Crane, P., Lane, M. *et al.*, Chronic spinal pain and physical-mental comorbidity in the United States: results from the national comorbidity survey replication, *Pain* 2005; 113:331-9.
- [38] Zautra, A.J. and Smith, B.W., Depression and Reactivity to Stress in Older Women with Rheumatoid Arthritic and Osteoarthritis, *Psychosom Med* 2001; 63:687-96.
- [39] Brage, S., Sandanger, I. and Nygard, J.F., Emotional distress as a predictor for low back disability: a prospective 12-year population-based study, *Spine* 2007 Jan 15; 32(2):269-74.
- [40] Castillo, R.C., McKenzie, E.J., Wegener, S.T. *et al.*, Prevalence of chronic pain seven years following limb threatening lower extremity trauma, *Pain* 2006; 124(3):321-9.
- [41] Sharpe, M. and Mayou, R., Somatoform disorders: a help or hindrance to good patient care?, *Br J Psychiatry* 2004; 184:465-7.
- [42] Kroenke, K., Patients presenting with somatic complaints: epidemiology, psychiatric comorbidity and management, *International Journal of Methods in Psychiatric Research* 2003; 12(1):34-43.
- [43] Mayou, R., Kirmayer, L.J., Simon, G. *et al.*, Somatoform disorders: time for a new approach in DSM-V, *Am J Psychiatry* 2005 May; 162(5):847-55.
- [44] Sullivan, P.F., Smith, W. and Buchwald, D., Latent class analysis of symptoms associated with chronic fatigue syndrome and fibromyalgia *Psychol Med* 2002 July; 32(5):881-8.
- [45] Aaron, L.A., Burke, M.M. and Buchwald, D., Overlapping Conditions among Patients with Chronic Fatigue Syndrome, Fibromyalgia and Temporomandibular Disorder, *Arch Intern Med* 2000 Jan 24; 160:221-7.
- [46] Aaron, L.A., Herrell, R., Ashton, S. *et al.*, Comorbid Chemical Conditions in Chronic Fatigue. A Co-twin Control Study, *J Gen Intern Med* 2001 January; 16:24-31.
- [47] Amital, D., Fostick, L., Polliack, M.L. *et al.*, Posttraumatic stress disorder, tenderness, and fibromyalgia syndrome: are they different entities?, *J Psychosom Res* 2006; 61(5):663-9.
- [48] Jaspers, J.P.C., Whiplash and post-traumatic stress disorder, *Disabil Rehabil* 1998; 20(11):397-404.
- [49] McCauley, S.R., Boake, C., Pedroza, C. *et al.*, Postconcussional Disorder. Are the DSM-IV Criteria an Improvement Over the ICD-10?, *J Nerv Ment Dis* 2005 August; 193(8):540-50.
- [50] Uhac, I., Kovac, Z., Muhvic-Urek, M. *et al.*, The prevalence of temporomandibular disorders in war veterans with post-traumatic stress disorder, *Mil Med* 2006 Nov; 171(11):1147-9.
- [51] McLean, S.A. and Clauw, D.J., Predicting chronic symptoms after an acute “stressor” - lessons learned from 3 medical conditions, *Med Hypotheses* 2004; 63(4):653-8.

- [52] Gamma, A., Angst, J., Ajdacic, V., Eich, D. and Rossler, W. (2007), The spectra of neurasthenia and depression: course, stability and transitions. *Eur Arch Psychiatry Clin Neurosci*, 257(2), 120-127. doi: 10.1007/s00406-006-0699-6.
- [53] Presidential Advisory Committee on Gulf War Veterans' Illnesses: Final Report, Washington, DC, USA: U.S. Government Printing Office; 1996.
- [54] Fiedler, N., Lange, G., Tiersky, L. *et al.*, Stressors, personality traits, and coping of Gulf War veterans with chronic fatigue, *J Psychosom Res* 2000; 48:525-35.
- [55] Southwick, S.M., Morgan, C.A., Nicolaou, A.L. and Charney, D.S., Consistency of memory for combat-related traumatic events in veterans of Operation Desert Storm, *Am J Psychiatry* 1997; 154:173-7.
- [56] Cano, A., Gillis, M., Heinz, W. *et al.*, Marital functioning, chronic pain, and psychological distress, *Pain* 2004; 107:99-106.
- [57] Papageorgiou, A.C., Macfarlane, G.J., Thomas, E. *et al.*, Psychosocial factors in the workplace – do they predict new episodes of low back pain? Evidence from the South Manchester Back Pain Study, *Spine* 1997 May 15; 22(10):1137-42.
- [58] Gatchel, R.J., Polatin, P.B. and Mayer, T.G., The dominant role of psychosocial risk factors in the development of chronic low back pain disability, *Spine* 1995 Dec 15; 20(24):2702-9.
- [59] Friedrich, M., Cermak, T. and Heiller, I., Spinal troubles in sewage workers: epidemiological data and work disability due to low back pain, *Int Arch Occup Environ Health* 2000 May; 73(4):245-54.
- [60] Feyer, A.M., Heribson, P., Williamson, A.M. *et al.*, The role of physical and psychological factors in occupational low back pain: a prospective cohort study, *Occup Environ Med* 2000 Feb; 57(2):116-20.
- [61] Croft, P.R., Papageorgiou, A.C., Ferry, S. *et al.*, Psychologic distress and low back pain. Evidence from a prospective study in the general population, *Spine* 1995 Dec 15; 20(24):2731-7.
- [62] Grotle, M., Vollestad, N.K. and Brox, J.I., Clinical course and impact of fear-avoidance beliefs in low back pain: prospective cohort study of acute and chronic low back pain: II, *Spine* 2006 Apr 20; 31(9):1038-46.
- [63] McLean, S.A., Clauw, D.J., Abelson, J.L. and Liberzon, I., The Development of Persistent Pain and psychological Morbidity after Motor Vehicle Collision: Integrating the Potential Role of Stress Response Systems into a Biopsychosocial Model, *Psychosom Med* 2005; 67:783-90.
- [64] Vlaeyen, J.W. and Linton, S.J., Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art, *Pain* 2000; 85:317-32.
- [65] Norton, P.J. and Asmundson, G.J., Amending the fear-avoidance model of chronic pain: what is the role of physiological arousal?, *Behav Res Ther* 2003; 34:17-30.
- [66] Brunello, N., Davidson, J.R., Deahl, M. *et al.*, Posttraumatic stress disorder: diagnosis and epidemiology, comorbidity and social consequences, biology and treatment, *Neuropsychobiology* 2001; 43(3):150-62.
- [67] Davidson, J.R., Stein, D.J., Shalev, A.Y. and Yehuda, R., Posttraumatic stress disorder: acquisition, recognition, course, and treatment, *J Neuropsychiatry Clin Neurosci* 2004 Spring; 16(2):135-47.

- [68] Pillemer, S., Bradley, L., Crofford, L. *et al.*, The neuroscience and endocrinology of fibromyalgia, *Arthritis Rheum* 1997; 40:1928-39.
- [69] Yehuda, R., Post-traumatic stress disorder, *N Engl J Med* 2002; 346:108-14.
- [70] McEwen, B.S., The neurobiology of stress: from serendipity to clinical relevance, *Brain Res* 2000 Dec 15; 886(1-2):172-89.
- [71] Korte, S.M., Koolhaas, J.M., Wingfield, J.C. and McEwen, B.S., The Darwinian concept of stress: benefits of allostasis and costs of allostatic load and the trade-offs in health and disease, *Neurosci Biobehav Rev* 2005 Feb; 29(1):3-38.
- [72] McBeth, J., Silman, A.J., Gupta, A. *et al.*, Moderation of Psychosocial Risk Factors through Dysfunction of the Hypothalamic-Pituitary-Adrenal Stress Axis in the Onset of Chronic Widespread Musculoskeletal Pain, *Arthritis Rheum* 2007 January; 56(1):360-71.
- [73] Duric, V. and McCarron, K.E., Persistent pain produces stress-like alterations in hippocampal neurogenesis and gene expression, *J Pain* 2006 Aug; 7(8):544-55.
- [74] Marshall, R.D. and Garakani, A., A Psychobiology of the acute stress response and its relationship to the psychobiology of post-traumatic stress disorder, *Psychiatr Clin North Am* 2002; 25:385-95.
- [75] Elzinga, B.M. and Bremner, J.D., Are the neural substances of memory the final common pathway in posttraumatic stress disorder (PTSD)?, *J Affect Disord* 2002; 70(1):1-17.
- [76] Staud, R., Craggs, J.G., Robinson, M.E., Perlstein, W.M. and Price, D.D. (2007), Brain activity related to temporal summation of C-fiber evoked pain. *Pain*, 129(1-2), 130-142. doi: 10.1016/j.pain.2006.10.010.
- [77] McLean, S.A. and Clauw, D.J., Biomedical models of fibromyalgia, *Disabil Rehabil* 2005 June; 27(12):659-65.
- [78] Meeus, M. and Nijs, J., Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome, *Clin Rheumatol* 2006; [Epub ahead of print].
- [79] Eriksen, H.R. and Ursin, H., Subjective health complaints, sensitization, and sustained cognitive activation (stress), *J Psychosom Res* 2004; 56:445-8.
- [80] Talley, N.J. and Spiller, R., Irritable bowel syndrome: a little understood organic bowel disease?, *Lancet* 2002 August 17; 360:555-64.
- [81] Verne, G.N., Himes, N.C., Robinson, M.E. *et al.*, Central representation of visceral and cutaneous hypersensitivity in the irritable bowel syndrome, *Pain* 2003; 103:99-110.
- [82] Nilsen, K.B., Sand, T., Westgaard, R.H., Stovner, L.J., White, L.R., Bang Leistad, R. and Ro, M. (2007), Autonomic activation and pain in response to low-grade mental stress in fibromyalgia and shoulder/neck pain patients. *Eur J Pain*, 11(7), 743-755. doi: 10.1016/j.ejpain.2006.11.004.
- [83] Heiden, M., Barnekow-Bergvist, M., Nakata, M. and Lyskov, E., Autonomic Activity, Pain, and Perceived Health in Patients on Sick Leave Due to Stress-Related Illnesses, *Integr Physiol Behav Sci* 2005 January-March; 40(1):3-16.

- [84] Dickens, D., McGowan, L., Clark-Carter, D. and Creed, F., Depression in rheumatoid arthritis: a systematic review of the literature with meta-analysis, *Psychosom Med* 2002; 64:52-60.
- [85] Neerinx, E., van Houdenhove, B., Lysens, R. *et al.*, Attributions in chronic fatigue syndrome and fibromyalgia syndrome in tertiary care, *J Rheumatol* 2000 Apr; 27(4):1051-5.
- [86] Damasio, A.R., *The feeling of what happens: body and emotion in the making of consciousness*, New York, USA: Harcourt & Brace; 1999.
- [87] McFarlane, A.C., Yehuda, R. and Clark, C.R., Biologic models of traumatic memories and post-traumatic stress disorder: The role of neural networks, *Psychiatr Clin North Am* 2002 June; 25(2):253-70.
- [88] van Houdenhove, B., Neerinx, E., Onghena, P. *et al.*, Daily hassles reported by chronic fatigue syndrome and fibromyalgia patients in tertiary care: a controlled quantitative and qualitative study, *Psychother Psychosom* 2002; 71(4):207-13.
- [89] Showalter, E., *Hystories: Hysterical epidemics and modern culture*, New York, USA: Columbia University; 1997.

Chapter 7 – EXPLANATORY AND PRAGMATIC PERSPECTIVES REGARDING IDIOPATHIC PHYSICAL SYMPTOMS AND RELATED SYNDROMES

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ABSTRACT

In recent years, a research methods literature mainly addressing controlled clinical trials has arisen regarding explanatory and pragmatic treatment trials. Explanatory trials tend to examine causal mechanisms and questions of efficacy and value internal validity (creating optimal study conditions) over generalizability (using study results to understand treatment effects in real-life patient populations). In contrast, pragmatic trials value “external relevance” (generalizability) of study results over “internal elegance” so that clinicians and health policy makers can better understand how treatments might impact their patients and policies. This chapter draws inspiration from these contrasting explanatory and pragmatic perspectives and develops them for clinical and research pertaining to idiopathic physical symptoms and related syndromes (e.g., somatization disorder, chronic fatigue syndrome, multiple chemical sensitivities, irritable bowel syndrome). Explanatory and pragmatic perspectives are used to examine these idiopathies with regard to causation, case-definition, labels, and treatment. It is concluded that idiopathic symptom syndromes are fundamentally pragmatic clinical and research challenges. For epidemiologic and methodologic reasons, the complex explanations for these syndromes remain largely elusive. Even so, scientific and clinical pragmatism offers the opportunity to reduce disagreement between competing medical disciplines and between clinicians and affected patients with regard to irreconcilable etiologic questions and to remain evidence-based in the care of patients.

7.1 INTRODUCTION

A burgeoning research methods and health services research literature has described the important differentiation between explanatory and pragmatic perspectives in medical research [1]. The explanatory perspective seeks to explain mechanisms, analyze components of an effect, and define efficacy under optimal therapeutic conditions. In contrast the pragmatic research perspective seeks answers to important applied health policy questions. To evaluate health policy questions, one must examine the answers to questions under the conditions of policy implementation [1].

The most natural and common scientific perspective is the explanatory perspective. Within this perspective, the internal validity of the research design (i.e., the extent that findings observed for the sample are credible) is maximized. However, maximizing internal validity, particularly in clinical research, can come at the expense of external validity (i.e., generalizability or the extent that the findings for the sample can be used to draw inferences regarding the larger population of interest). For example, to learn whether drug A can improve the status of condition B requires that one identify a homogeneous sample of individuals with condition B and no other conditions that might interfere with response to drug A and to randomly assign them to receive drug A or placebo. This approach reveals one consequence of the explanatory research perspective: when testing a hypothesis, one wants to maximize the certainty with which the null hypothesis (in this case, that drug A and placebo have comparable effects on condition B) is rejected when a true drug A effect is present. The logic here is that if the null hypothesis is not rejected under conditions that are optimal for detecting a drug A effect, then

drug A will be similarly ineffective when used in the applied clinical setting. In these routine clinical settings complicating medical illness, comorbid psychiatric disorders, inadequate dosing, non-expert clinicians, and other factors tend to diminish the average benefit a “real” patient experiences.

The pragmatic perspective, most often represented by clinicians and health policymakers, cares mainly about the extent that available medical research evidence can define optimal practice for usual patients and average clinical settings. Internal validity remains important, but particularly when sound explanatory (efficacy) studies have already been performed, the top priority is external validity (generalizability). Studies designed from the pragmatic perspective are designed to maximize eventual generalizability of findings to the patients or settings of interest. As Barbara Starfield has eloquently suggested, a pragmatic perspective frequently involves exchanging “internal elegance” for necessary “external relevance” [2].

This chapter draws inspiration from these notions and addresses the issue of pragmatic and explanatory perspectives as it applies to research and clinical practice involving idiopathic physical symptoms and related syndromes. The prototypical examples of these idiopathic symptom syndromes are:

- Somatization disorder;
- Chronic fatigue syndrome;
- Fibromyalgia; and
- Multiple chemical sensitivities.

It is argued that idiopathic physical symptoms present both explanatory and pragmatic challenges, but they are best viewed through a pragmatic lens, a lens that diminishes the importance of somatoform disorders as a fundamental psychiatric diagnostic category. This assertion may seem radical, but it is not. In the past year international leaders in the field of somatization from the disciplines of medicine and psychiatry called for the abolition of somatoform disorders as a diagnostic category in DSM-V [3], [4].

Etiologically, phenomenologically, and epidemiologically, idiopathic physical symptom syndromes are fundamentally heterogeneous and multi-factorial problems [5]-[7]. To the practicing primary care clinician, idiopathic symptoms represent the prototypical pragmatic challenge, affecting at least a third of patients and offering few easy medical explanations or solutions [8]. For these clinicians an explanatory approach, particularly a dualistic one that attempts to discriminate medical from psychiatric causes, is usually unhelpful and often leads to physician-patient disagreement and conflict [9].

7.2 IDIOPATHY, EXPLANATION AND PRAGMATISM

In medicine we sometimes refer to a clinical phenomenon of unknown origin or etiology as an idiopathy. The adjective “idiopathic” is used to describe an illness for which we cannot establish a root cause. Idiopathy is a word derived from the Greek *idios*, meaning personal or private, and *pathos*, meaning to suffer [10]. Indeed, private suffering aptly describes the most readily observable manifestations of idiopathic pain, fatigue, and other symptoms that commonly compel patients to visit doctors. For most affected patients, there are no reliable diagnostic tests or hard physiologic indicators that can serve as a public disease marker to prove to others that they are suffering; indeed, when idiopathic symptoms are chronic, the quest for a public disease marker can sometimes become a major patient preoccupation. This is one reason many prefer the designation of “illness” (the subjective experience and observable behavioral manifestations of suffering) over “disease” (objectively defined structural injury or abnormal laboratory parameter) when describing the basic nature of idiopathic symptom syndromes.

Idiopathy as a diagnostic group is fundamentally pragmatic. This statement is true in part for all diagnostic groupings but all the more the case for idiopathies. When we say that symptoms lack an established root cause, we are not asserting they have no cause. Instead we are asserting that the cause is practically indeterminate. Symptoms that are idiopathic today may progress into a something more recognizable over time. Similarly, new technologies constantly develop and redefine the boundaries between what is idiopathic and what is explained. For example, the discovery of *Helicobacter pylori* as a common cause of gastric ulcers led to a reconsideration of the extent to which peptic ulcer disease is idiopathic. The reverse is also sometimes true – new technologies may result in explanations that subsequently get reconsidered in the light of new technology assessment. For example, magnetic resonance imaging often reveals bulging discs in areas that might explain back pain symptoms. These findings are sometimes used to differentiate idiopathic from surgical back pain. When research found that bulging discs occurred in over half of patients without back pain [11], it presumably caused a redefinition of some patients' back pain from nerve impingement to idiopathy.

One leading fibromyalgia expert has offered a harsh but illustrative judgment regarding the centrality of the pragmatic perspective when studying and providing care for patients with idiopathic symptom syndromes: *"...fibromyalgia cannot be characterized as a true disease because it lacks a uniquely defining tissue pathology or biochemical marker. Contemporary fibromyalgia researchers seldom waste their time with such tautologic arguments, as the practical problems of understanding and managing fibromyalgia patients will remain the same whether one views it as a disease, a disorder, a syndrome, a psychosocial construct, or a somatoform disorder."* [12].

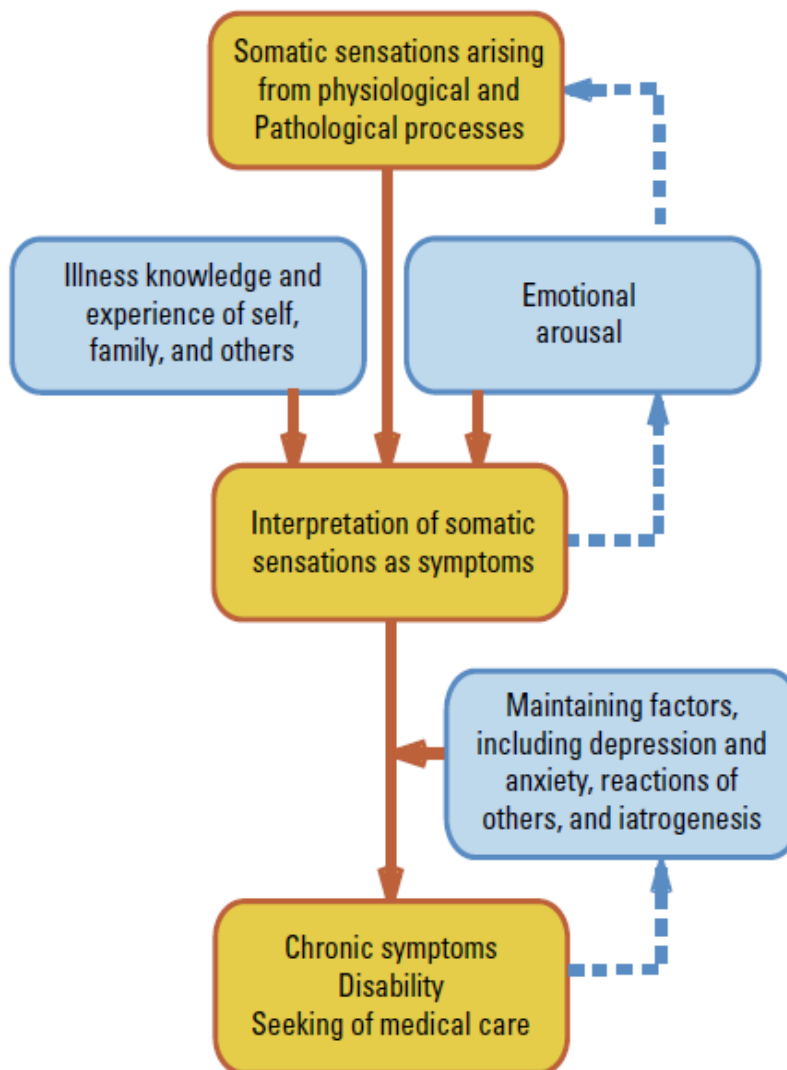
7.3 IDIOPATHY, SOMATIZATION, AND CAUSATION

As research has matured for some idiopathic symptom syndromes, namely somatization disorder, chronic fatigue syndrome, and fibromyalgia, awareness has developed that case-definitions based completely upon physical symptom phenomenology in the absence of objective examination signs or test results have not yielded etiologically homogeneous patient samples [13]. Leading investigators currently view idiopathic physical symptoms as the final common manifestation of multiple etiological pathways [3], [14].

The causes of idiopathic physical symptoms are exceedingly complex and multi-factorial. This is represented in state-of-the-art biopsychosocial explanations of somatization as a multi-step process rather than an easily defined defect in a single causal pathway (see Figure 7-1) [15]. For example, idiopathic symptoms involve a perceptual step (a person "feels" symptoms), a cognitive psychological step (the symptomatic person decides the symptoms are ominous), and social behavioral step (the person with symptoms visits a doctor for help).

FIGURE.

Potential etiologic model for idiopathic physical symptoms: a complex multifactorial biopsychosocial pathway¹⁵



Mayou R, Bass C, Sharpe M. Overview of epidemiology classification and aetiology. In: Mayou R, Bass C, Sharpe M, eds. *Treatment of Functional Somatic Symptoms*. London, England: Oxford University Press; 1995:42-65.

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Figure 7-1: Potential Etiologic Model for Idiopathic Physical Symptoms – A Complex Multi-Factorial Biopsychosocial Pathway (reprinted from Ref. [30], Chapter 3, p. 59).

Psychiatrists have long struggled with somatization as an explanatory and diagnostic construct. In simple terms, somatization may be defined as physical symptoms and related functional impairment resulting from psychiatric disorder and psychosocial distress rather than physical disease. From an explanatory perspective, as elusive as somatization has been as a construct, few would argue its validity. From a pragmatic perspective, however, somatoform disorders have largely failed as a diagnostic grouping [3], [4]. The reasons for this failure are:

- 1) The diagnoses are widely unpopular with affected patients (they often experience them as invalidating);
- 2) Somatization and physical disease are not mutually exclusive explanations as these diagnoses might suggest;
- 3) Somatization is invariably difficult to prove and can lead to irreconcilable differences between physician and patient or adversarial parties in a legal proceeding or disability compensation determination; and
- 4) Primary care is the setting in which most affected patients prefer to receive health care, but primary care physicians tend to use other available syndromic labels (fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome and so on).

In contrast to psychiatric (somatoform) explanations for idiopathic symptoms, case-definitions based around medical explanations have achieved broader clinical use. Fibromyalgia in particular was originally conceptualized as a connective tissue disease, but most explanatory research currently focuses on central and autonomic nervous system mechanisms, central pain pathways, and neurotransmitters [16]-[18]. Fibromyalgia has become a widely used diagnosis for patients with multiple idiopathic symptoms that include widespread chronic pain. Many non-psychiatric physicians are comfortable making this diagnosis, and patients generally find it acceptable.

One challenge to convincing identification of explanatory mechanisms for idiopathic physical symptoms, as is discussed earlier, is the problem of etiologic and phenomenologic heterogeneity. From an epidemiologic and measurement perspective, the best way to achieve homogeneity is to study symptoms in an isolated state (e.g., patients that only have low back pain or only constipation). However, in practice these patients are rare. The patients of greatest pragmatic clinical consequence are those with chronic, intense, and disabling symptoms. Few of these patients have a single isolated symptom and nearly all have several symptoms, introducing sample heterogeneity that makes it less likely that an etiologic “signal” can be identified from within the “noise” due to sample variation.

The epidemiology of idiopathic symptom syndromes also makes it difficult to obtain the early involvement in prospective studies that is essential to maximizing potential for convincing identification of pathogenesis [19]. These syndromes are characteristically chronic with an insidious onset, sometimes in the third decade or earlier. By the time the syndrome is identified as a problem and then clinically characterized, most patients are years into their course, have visited multiple physicians, suffer from comorbid psychiatric conditions, and have exposed their central nervous system to many different treatments. All of these and other factors may confound or modify the effect of various hypothesized influences within a given pathogenic illness model. Schizophrenia, by comparison, is often an early onset brain disease and suffers from some similar challenges to identifying early pre-treatment samples for etiologic studies. However the manifestations of acute psychosis are usually difficult to miss and the affected individual lacks sufficient insight to seek assistance. With work vigilant investigators can identify pre-treatment samples. The insidious onset of idiopathic symptom syndromes and the tendency for those who suffer with them to have a low threshold for seeking medical advice and accepting pharmacologic therapies represent obstacles to scientifically sound studies of causal mechanisms and reliable pathogenic models.

Should we avoid these challenges? Of course not, but an awareness of these issues is necessary, so we do not underestimate the magnitude of the challenge and the chances for success. There is a need to broaden research

questions to include pragmatic perspectives that may offer important daylight for affected patients and their doctors.

7.4 IDIOPATHIES AND DIAGNOSTIC LABELS

The labels used for various idiopathic symptom syndromes may also be viewed from explanatory and pragmatic perspectives. From the explanatory perspective, labels are chosen based on actual or suspected pathogenesis. For example, physicians and researchers have sometimes used labels communicating a psychiatric cause (e.g., hysteria, somatization disorder), on the presumption that all physical causes have been excluded. Other times, as previously described, a medicalized label is used that communicates a hypothesized medical explanation (e.g., chronic Lyme disease, multiple chemical sensitivities).

Wessely and colleagues have suggested that in practice the precise diagnosis a physician makes for idiopathic symptoms depends more on his or her specialty than on actual differences in patient presentation [20]. This assertion is supported by an expanding research literature identifying extensive phenomenologic overlap between various idiopathic symptom syndromes [21]. It has been further noted that various idiopathic symptom syndromes have independently arrived at quite similar risk and prognostic factors, natural histories, and evidence-based treatment profiles [20]. The diagnostic and treatment distinctions between chronic fatigue syndrome and fibromyalgia are so subtle that one evidence-based clinical practice guideline for “medically unexplained symptoms” juxtaposes evidence for each syndrome so one can more easily find the few places where clinical recommendations might differ [22].

From the pragmatic perspective diagnostic labels are evaluated as a treatment rather than for their fit to prevailing ideas regarding causal mechanisms. A pragmatic labeling perspective toward idiopathic symptom syndromes seems wise given the lack of consensus regarding various explanations, the dislike many affected patients have for somatoform (psychiatric) labels, and completed longitudinal studies suggesting that certain labels may prolong the course of idiopathic symptoms [23]. A wide range of pragmatic labels have been used for idiopathic symptoms (see Table 7-1). A label is a practical device only to the extent that it leads to improved patient status and prevents iatrogenic problems. For idiopathic physical symptoms key sources of iatrogenic harm include irreconcilable debates, patient provider differences, and unnecessary medications and invasive procedures.

Table 7-1: Examples of Pragmatic Diagnostic Labels Used for Idiopathic Physical Symptoms and Related Syndromes.

Idiopathic symptoms
Idiopathic symptom syndromes
Multiple idiopathic symptoms
Chronic pain
Pain disorder
Somatic symptoms
Functional somatic symptoms/syndromes
Medically unexplained symptoms
Unexplained physical symptoms
Chronic fatigue syndrome

These considerations lead to a number of potentially important diagnostic label characteristics that may mediate positive or negative labeling effects. Some of these are the extent that a given diagnostic label:

- 1) Is contested or accepted by clinicians;
- 2) Is contested or accepted by affected patients;
- 3) Conveys a psychiatric or medical explanation;
- 4) Inhibits or promotes a constructive doctor-patient relationship;
- 5) Conveys a trivial or catastrophic symptom explanation;
- 6) Conveys a good or bad prognosis;
- 7) Is experienced by the patient as distressing or reassuring;
- 8) Conveys the sense that responsibility for healing lies with the clinician or the patient;
- 9) Leads to effective patient and clinician management strategies;
- 10) Leads to patient adherence to prescribed treatment strategies; and
- 11) Increases or decreases the stigma for the affected individual.

From the pragmatic perspective, diagnostic labels should be empirically studied on these and other label domains. Furthermore, the same experimental methods that are used to test the efficacy of medications, psychosocial interventions, and screening programs should be adapted to evaluate the impact of diagnostic labels. A few of the relevant outcomes include:

- Symptom severity;
- Health beliefs;
- Health behaviors; and
- Therapeutic alliance.

Idiopathic physical symptoms and idiopathic symptom syndromes, the pragmatic labels chosen for the reviews in this issue of *CNS Spectrums* [24]-[26], were selected for use based on clinical experience but without the benefit of empirical data. For example, in the author's experience, primary care clinicians find the label fair, acceptable, and already in common use. Patients find the label neither unfairly trivializing nor stigmatizing. It communicates gravity, but it is not overly distressing or portentous. The label fosters physician-patient dialogue around the meaning of "idiopathic", a brief conversation that is used to inform patients that many symptoms people experience are idiopathic, that highly effective medical therapies are few, and that active coping and self-management strategies can have significantly impact life quality. The potential for future research on the impact of labels on patients with idiopathic physical symptoms is wide open, though methodologic challenges exist. For example, a valid experimental study comparing the impact of two or more labels is likely to require some short-term participant deception. A few institutional review boards may not allow such deception. However most ethical analyses assume that deception can be acceptable provided it does not conceal known risks to subjects [27].

7.5 IDIOPATHIES AND TREATMENT RESEARCH

The medical model operates on the assumption that discovering the explanation for a disease must precede its cure. This approach has led to revolutionary therapeutic discoveries, particularly for acute illnesses such as infectious disease. Arguably, however, these therapeutic successes have yielded an unquestioning allegiance to

uncovering disease explanations even when their value is limited. For example, for idiopathic symptoms, extensive searches for physical explanations may only distract clinicians from implementing effective treatments to reduce morbidity and improve life quality and may lead patients to feel as though their role in the healing process is passive.

By now it is probably clear that a pragmatic perspective is a utilitarian one in which every clinical action is ultimately viewed and evaluated as a therapy. Taken to its logical extreme pragmatism only makes room for those parts of the clinical endeavor that improves important outcomes. Time and effort spent, for example, discriminating between idiopathic symptoms of fibromyalgia and those of somatization disorder, even one could do it (one cannot), is wasted if the treatment is the same for both illnesses. In short, sleuthing solely for explaining is inefficient and unjustifiable.

We will not revisit explanatory versus pragmatic clinical trials, though it is worth brief discussion of factors that can threaten generalizability of explanatory study findings to patients with idiopathic symptoms in real-life settings. Well-known factors such as comorbid mood and anxiety disorders, substance use disorders, and chronic disease are usually excluded from explanatory studies because they may reduce the impact of a given treatment. When evaluating therapies for idiopathic symptom syndromes and estimating to what extent results will generalize to specific settings, it is similarly important to consider what common “overlapping” symptom syndromes are present [28]. Aaron and Buchwald have extensively studied the large degree to which idiopathic symptom syndromes are overlapping (see Table 7-2) [28]. These comorbid idiopathic symptom syndromes are important to take into account in clinical settings too, as they represent markers of overall illness severity and may also lead to modifications in the therapeutic plan with affected patients.

Table 7-2: Screening Questions for Overlapping Symptom Syndromes with Published Criteria that Commonly Co-occur with Fibromyalgia (Reprinted from Aaron and Buchwald [28]).

Condition	Screening Questions	Published Criteria
Chronic fatigue syndrome	Unexplained persistent or relapsing fatigue for >6 months?	1994 Centers for Disease Control and Prevention criteria ²⁶
Irritable bowel syndrome	Abdominal discomfort or pain accompanied or affected by constipation or diarrhoea for >3 months in the past year?	Rome II criteria ²⁷
Temporomandibular disorders	Recurrent facial/jaw pain and/or limitation in jaw opening occurring?	1992 research diagnostic criteria ²⁸
Multiple chemical sensitivities	Symptoms in multiple organ systems reliability occurring on exposure to multiple unrelated chemicals?	Bartha et al 1999 consensus criteria ²⁹
Tension and migraine headache	Recurrent headaches (≥5 for migraine, ≥10 for tension-type) lasting >30 min occurring in the past 6 months?	1988 International Headache Society criteria ³⁰
Intestinal cystitis	Symptoms >9 months of bladder pain, urinary urgency and frequency (voiding >8 times during the day, >2 times during the night), and a negative urine culture?	1987 National Institutes of Health criteria ³¹
Localized myofascial pain disorder	Localized muscle pain for ≥3 months?	1986 International Association for the Study of Pain criteria ³²

*Positive responses to screening questions warrant further clinical evaluation and possible laboratory testing as recommended by individual criteria.

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With widespread disagreement with regard to the explanations for idiopathic symptoms and related syndromes and no demonstrably reliable method for even identifying clearly distinct and relevant syndromes (for example, syndromes that might differ from one another with regard to preventable risk factors, a disease-specific treatment, or predictors of natural history), it would appear that clinicians are obligated to acknowledge uncertainty when caring for patients with these symptoms. Part of the clinical act of respecting medical uncertainty is acknowledging the complex and non-linear etiologic relationship between idiopathic symptoms, personality factors, psychiatric disorders, and associated distress and disability. It follows logically and ethically that in the presence of etiological heterogeneity and medical uncertainty, clinicians should generally elicit, validate, and even adopt the patient's perspective when designing, communicating, and implementing a the treatment plan. In contrast, others have already observed the ethical tension present when, for fear the diagnosis will be rejected along with the treatment and even the clinician, patients are rarely told that a somatoform diagnosis has been made [29].

7.6 DISCUSSION

The tradition in psychiatry has long been to view idiopathic physical symptoms and related syndromes through an explanatory lens. We view these symptoms as psychiatric (somatization) and routinely applied psychiatric (somatoform disorder) labels like somatization disorder and hypochondriasis with little or no thought to the acceptability of these labels to patients, the ease (or lack of it) that primary care clinicians experience when using them, and the impact of the label on the physician-patient relationship and overall treatment. Consequently, while it is clear that somatization is a complex but valid and clinically significant construct, our categories and our case definitions are failing those who should benefit most from them; that is, patients with idiopathic physical symptoms and the primary care clinicians who provide care for them.

A movement has gradually gathered momentum within progressive iterations of the DSM and among somatization experts, a movement toward a more pragmatic perspective that relies on increasingly practical and generic labels for what are best conceptualized as idiopathic physical symptoms. In some respects, an atheoretical and phenomenological movement within the field of somatoform disorders is long overdue and simply represents another step in the progressively more pragmatic psychiatric nomenclature overall. With the dissemination of DSM-III, psychiatry first committed to an atheoretical and phenomenological view. This was of course done to overcome etiological disagreement within psychiatry, disagreement that pertained to nearly all psychiatric disorders of that time. In a remarkably similar way, there is now wide disagreement within various medicine specialties with regard to etiologically framed but phenomenologically indistinct categories of what are fundamentally idiopathies (e.g., fibromyalgia, chronic fatigue syndrome, multiple chemical sensitivities, and irritable bowel syndrome).

Now just as then, solutions and consensus will only come with continued movement toward scientific pragmatism in research methods and in clinical practice.

7.7 DISCLOSURES

The author does not have an affiliation with or financial interest in any organization that might pose a conflict of interest.

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7.9 REFERENCES

- [1] Godwin, M., Ruhland, L., Casson, I. *et al.*, Pragmatic controlled clinical trials in primary care: the struggle between external and internal validity, *BMC Med Res Methodol*, 2003; 3:28.
- [2] Starfield, B., Quality-of-care research: internal elegance and external relevance, *JAMA* 1998; 280(11):1006-8.
- [3] Mayou, R., Kirmayer, L.J., Simon, G., Kroenke, K. and Sharpe, M., Somatoform disorders. Time for a new approach in DSM-V, *Am J Psychiatry* 2005; 162:847-855.
- [4] Sharpe, M. and Mayou, R., Somatoform disorders: a help or hindrance to good patient care?, *British Journal of Psychiatry* 2004; 184:465-467.
- [5] Wilson, A., Hickie, I., Hadzi-Pavlovic, D. *et al.*, What is chronic fatigue syndrome? Heterogeneity within an international multicentre study, *Aust N Z J Psychiatry* 2001; 35(4):520-7.
- [6] Schweickhardt, A., Larisch, A. and Fritzsche, K., Differentiation of somatizing patients in primary care: why the effects of treatment are always moderate, *J Nerv Ment Dis* 2005; 193(12):813-9.
- [7] Turk, D.C. and Okifuji, A., Pain in patients with fibromyalgia syndrome, *Curr Rheumatol Rep* 2000; 2(2):109-15.
- [8] Kroenke, K., Patients presenting with somatic complaints: epidemiology, psychiatric comorbidity and management, *Int J Methods Psychiatr Res* 2003; 12(1):34-43.
- [9] Walker, E.A., Katon, W.J., Keegan, D., Gardner, G. and Sullivan, M., Predictors of physician frustration in the care of patients with rheumatological complaints, *Gen Hosp Psychiatry* 1997; 19(5):315-23.
- [10] American Heritage Dictionary of the English Language, Fourth Edition, Houghton Mifflin Company, 2004.
- [11] Jensen, M.C., Brant-Zawadzki, M.N., Obuchowski, N., Modic, M.T., Malkasian, D. and Ross J.S., Magnetic resonance imaging of the lumbar spine in people without back pain, *N Engl J Med* 1994; 331(2):69-73.
- [12] Bennett, R., Fibromyalgia. Present to future, *Curr Rheumatol Rep* 2005; 7:371-376.
- [13] Hyams, K.C., Developing case definitions for symptom-based conditions: The problem of specificity, *Epidemiol Rev* 1998; 20(2):148-56.
- [14] Wessely, S., Hotopf, M. and Sharpe, M., *Chronic fatigue and its syndromes*, New York, NY, USA: Oxford University Press Inc.; 1998.

- [15] Mayou, R., Bass, C. and Sharpe, M., Overview of epidemiology classification and aetiology, in *Treatment of Functional Somatic Symptoms*, Edited by Mayou R, Bass C, Sharpe M., London, Oxford University Press, 1995: 42-65.
- [16] Vollestad, N.K. and Mengshoel, A.M., Relationships between neuromuscular functioning, disability and pain in fibromyalgia, *Disabil Rehabil* 2005; 27(12):661-673.
- [17] Dadabhoy, D. and Clauw, D.J., Fibromyalgia. Progress in diagnosis and treatment, *Curr Pain Headache Rep* 2005; 9:399-404.
- [18] Inanici, F. and Yunus, M.B., History of fibromyalgia. Past to present, *Curr Pain Headache Rep* 2004; 8:369-378.
- [19] Engel, C.C., Unexplained physical symptoms: medicine's "dirty little secret" and the need for prospective studies that start in childhood, *Psychiatry* 2000; 63(2):153-9.
- [20] Wessely, S., Nimnuan, C. and Sharpe, M., Functional somatic syndromes: one or many?, *Lancet* 1999; 354(9182):936-9.
- [21] Aaron, L.A. and Buchwald, D., A review of the evidence for overlap among unexplained clinical conditions, *Ann Intern Med* 2001; 134(9 Pt 2):868-81.
- [22] VA/DoD Clinical Practice Guideline Working Group. Medically Unexplained Symptoms: Chronic Fatigue and Pain. Washington, DC, USA, Veterans Health Administration, Department of Veterans Affairs, and Health Affairs, Department of Defense, Office of Quality and Performance publication 10Q-CPG/CF&P-01; August 2002 [Accessed on December 22, 2005 at http://www.oqp.med.va.gov/cpg/cpgn/mus/MUS_Gol.htm].
- [23] Hamilton, W.T., Gallagher, A.M., Thomas, J.M. and White, P.D., The prognosis of different fatigue diagnostic labels: a longitudinal survey, *Fam Pract* 2005; 22(4):383-8.
- [24] Escobar, J.I., Interian, A. and Díaz-Martínez, G.M., Idiopathic physical symptoms: a common manifestation of psychiatric disorders in primary care. *CNS Spectr.* 2006;11:201-210.
- [25] Salmon, P. The potentially somatising effect of clinical consultation. *CNS Spectr.* 2006;11:190-200.
- [26] Jackson, J.L., O'Malley, P.G. and Kroenke, K. Antidepressants and cognitive-behavioral therapy for symptom syndromes. *CNS Spectr.* 2006;11:212-222.
- [27] Wendler, D. and Miller, F.G., Deception in the pursuit of science, *Arch Intern Med* 2004; 164(6):597-600.
- [28] Aaron, L.A. and Buchwald, D., Chronic diffuse musculoskeletal pain, fibromyalgia and co-morbid unexplained clinical conditions, *Best Pract Res Clin Rheumatol* 2003; 17(4):563-74.
- [29] Wessely, S., To tell or not to tell: the problem of medically unexplained symptoms. *Ethical Dilemmas in Neurology*, A. Zeman, L. Emanuel, Editors, London, UK: Saunders 1999; 41-53.
- [30] Mayou, R. (1995), *Treatment of Functional Somatic Symptoms*, Edited by R. Mayou, 1995, Oxford University Press.



Chapter 8 – DEVELOPMENT OF A DAY TREATMENT PROGRAM FOR MEDICALLY UNEXPLAINED PHYSICAL SYMPTOMS (MUPS) IN THE DUTCH ARMY

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ABSTRACT

BACKGROUND: A group of servicemen can be identified that seek disproportionately amount of health care in comparison to diagnostic and therapeutic perspective. This group can be identified on the basis of an absence of a structural medical explanation for their symptoms. Symptoms manifest predominantly as fatigue and pain, and are often chronic. Based on reviews, expert recommendations and clinical demand a specialized treatment program for soldiers with Medically Unexplained Physical Symptoms (MUPS) has recently been developed and implemented in the system of health care in the Netherlands Armed Forces. While consensus on the biological basis for these complaints is lacking awareness on the need for effective treatments for this patient group is high. METHOD: Patients with MUPS often have multiple and complex problems that would be best treated by a team of cooperating medical specialists and paramedics. We developed a functional rehabilitation program with blended care elements of Cognitive Behavioral Therapy (CBT), physical therapy, case management and psychoeducation, embedded in a day treatment setting. RESULTS: The program scores high on team as well as participants satisfaction. We illustrate the program by two clinical vignettes. CONCLUSION: The military is characterized by high loyalty towards peers and leadership. A blended care program for medical unexplained physical symptoms offers a more holistic and preventive approach that focuses on allostatic load awareness contributes to a reduction of unnecessary medical consumption and increases job participation. We recommend that the development of guidelines for diagnoses and treatment of these complaints in military setting will improve the quality of patient care, reduce disability, facilitate reintegration and encourage scientific research.

8.1 BACKGROUND

The reported prevalence of Medical Unexplained Physical Symptoms (MUPS) in the Dutch military population varies from 5% to 20% [1], [2]. The Dutch Military Mental Health Care (MMHC) and the Central Military Hospital (CMH) in The Netherlands appreciated the clinical need and responsibility towards the service members to offer an effective treatment program for MUPS in the military population. The complaints are characterized by persistent physical symptoms such as fatigue, headaches, joint pains [3], [4], [5], causing significant distress or functional impairment in the absence of disease or clear cause after appropriate and directed clinical assessment. MUPS are neither a disease nor have a specific diagnostic category. These non-specific symptoms have a variety of potential causes. MUPS are related to a high medical consumption [6]. This situation is not typical for service members. Approximately two thirds of the general population experience one or more painful or distressing symptoms in an average month, and studies show that in routine practice 25 – 30 % of symptoms remain unexplained. Scientific and clinical investigations typically do not provide answers to the complex causal questions that arise in defining and responding to these common persistent symptoms.

Successful diagnostic assessment and treatment is of key importance for service members that may experience persistent work-related symptoms or injuries. Rather than expanding care to exhaustive biomedical diagnostic

evaluations or implementing invasive interventions or treatments targeting a narrow set of symptoms, a comprehensive approach is necessary to balance necessary diagnostic assessment and prevent unnecessary medical overconsumption.

The purposes of this paper are to:

- 1) Present the development of a blended care program for service members with MUPS within the Dutch Department of Defense; and
- 2) Justify the blended nature and ingredients of the program, as an intensive outpatient program.

Elements of this approach are used in chronic pain centers internationally. We will describe the more holistic treatment approach to highly loyal service members with persistent, disabling physical symptoms. We will illustrate the program with two vignettes of a patient with MUPS. The specialized care program is a multi-disciplinary group treatment program that is developed for servicemen with MUPS. It is based on a treatment program, which is implemented at the Walter Reed Army Medical Center (WRAMC) in Washington, DC, USA [3]. The specific mission of the program is to provide a 12-week, intensive outpatient, multi-disciplinary treatment program for people with persistent MUPS. Objectives are to help those with these symptoms and improve their quality of life, functional status, and occupational performance. The program works with each individual to:

- 1) Maximize awareness over symptoms;
- 2) Maximize awareness of factors that prevent reduction of symptoms;
- 3) Maximize successful coping with persistent and disabling physical symptoms;
- 4) Obtain a consistent, primary care-based follow-up plan;
- 5) Address psychosocial contributors to symptom-based disability;
- 6) Improve relationships with health care providers and significant others;
- 7) Reduce excessive and potentially harmful use of the health care system;
- 8) Initiate a program of physical activation that takes into account an individual's unique musculoskeletal limitations; and
- 9) Improve understanding of the known health consequences of the military profession.

The treatment program consists of a day program, occurring one day per week for 12 subsequent weeks and containing of a blend of ingredients:

- 50% specialized physical therapy;
- 20% Cognitive Behavior Therapy (CBT);
- 10% psychomotor therapy;
- 10% health education; and
- 10% case management.

Health education consists of seminars provided by varying specialists. The case manager links the separate therapies during the day and monitors the general needs of the patients.

8.2 CLINICAL CHALLENGES

General practitioners are not always aware of ill-defined conditions or MUPS, and are, therefore, often hesitant to mention them [7]. Patients with MUPS symptoms are complicated for doctors in different ways [8]. Differences in opinions and expectations influence a doctor-patient relationship in many ways. Patients with MUPS may lack confidence in the regular health care system and may look for a solution in complementary or alternative treatments. When a medical diagnosis is lacking, treatment cannot be justified and therapy remains absent. Referrals to external facilities often result in long delays, and lack specific understanding of military setting and demands of the service. These factors contribute to the fact that undiagnosed patients feel as though they are not understood, are not cared for and may feel despair as a result. In case of external attributions, they may deplete the sources of medical system, since their attributions cannot always be corroborated. They may seek negative attention in their environment and in a public arena, such as the media. Some may develop compensation seeking behavior, yet can be stuck in a high loyalty to their employer, peer group, commander or the military service in general. Patients typically look for acknowledgment. The authors of this paper feel that quite often there is a generalized blame to the army for their physical complaints, which sometimes can be reduced to specific encounters or conflicts with key persons. Finally, when a patient is referred for medical treatment, they may not feel understood by their social environment, doctor or command line. Medical consumption is typically high in this group, and characterized by an abundance of diagnostic assessments. There is often chronic functional impairment on cognitive, emotional, behavioral and social domains. These factors contribute to disproportionately high costs for patients with MUPS in the absence of proper recognition of potential factors that address issues that contribute to therapeutic change.

8.3 CASE REPORTS

8.3.1 Case 1

Patient is a 34-year-old captain in the Dutch Army. She was deployed in 2010 to Afghanistan. She had served the army since 1996. She felt a bit insecure because of last minute preparation (e.g., there was no time for measurement of her protective gear, which was given to her during the last stop over before arrival in Kandahar). These and similar experiences had made her feel a bit insecure. She was assigned a job for which she frequently had to go out of the army basecamp into unsafe areas. One occasion changed the course of her deployment. She went out to visit a children's home. On the way back they came to a crowded market. The vehicle got stuck; there were locals all around them. They were ambushed, with high threat, while she was very aware of being the only woman in an army vehicle that provided no protection in case of an ambush. The driver tried to escape by high speed driving through the crowd. During the escape, her vest was so tight that it hurt her and impeded her breathing. Because of the high alert she didn't notice it at that time, but being back at the base an intense chest pain started. She collapsed, fell and was heavily bruised. She suffered from nervous palpitations and strong chest pains, spreading from her chest to her throat. She was admitted to the role-2 hospital, scans were taken, without any signs of fractures. She was diagnosed with a non-specific costosternal pain. Morphine was given and they decided to repatriate her. The flight surgeon was not sure if air transportation would be safe for her, so additional painkillers were given. In retrospect, she was uncomfortable that pre-safety procedures had not been followed correctly. The men who accompanied her had appeared nervous. During the visit they had taken off their protective gear and went outside the house. This had made her fearful. At the hospital she was in so much pain that again she collapsed. She was repatriated. At the airport at that moment a few rocket attacks commenced. Upon arrival in the Netherlands only her boyfriend met her at the airport, nobody from the medical team or the Dutch Army was present to pick her up and guide her to the Military Hospital. She went there herself, was assessed, put on painkillers and sent home. In the absence of

follow-up she continued taking the painkillers. Her commander told her to come back to work when everything was all right. She felt she was left alone. She continued to be worried about the pain. Very little was done to get her back to work. A proper diagnosis was lacking. She started to suffer from addiction to pain medication, started physical therapy with very little result. Her symptoms became worse, now spreading out to her whole body. She felt a stiffness of her body, suffered pain in both her feet, had difficulties walking the stairs, had swollen fingers, pain in her right clavicular bone, neck pain, and shoulder pain. The stiffness and pain contributed to making her feel fatigued.

Her cognitions about her symptoms were that she thought her vest had been too tight. In her family there were some rheumatic diseases, but although the fact that she was examined by a rheumatologist, and that rheumatic diseases were ruled out, she was still not relieved. Emotionally she was upset that the army had not given her proper material and that safety instructions had not been carried out properly during her last trip. Having arrived at the airport with no pick up and no proper reintegration schedule from work she felt abandoned and as though she was not being taken care of.

She started to become frustrated that the pain did not dissipate by itself. She had always been an active woman. She started to be hopeless but wanted to keep strong. She did not want to give up. In her coping she avoided physical exercise since this made her symptoms worse. She also noticed that she was negatively affected by stress. Her breathing was superficial and her muscles tight. She was still taking care of her household; she would not give that away. Her social system, including her husband, started to become worried. At the assessment she was not on sick leave; all of her energy went into her working day. She did not want to fail in her job. In her character she was described as a perfectionistic, active person, who liked to be in control.

8.3.2 Case 2

Patient is a 54-year-old sergeant, who had served in the army for 30 years. He had been deployed 6 times: to the Gulf, Iraq, twice to Bosnia, Kosovo and Uruzgan during his career. In several deployments, he was exposed to situations of high threat and deadly violence. He had been in many dangerous operations himself, but was never injured. In his role as a medic he had witnessed several atrocities, had been near explosions and shootings and had seen many people die. Since 2000, he reported he suffered from physical pains, which gave him a lot of distress. His body hurt; mainly he had pains in his joints. He consulted several medical specialists in the hospital, yet no somatic diseases were found. In 2007 he was sent to a psychiatrist for the first time, in particular since he persistently attributed his symptoms to having been exposed to Sarin gas, pyridostigmine, multiple vaccinations and depleted uranium and there were no further options in the somatic area. Though he had witnessed several traumatic incidents he was not diagnosed with PTSD. He received trials of medication such as benzodiazepines, SSRIs, and pregabalin of which only duloxetine gave some relief, yet with only partial effect. He was guided in his desire to seek help in alternative medicine. His muscle stiffness and pains had set a pattern of physical therapy twice per week for the last years. He was described as a man with high loyalty towards his employer and is very sensitive to authorities. He scored negative on depression and anxiety. He was perceived as rigid in his thinking, never shared anything about his deployments with his wife or children, and wanted to keep them away from his experiences. Though he suffered much, he has skipped only a few days from work. A medal of honor that he applied for, was turned down, which he felt as a great rejection. He blamed the army; he persisted to refer to his pains to being exposed to Sarin during his deployment. When he was admitted to our specialized program for screening he shared with us that he could not have PTSD because he was a soldier and everything he did or saw was part of the job. Two years before his retirement he disclosed to the researchers that he feared retirement, and was afraid of losing the health benefits that kept him doing his job so far.

8.4 RESEARCH IN DUTCH COHORTS

Netherlands Armed Forces is confronted with soldiers and veterans who after deployment report medical unexplained physical symptoms that demand medical attention and care. For the Dutch situation these symptom complexes are reported after deployment to Desert Shield/Desert Storm, UNTAC (Cambodia), and UNPROFOR (Lukavac, Bosnia), as well as Dutchbat (Srebrenica). In many cases a pathophysiological substrate is not found after careful diagnosis [9], [10]. The symptoms are usually attributed to the deployment(s) because they arose a shorter or longer time afterwards. They do not respond to reassurances or forms of classical symptom management and can develop into a chronic disease with severe functional limitations, resulting in disability. An accurate estimate of the incidence is difficult. In a group of 2700 Cambodia veterans at the VU Amsterdam and the University of Nijmegen, extensive research was performed into possible causal factors of unexplained health problems [11].

Microbiological, immunological, toxicological and vaccination studies yielded no evidence for causes that could explain the symptoms. However, a relationship was found with the daily activity level, exercise tolerance and psychological functioning in particular lack of low self-efficacy, somatisation, and negative social interactions.

Recently, a study into the general health of veterans from Lebanon was performed through a written survey. A total of 1835 veterans responded. These patients, 25 years later, still scored above the average standard complaints in the MUPS and PTSD spectrum [12]. The health perception in general was lower than the average standard for a similar group. This can partly be explained by a response bias. At the same time this can indicate that if there are health problems, these can be protracted.

8.5 SYMPTOM PRESENTATIONS

MUPS in soldiers can be seen as a symptom complex without organic basis. As has been reviewed here, the complaints include:

- Chronic fatigue;
- Joint pain;
- Pain (head and spine);
- Painful muscles and joints;
- Vertigo;
- Skin irritation;
- Sore throat;
- Symptoms of the respiratory or gastrointestinal tract;
- Arousal (alertness, but also increased sweating);
- Sexual problems;
- Sleep disorders;
- Memory/concentration problems; and
- Others.

These complaints result in functional limitations, disability and reduced quality of life. In the phenomenology there is a strong resemblance with the chronic fatigue syndrome [13], [14]. The first case presented had similar features as in the early descriptions of Da Costa's syndrome. The symptoms are predominantly physical in their presentation. From a psychiatric perspective there are similarities with comorbid symptoms found in patients with PTSD, atypical depression, hypochondriasis, undifferentiated somatoform disorder, somatoform disorder with autonomic dysfunction and with a pain disorder. Differential diagnosis always needs to be made to exclude these disorders. There are also descriptions in the literature with characteristics such as migraine headaches, unexplained abdominal discomfort and multiple chemical sensitivity [15], [16], which the second case demonstrated. Cognitive disorders (attention and memory) and mixed anxiety and mood disorders [17] are also frequently mentioned.

Both medically unexplained symptoms, in general, and among soldiers after deployment, in particular, often express loss of function that is disproportionate to the findings at physical examination, diagnostic and inconsistent with laboratory findings. Often it is thought that these people are out on secondary gain. An association with stress and psychosocial factors is assumed [14], but has not been systematically investigated. Many patients have a long and complicated history with several consultations in primary and secondary care specialists. Several studies or interventions have occurred without conclusive results. In the Netherlands the term 'somatic fixation' has been common practice [18]. In this perspective, the patient is convinced that there is something wrong with him/her and often has a specific attribution for the complaints. The symptoms often refer to different organ systems. The course of the disorder is chronic and is associated with, or leads to, impairments in social, interpersonal and system interactions. Given that, the physical presentation is not primarily thought to be a psychological or psychiatric attribution of symptoms, which frequently in hindsight it appears to be the case.

It is important to note that these physical complaints and reports are typically outside the purview of psychiatry. They are manifest in general practice, general physicians, and further to medical specialists as neurology, internal medicine and orthopedics, as well as in cardiology, pulmonary and ENT. Sometimes there is also resistance to a descriptive psychiatric explanation for the symptoms.

8.6 DEVELOPMENT OF BLENDED CARE PROGRAM

In a ministerial report that was written after assessment of the studies in Cambodia [1], recommendations were made with regard to health care programs. Soldiers with ill-defined medical complaints after deployment would submit to a detailed integrative medical plan tailored to the individual. The symptoms or complaints could not directly be traced back to a medical and/or psychological component in all cases. Nevertheless, a plea was made to investigate these complaints seriously. If no biomedical explanation could be found, a clear course needed to be followed. It was advised that nurturing cognitive behavioral treatment needed to be an important aspect of the program (Ref. [1], p. 6). An 'overall plan' should contain synchronized medical and psychological help with the support of the social system, as well the physical rehabilitation (fitness) and the return to work (reintegration).

The Central Military Hospital (CMH) translated the recommendations of the Tiesinga Committee into a blended care specialized program. The aspects of the program developed were derived from various sources, such as mentioned above, and the literature on MUPS. This literature focused on treatment strategies in the context of the Gulf War syndrome, in which interventions in the field of activities, effort and psychology were emphasized [19]. This has led to a treatment model that is operated in an outpatient setting, for a period of 4 months (12 weeks) in day treatment. The treatment was designed as closed group therapy, in which six to eight participants per module could participate.

The term blended refers to the notion that there is no competition in the treatment strategies of the participating therapists. All participating therapies blend in the service of the benefit of the patient. This is achieved and maintained in frequent multi-disciplinary encounters. All therapies refer to a context of healing.

8.7 OUTPATIENT DAY TREATMENT PROGRAM

It is important to once more note that MUPS is a working diagnosis only. Despite the acronym MUPS, one should not assume that this is a specific diagnosis or disorder. There is also no golden standard assessment for MUPS. Medical screening is preferentially performed by a family physician who may act in concert with a team of medical specialists, including:

- Neurologist;
- Internist;
- Psychiatrist;
- Rehabilitation specialist;
- Cardiologist;
- ENT doctor;
- Clinical psychologist regarding diagnosis; and
- Need for additional provisions/operations.

The day treatment program was launched in 2009. First, the patient is seen at the outpatient clinic by the family physician and if indicated by other medical specialist (once) for additional research. During the intake the history of the physical complaints is documented in patients own words. Detailed medical history is collected from previous consultations and reviewed on course, consistency, completeness and systematicness. This assessment is to find a somatic basis or explanation for the reported symptom complaints. Indeed, only if this basis is lacking, a patient may be referred to the outpatient treatment. Other physical causes of illness are also ruled out.

A willingness to participate in a constructive way is then explored with the person, focused on attribution, perception, coping, body image, ego-strength and ability to self-reflect. Also, an analysis is made on the meaning of this in the family situation. The patient's partner preferably participates in the intake and periodically throughout the treatment. We examined whether patients are able to take responsibility for their complaints to investigate and to find ways to reduce or to modify them. Relative contraindication to our treatment are on-going diagnostic efforts into a medical explanation for the symptoms (i.e., research into a pathophysiological substrate), an insurance procedure in relation to these complaints (progress of the treatment could be affected), severe psychiatric problems, such as:

- Depression;
- Psychoses/delusions;
- Addiction;
- Obsessive-compulsive disorders;
- Anxiety disorders; and
- Behavioral or personality disorders.

Also a highly disordered (illness perseverant) home system could prevent healthy development. Based on these questions, additional assessment may be indicated. When the diagnosis is complete and adequate, the patient is discussed in a consensus meeting with the whole team.

As a minimal set, the following factors must be assessed:

- Do co-morbid disorders such as mood/anxiety disorders, PTSD, and depression play a role?
- Are there objective somatic disorders?
- Are there any pre-existing conditions?
- Are there any predisposing factors?
- Are there any illness-perpetuating factors?
- Are there stressors in the private and/or work environment that are important?
- Do physical complaints or limitations exist?
- Has there been adequate therapy/counseling (not only insightful therapy)?
- What has thus far been the primary focus of the treatment?
- According to this treatment, what have been the main obstacles to recovery?

We chose to be stationed at the front door of the general hospital, rather than within the walls of in the mental health care unit. We made this choice based on the fact that MUPS is neither fully somatic nor fully psychologically explained. In addition, soldiers who come back from combat usually have difficulties seeking medical care for mental problems, are fearful of stigma and other barriers to care. [20]. Therefore, we formed a multi-disciplinary team comprised of individuals with a variety of medical disciplines. The team consisted of:

- Two general family physicians;
- One psychiatrist;
- Two psychologists/psychotherapists;
- One psycho-educative nurse;
- One behavioral therapist; and
- One neurologist.

The program had two elements:

- 1) Diagnostic assessment; and
- 2) Treatment.

8.7.1 Assessment

In the anamnestic phase the interviewer checks besides the somatic field the fields of cognition, emotional, behavioral and socials, according to the SCEBS (Somatic, Cognitions, Emotions, Behavior, Social system) communicative model. When a patient is likely to have MUPS, he or she is seen for a meeting with the physiotherapist and psychologist of our team. The GP's at the outdoor clinic also offer guidance to medical health care workers who seek advice for MUPS issues.

The physiotherapist is consulted if a patient is fit to participate in the program, and a psychologist of the team assess if the person is mentally capable to be admitted to group therapy. Any psychiatric disorder should be ruled out. MUPS is associated in 30% with anxiety and or depression. If a patient is seen by all of these professionals, then the team as a whole makes a decision as to whether participation is worthwhile for this patient.

8.7.2 Treatment

Previous studies showed that physical exercise in combination with body awareness and CBT could be effective in those suffering from unexplained physical symptoms [25]. The treatment program for MUPS consisted of 12 days of group therapy, once a week. Group therapy proved to be effective [21]. We chose to offer multi-disciplinary treatment, which we call blended care. It is based on the ‘protocol of treatment for patients with MUPS’ by Speckens *et al.* [22]. This protocol offered guidelines for treatment for MUPS with CBT and graded exercise. According to needs, it leaves time in the program for different modules for example relaxation, psychomotor therapy, EMDR and psycho education. Furthermore we used the Dutch Multi-disciplinary Guideline for medically unexplained symptoms and somatic disorders 2010 [23]. We also used recommendations from treatment programs for somatoform and somatoform-like disorders and the stepped-care guidelines for evidenced-based treatment [24].

8.7.2.1 Specialized Physical Therapy

Physical exercise is based on a model of Allostatic Load Awareness (ALA). This is based on the model of allostatic load by McEwen [26], in which a balance (homeostasis) has been established against a price, of an altered ‘set-point’ (allostasis) (e.g., high blood pressure, headache, fatigue). Members learn how to exercise while becoming aware of the load that their body takes in a playful interactive way. Patients often experience their bodies as ‘heavy,’ or move beyond their physical limits and ignore body signals and limitations. This takes a toll on body reserves. When they feel good they ‘overreact,’ for which the next day they pay the price of pain or exhaustion. Others were afraid that they could harm their bodies. They ended up in a spiral of inactivity and develop a loss of physical condition.

8.7.2.2 CBT According to the ‘Model of Causes’

We work according to the ‘model of causes’. This model is a kind of CBT but the focus is put not on the physical complaint itself but the effects in daily life resulting from these physical complaints. The model and its therapeutic implication provide a tool to focus on improvement of daily life and general feeling of the patient. The improvement of activities that the person assumed could no longer be performed, and the focus on abilities rather than disabilities ensures positive reinforcement. Usually health complaints diminish secondarily in response to reengaging in these activities.

8.7.2.3 Psychomotor Therapy

This is an intensive training that confronts the participants with their subtle bodily signals and how these are related to their emotions and cognitions; it is an experimental treatment which uses non-verbal methods. Central to this approach is that the patient learns to become aware of the connections between emotions and physical signals.

8.7.2.4 Psychoeducation

In this part researchers offer different educational modules (e.g., education about work and health), communication with the general physician, ‘taking care of yourself’ and working on your social environment. Sessions last approximately an hour and are interactive.

8.7.2.5 VIP

At two times during the program there is a so-called VIP day where the spouse or another important person of the patient also takes part in the program. This allows the team to collect information about the social system, and also allows the VIP an appreciation of the intensity of the treatment.

8.8 THERAPEUTIC COURSE

8.8.1 Case 1

During therapy, the soldier learned that while engaged in sports and play not to be afraid to move and make movements slowly and smoothly. We encouraged her to make 'big' movements, so her body would be relaxed and her body language would be open. During CBT, according to the model of causes, we showed her that doing everything on her own while having many symptoms would make her tired. This was manifested in tense muscles with intense pains, but the more she tried, the less it worked. The team taught her to take brief breaks and rest at discrete moments during the day, to relax and to let go. If she would learn how to relax her muscles, she would be less tense and would be more relaxed. If she could relax her muscles, she would experience less pain. During psychomotor education, we explored her emotions at different points throughout the education process. She learned that her muscles would tighten when she feels angry and insecure, and relax if she is not angry. During psychotherapy we focused on letting the anger and insecurity out. The circle "being angry or insecure – tighten muscle -muscle pain and stiffness – not being able to do the things she wants – angry about not being able to do the things she wants – tighten and so on." She gained insight in the fact that before going to her deployment she felt unsafe and insecure. During specialized physical therapy she found out that the stiffness and pain of the muscles reminded her of the horrible trip in the car. She was aware that her complaints were a physical reminder of a stressful experience. After the 12-week treatment, her complaints were fully gone, and she was maximally aware of her boundaries. She could feel when she had to stop and take a rest. She knew that regular physical exercise would keep her body relaxed and in shape. She could put her complaints in a framework of cause and effect. To let go of her anger against "the army" she wrote a letter to a high commanding officer. He replied. This gave her satisfaction and made her feel at ease. In a six month follow up after treatment, she was back to work full-time.

8.8.2 Case 2

The officer learned during playful group physical exercises that he could do more than he was aware of and that this did not negatively affect symptoms. During physical therapy, he also discovered that being part of a group could be quite fun and that the group could be supportive in times of need. He found much support and started to share his thoughts and feelings. It was good for him to know that, being a soldier, emotions would not make him less appreciated. During the CBT, which was based on the model of causes, he learned that the pain he felt in his body was a pain he could not express in emotions. Because he always focused on his physical complaints, everybody was focused on his physical symptoms and not on his mental pain. Psychomotor therapy had taught him that his pain actually was, in part, mental imprints that he had been very afraid to feel. When slowly during therapy some physical complaints started to change, his symptoms shifted: he started to have nightmares and flashbacks of previous deployments. He felt an urge to talk about experiences that he never disclosed to anyone. It was two months before his retirement. His diagnosis changed to PTSD in conjunction with chronic pain. He blamed himself for not earlier disclosing his experiences during deployment. He noticed that physical complaints came when mental pain was not accepted. After completion of the day treatment, he continued with narrative exposure therapy in which his wife was also involved. After day treatment, he had developed delayed onset PTSD.

These vignettes demonstrate the clinical course of participation in a blended care, multi-disciplinary treatment program. Central in the program is the notion that a context is created in which healing is facilitated. Sometimes this leads to identification and amplification of factors that contribute to successful coping (see Case 1), but in other cases (Case 2) this is only first realized after breakdown of maladaptive coping.

Since the start of 2009, a total 104 soldiers have been admitted to our specialized program. Of this group, 32 followed the day treatment program, which was divided into six groups over the course of three years. Of the 72 that were not admitted to the program, 34 received another diagnosis, among which are gastric ulcer, Epstein Barr infection and auto-immune disease. Fifteen received a psychiatric diagnosis, mostly depression, hypochondria or anxiety disorder. The remaining group of 38 was not admitted because they did not meet inclusion criteria. We gave 28 patients in this group personal counseling. The last 10 referred patients did not participate because of other reasons (e.g., some left the army, some felt well for no reason, or developed another illness).

We then looked at medical consumption and work recovery as means of functional impairment. We checked the files of the primary health care of the patients. All patients gave signed permission to look at their files. We included the doctors' visits three months prior to treatment and three months after treatment. If the amount of visits was lower, we called this less medical consumption. We also checked if three months prior to treatment if there was sick leave and the percentage of sick leave. We checked after treatment how many of those with sick leave had returned to work full time. The participants were also tested on physical complaints, coping and personality.

A total of 32 patients entered and completed the 12-week program. In 69% of them, their physical symptoms had fully receded. Medical consumption was counted three months prior to treatment and three months after treatment. Before day treatment, a number of consultations in three months averaged 3.8 (0 – 9). After day treatment had dropped to 1.7 (0 – 5).

From the total of 32 patients, 21 were on sick leave before treatment, 10 had short sick leave (defined as three periods of three days sick leave in three months) and 11 had continuous sick leave. After treatment, 18 had a full work recovery without sick leave, only one had a period of short sick leave. One had no recovery and two had left the army. Three patients who were not fit for the military before treatment were considered fit for military service after medical re-evaluation after the treatment.

On qualitative assessment, overall, the patients felt happier, less frustrated, and physically and mentally more fit. Also their spouses and support system was more satisfied with their lives than before. Of importance, there were no claims whatsoever against any of the workers at the program or at the outdoor clinic in general. Overall they were satisfied that their employer gave them the opportunity to get better.

8.9 CONCLUSION

As is outlined in this paper a MUPS program that is based on a blended care, multi-disciplinary 12-week day treatment approach has a beneficial value on the outcome of the patients' quality of life and overall functional improvement. A short program like the one we offered (total number of treatment days is 12) gives patients time to work on different parts of the negative spiral they are in. In post-deployment care, attention should be paid to those suffering from MUPS. We cannot avoid that sometimes people, as different as they are, do not fit into our traditional health care system. For these people, MUPS treatment as described can have a miraculous effect. The additional effect of the group for support and sharing experience and attention was significant. It gives them tools for the future.

Understanding MUPS and other ill-defined medical conditions and the necessary ingredients for successful treatment is still in its infancy. The following themes and questions could play a role in future studies:

- 1) What factors influence improvement and are these factors integrated in the treatment?
- 2) Is there an optimal activity level for patients with MUPS for optimal physical function and participation and what is the role of physical activity and its influence on the symptoms?
- 3) What are the long-term effects of the current treatment program and is a follow-up trajectory needed for more enduring effects?
- 4) If the answers are known and positive, what should such a trajectory consist of?
- 5) What is the most optimal composition of the multi-disciplinary elements?

It could be that the current elements can be optimized or that other disciplines need to be involved. This also applies to the duration and intensity of the treatment program. Finally, cost effectiveness should be examined in more detail.

Incidentally MUPS are observed in veterans who do not meet all criteria for PTSD [27]. The causal relationship between many physiological abnormalities in PTSD patients and perceived stress load has been confirmed in animal models [28]. Besides some basic changes herein, a picture of generalized hyper responsiveness of physiological systems can be seen that may potentially contribute to physical complaints. Not only the external (stress) load plays a role, but also the individual vulnerability (e.g., as a result of traits or experiences earlier in life). Parameters of functional impairment-oriented research are:

- General physical health.
- General health history.
- Medical history, including:
 - Personality and temperament;
 - Neuroendocrine;
 - Cardiovascular;
 - Gastrointestinal and immune functions; in addition to a
 - Test for sensitivity.

Future scientific research will have to increase the understanding of the nature of this diagnostic ‘category’. The homogeneity of the symptom complexes now is the first point of attention. Not infrequently a post-deployment syndrome gradually developed into a recognizable PTSD or other disorders from psychiatric diagnostic classification. Professionals would be well-advised to look for common elements, such problems in impulse control and psychophysiological hyper reactivity [29]. Such properties may have been acquired, but even in early childhood arise or even congenital and service experiences strengthened. Such insights will in turn clarify the therapeutic potential and hopefully expand it as well. This means that coupling clinical treatment to scientific research, as was already recommended by the Tiesinga Committee in 1999, is essential.

We live in an age in which people scrutinize their health and the health implications of the workplace to a very high degree. As we outlined a program that is providing health care for people deploying to unpredictable, traumatic, and potentially toxic environments must prepare to implement coordinated, multi-disciplinary medical evaluations for those. We described a framework for a program that is in a team-based setting as described and allows the patient to feel understood, warrants job satisfaction, and could be cost-effective. Such a treatment

seemed to be timely, innovative, and effective health care to those with persistent ill-defined post-deployment physical symptoms.

8.10 REFERENCES

- [1] Commissie-Tiesinga, Rapportage Begeleidings Commissie Post Cambodja Klachten Fase II, 12 December 2000.
- [2] Vries, M. de, Soetekouw, P.M.M.B., Meer, van der J.W.M. and Bleijenberg, G., Natural course of symptoms in Cambodia veterans: a follow-up study, *Psychol Med* 2001; 31:331-333.
- [3] Engel, C.C., Hyams, K.C. and Scott, K., Managing future Gulf War Syndromes: international lessons and new models of care, *Philosophical Transactions of the Royal Society B* 2006; 1468:707-720.
- [4] Barrett, D.H., Gray, G.C., Doebbeling, B.N., Clauw, D.J. and Reeves, W.C., Prevalence of Symptoms and Symptom-based Conditions among Gulf War Veterans: Current Status of Research Findings, *Epidemiological Reviews* 2002; 24:218-227.
- [5] Vermetten, E. and Linn, F.H.H., 2008, Onbegrepen klachten bij militairen na uitzendingen, *Bijblijven* 2008; (8):55-62.
- [6] van der Gulden, J.W., Onverklaarde chronische klachten, Houten: Bohn, Stafleu van Loghum, 2006.
- [7] Olde Hartman, T., van Ravesteijn, H. and Lucassen, P., Onverklaarde lichamelijke klachten, *Huisarts & Wetenschap* 2012; 55:301-305.
- [8] Thomas, S., Dealing with medically unexplained symptoms in general practice: from irritation to “the tricks of the trade”, *Abstract, Netherlands Tijdschrift Geneeskunde* 2006; 150:657-9.
- [9] Mulder, Y.M. and Reijneveld, S.A., Gezondheidsonderzoek UNPROFOR. Een onderzoek onder militairen die uitgezonden zijn geweest naar Lukavac, Santici en Busovaca, (Bosnie-Herzegovina) in de periode 1994-1995, Leiden: TNO Preventie en Gezondheid, 1999.
- [10] Soetekouw, P.M., Vries, M. de, Preijers, F.W., van Crevel, R., Bleijenberg, G. and van der Meer, J.W.M., Persistent symptoms in former UNTAC soldiers are not associated with shifted cytokine balance, *Eur J Clin Invest* 1999; 29(11):960-3.
- [11] Vries, M. de, Soetekouw, P.M., van der Meer, J.W.M. and Bleijenberg, G., The role of post-traumatic stress disorder symptoms in fatigued Cambodia veterans, *Mil Med* 2002; 167(9):790-4.
- [12] Mouthaan, J., Libanon, 25 jaar later: Het laat ons nooit meer los, Veteraneninstituut, Interne Publicatie, 2005.
- [13] Aaron, L.A. and Buchwald, D., A review of the evidence for overlap among unexplained clinical conditions, *Ann Intern Med* 2001; 134(9 Pt2):868-81.
- [14] Henningsen, P., Zimmermann, T. and Sattel, H., Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review, *Psychosom Med* 2003; 65(4):528-33.

- [15] Nisenbaum, R., Barret, D.H., Reyes, M. and Reeves, W.C., Deployment stressors and a chronic multisymptom illness among Gulf War Veterans, *J Nerv Ment Dis* 2000; 188:259-266.
- [16] Reid, S., Hotopf, M., Hull, L., Ismail, K., Unwin, C. and Wessely S., Multiple chemical sensitivity and chronic fatigue syndrome in British Gulf War veterans, *Am J Epidemiol* 2001; 153:604-609.
- [17] David, A.S., Farrin, L., Hull, L., Unwin, C., Wessely, S. and Wykes, T., Cognitive functioning and disturbances of mood in UK veterans of the Persian Gulf War: a comparative study, *Psychol Med* 2002;32(8):1357-70.
- [18] Grol, R.P.T.M., Huisarts en somatische fixatie, Bohn, Scheltema& Holkema, 1983.
- [19] Engel, C.C., Roy, M., Kayanan, D. and Ursano, R., Multidisciplinary Treatment of Persistent Symptoms after Gulf War Service, *Mil Med* 1998; 163:202-208.
- [20] Hoge, C.W., Castro, C.A., Messer, S.C., McGurk, D., Cotting, D.I. and Koffman, R.L. Combat Duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to Care. *The New England Journal of Medicine*. 2004; 351-1:13-22.
- [21] Zonneveld, L.N., van Rood, Y.R., Timman, R., Kooiman, C.G., Van't Spijker, A. and Busschbach, J.J. (2012), Effective group training for patients with unexplained physical symptoms: a randomized controlled trial with a non-randomized one-year follow-up. *PLoS One*, 7(8), e42629. doi: 10.1371/journal.pone.0042629.
- [22] Speckens, A.E.M., Van Hemert, A.M., Spinhoven, P. *et al.*, Cognitive behavioural therapy for medically unexplained physical symptoms: a randomised controlled trial. *British Medical Journal* 1995;311:1328. [PMC free article] [PubMed]
- [23] Trimbos Instituut/Netherlands Institute of Mental Health, Addiction (Multidisciplinary guidelines medically unexplained symptoms and somatoform disorders), Houten: Ladenius Communicatie, 2010.
- [24] van Rood, Y.R., Treatment program somatoform and somatoform-like disorders, Stepped-care guidelines for an evidenced-based treatment, 2007.
- [25] Donta, S.T., Clauw, D.J., Engel, C.C., Guarino, P., Peduzzi, P., Williams, D.A., Skinner, J.S., Barkhuizen, A., Taylor, T., Kazis, L.E., Sogg, S., Hunt, S.C., Dougherty, C.M., Richardson, R.D., Kunkel, C., Rodriguez, W., Alicea, E., Chilaide, P., Ryan, M., Gray, G.C., Lutwick, L., Norwood, D., Smith, S., Everson, M., Blackburn, W., Martin, W., McLeod Griffiss, J., Cooper, R., Renner, E., Schmitt, J., McMurtry, C., Thakore, M., Mori, D., Kerns, R., Park, M., Pullman-Mooar, S., Berntstein, J., Herschberger, P., Salisbury, D.C. and Feussner, J.R., For the VA Cooperative Study #470 Study Group. Cognitive Behavioral Therapy and Aerobic Exercise for Gulf War Veterans' Illnesses, *The Journal of the American Medical Association*, 2003; 19:1396-1404.
- [26] McEwen, B.S. and Wingfield, J.C., The concept of allostasis in biology and biomedicine, *Horm Behav* 2003; 43(1):2-15.
- [27] De Loos, W.S., Somatic war syndromes: no man's land between the trenches?, *Eur J Clin Invest* 2000; 30:566-569.

- [28] Stam, R., PTSD and stress sensitisation: a tale of brain and body. Part 2: animal models, *Neurosci Biobehav Rev* 2007; 31(4):530-57.
- [29] Vermetten, E. and de Loos, W., Medisch Onbegrepen Lichamelijk Klachten bij Veteranen; het Post-Deploymentsyndroom, diagnose en zorg in ontwikkeling, *Veteranenbundel*, pp. 51-63, 2004.



Chapter 9 – MUPS IN MILITARY SETTING: AN ORGANISATIONAL PERSPECTIVE

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9.1 INTRODUCTION

In the military it is common to presume that soldiers are able and motivated to contribute always at their best. This expectation, however, is not always met – frequently the lack of skills or abilities is referred to as a reason but more often than we like to admit, a poor functional condition or just a lack of motivation can be the reason of soldiers' failed or meagre performance. Similarly to all goal orientated establishments, a high performing workforce is the key variable for military organisations too having has a significant impact on the operational effectiveness of a military system. Adaptation to future complex environments within which NATO forces are operating requires to be manned with a healthy, high performing staff. The achievement of difficult goals in demanding environments needs not only skills and abilities, but also performers' good health and sustained efforts to implement their skills and abilities over time.

MUPS is expressed in spectrum of medically unexplainable but physically painful and distressing symptoms. The vague nature of “medically unexplained” [1] but objectively afflicting condition challenges military organisations impairing potentially the health and expected performance of service personnel. In the one hand, it is a medical concern because the missing definition makes the condition difficult to point and treat. In addition, there is always a risk, particularly with somatoform disorders, that medically unexplained physical complaints are just masking some serious disorder and contextual barriers (i.e., language or cultural) can cause a delayed or misdiagnosing [2]. Drawing a parallel with other stress-related or somatoform diseases, the relatively high importance of psychogenic etymology in onset of MUPS could be presumed. Studies exploring relations between psychological well-being or job satisfaction and physically manifesting symptoms serve as good example here. If people are unsatisfied with their jobs, residual effects of this dissatisfaction will affect the quality of life and health as well [3]. So, in the other hand it can be also a concern of leadership and related with soldiers' poor well-being or motivational deficits.

Integrating domains of health and functioning, a new holistic approach is recently introduced as Total Force Fitness paradigm. In their article Jonas et al. state that although major medical diseases require standard medical treatment, non-medical approaches may well prevent the progression of PTSD and developing of chronic pain. As first layers of foundation of total force fitness a risk reduction (prevention) and health (well-being) are named [4]. In the same volume Bates et al. describe a system model (Military Demand Resources model) that accounts for key interactions across the full range of demands and resources in predicting resilience and performance outcome and is based on the proposition that, similar to physical fitness, it is possible to identify and develop psychological fitness [5]. Research results show that when trajectories of PTSD symptomatology were explored through the deployment cycle – relative to other individuals, resilient individuals perceived fewer deployment hassles and reported, on average, less previous trauma, stress reactivity depression, alcohol use, and aggressive behaviours [6]. Military organisations that are successful with promoting psychological resilience (for exhaustive overview, see [7]) among their service personnel may be able to reduce MUPS-related treatment costs, prevent declined performance related to unreported symptoms as well as maintain and fortify moral in their units.

9.2 ORGANISATIONAL CONCERNS

Organisational concerns are divided into two broad categories – health-related and performance-related issues. Figure 9-1 is provided to map the adverse organisational effects related to MUPS in military environment. Both of those closely related categories can be addressed from the perspective of medical care and human resources management.

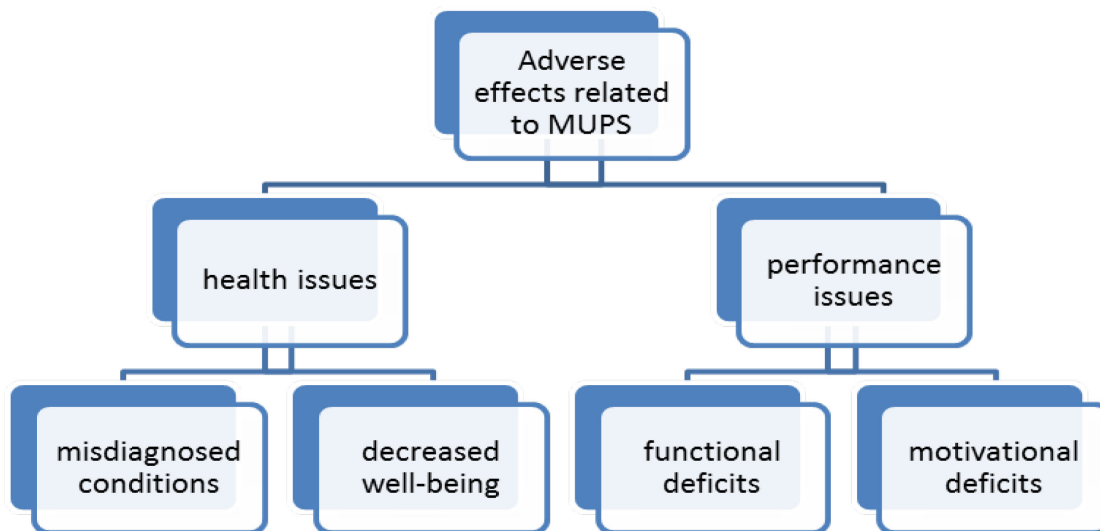


Figure 9-1: Adverse Organisational Effects Related to MUPS.

9.2.1 Health

Beside of financial expenses invested to medical treatment based on inaccurate diagnosis (and thus of no effect), consequences of false-positives and false-negatives conditions must be highlighted too. It is stated that all complaints are not necessarily symptoms, and perceptions of bodily irregularities are not necessarily complaints and suggested that from clinical perspective, it could be useful to differentiate between the conditions of benign everyday phenomena and cases what really need clinical attention [8]. Discussing the problem of false positives (diagnosis that mistakenly attribute disorder when it does not exist), Wakefield [9] has pointed out the fact that the symptom-based system at all has been developed in a way that fails to distinguish normal distress from disorder. Two of his suggestions how to distinguish between disorder and non-disorder are relevant to mention here – taking account the context of the symptoms (i.e., normal reactions to abnormal situations) and the power of meanings what can modify emotional responses (i.e., feeling of being entrapped or humiliated).

For some cases occupation or specific activity-related distress can elicit psychological symptoms. There are evidences, for example, that being tasked to ease the chaotic lives of other people has a negative influence to performer physical and mental health [10] and that the level of perceived stress is positively correlated with the level of unexplained medical symptoms [11]. Both of those findings may appear to be relevant also in military (deployment) environment. NATO is, and will be required to effectively operate in increasingly complex situations within both Article 5 and OOTW (e.g., Humanitarian Assistance/Disaster Relief missions). Deployment situations show the need for soldiers not only fighting an enemy but, for example, provide humanitarian assistance, build schools, hold warring tribes apart, help local population. These diverging tasks mean that soldiers have to be able to switch between roles. On the one hand a soldier must be able to fight and use force,

on the other hand they must be able to help, mediate and protect people [12]. Findings reveal that although troops are generally able to adapt with demands of their immediate environment, there are soldiers for whom the particular type of deployments are psychologically more difficult to endure [13].

One should also be aware of the problem of false negatives – not seeing the problem when it is actually there, and/or not being able to identify the right problem. As the military culture appears to be rather masculine, reporting physical symptoms may seem to be easier and less career damaging than reporting psychological symptoms. To a certain degree, a tendency toward false negative findings is suggested to be present also in general population due to substantial proportion of patients who prefer to interpret their physical symptoms as “medical” and not “psychological” [8]. MUPS, when unrecognized, may have a significant impact on the consultation load of physicians and lead to an increased utilization of medical care. Being trained to identify MUPS, health care providers could rule out somatic and psychiatric causes and avoid delayed return to work but also encourage patients to increase their activities and return to work [14].

Another important health issue is psychological well-being (or mental health state in general) which is shown to be related to job performance ratings [15]. Organisations should concern for employees mental health state, because it affects not only workers’ well-being but also organization productivity [3]. It is reported that stress and lack of well-being in the workplace cost around £25.9 billion per annum in terms of sickness absence, presenteeism and labour turnover [16]. Pronounced differences were reported between individuals having contrasting profiles of psychological well-being, with lower levels of both general and musculoskeletal symptoms among those with higher levels of psychological well-being [17]. This research is important also from the preventive point of view because the environmental mastery popped up as a substantial component of well-being. Authors proposed that higher cortisol release in individuals with lower psychological well-being may reflect anticipatory stress associated with doubts concerning one’s ability to handle or control the environment.

9.2.2 Performance

Severe MUPS is found to be associated with a high prevalence of depressive and anxiety disorders, distress, health anxiety and functional limitations as well as with prolonged and frequent sickness absence [14] representing a serious threat to any performance. Direct relationship between psychological and physical symptoms has been also found in study where extended shifts influence on workers’ health was explored [18]. From prevention perspective it is important to note that according to this research negative health effects can be alleviated by social support from various sources (supervisors, co-workers and family). The positive effect of supervisor support on workers mental health (as well as job satisfaction) is referred also in another study with recommendations that mental health can be enhanced by developing job satisfaction and conducting supervisor training program [3].

It is known that the characteristics of the work environment may be responsible for positive and negative effects on performance and on well-being of the performer [19] and a moderate level of stress can have positive effects on job satisfaction and organizational commitment while reducing turnover intent [20]. However, environmental stimuluses’ are experienced differently depending on the resources of a given individual [21], and if the level of stress is appraised as moderate is related with individual differences. It is shown also that perceived capability to cope with stress determines how a person appraises a stressful situation [22]. In the same vein, reviewing different theories of subjective well-being Diener [23] states that when a person is involved in an activity in which their skills and the challenge of the task are roughly equal, a pleasurable flow experience will result. But this equality, too, perceived as the challenge by one person can be perceived as a full stressor by another one. Challenge “stressors”, because they are appraised as having the potential to promote personal gain or growth, trigger an active or problem-solving style of coping. Threatening or hindering stressors, because they are

appraised as having the potential to harm personal growth or gain, trigger a passive or emotional style of coping [24]. Personality is related with coping under stress [22] and soldiers who perceive more situations as threatening are subject to an increased risk for developing stress-related symptoms [25].

Any stressor from environment does not automatically create the stress experienced by individual, but is influenced by the person's perceptions, past experiences, social support and individual differences [26]. Related to peculiarities of military environments it is relevant to refer to another study where the *Sick building syndrome*¹ was explored and strong correlations between several psychosocial variables and symptom-reporting was found [27]. Findings in general referred that the psychological working environment makes significant contribution to self-reported symptoms. Particularly under condition of low job control where job-related mood is negative and negative affectivity is high, employees report more somatic complaints when in their work environment.

In simplified way organisational HR challenges can be summed up in axes of *Functional condition* (High: well-functioning, Low: ill-functioning) and *Motivation to serve* (High: motivated, Low: unmotivated) resulting with four categories:

- Soldiers who function well and are motivated to serve;
- Soldiers who do not function well, but are motivated to serve;
- Soldiers who feel unmotivated and are in poor functional condition; and
- Soldiers who are functioning well but are unmotivated to serve for some reasons.

For illustration the Figure 9-2 is provided below.

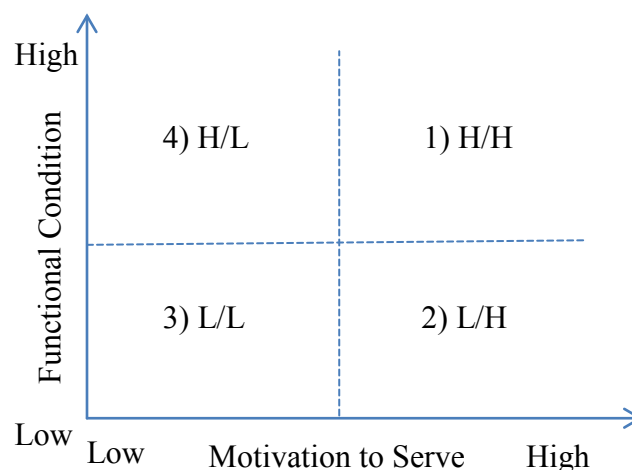


Figure 9-2: HR Challenges in Military Organisations.

Framed in this way, organisational HR challenge is to move individuals from L/L, H/L and L/H to H/H group. Based on where the potential root of problems is, different interventions could be needed. While medical

¹ Refer to a range of physiological, cognitive, psychological and neurological symptoms that typically worsen when employees are at work and diminish when they leave.

responsibility is to identify adequately L/L individuals but also L/H what is even more difficult because they can leave their symptoms (un-)wittingly unnoticed, leadership should consider how to motivate H/L to avoid attrition but also maintain the motivation in H/H group. Remaining unnoticed, the migration from H/H to H/L can happen (risk to leave service) where there is hypothetical risk to develop physical complaints and appear in L/L group (become treatment subjects).

9.3 CONCLUSION AND RECOMMENDATIONS

It is claimed that employees mental capital, defined as a metaphorical ‘bank account of the mind’, gets enhanced or depleted throughout the life course and well-trained leaders managing people by praise and reward and not by constant fault finding and supporting a less “long hours culture” is one potential way to deal with it [16]. Even the most sophisticated medical interventions are inefficient to increase soldiers’ motivation, and even the most skilful military leaders are not able to deal with functional impairments. It seems reasonable to assume that the best result dealing with MUPS in military organisations could be achieved by combining medical care and leadership efforts. In order to be effective, cases where the low motivation or job dissatisfaction can be the root of expressed complaints should be differentiated from cases where clinical attention is really needed.

Service members whose individual characteristics are matched to their task-environments may be better motivated for their assignments, have a potential to grow thorough challenging situations and recover faster from their professional exertions. A consideration of complex relationships between job characteristics and individual factors was recently supported by Chung-Yan and Butler [28]. They demonstrated that, not only did job complexity and proactive personality interact to predict work-related outcomes but they can also be both beneficial and detrimental depending on the level of the variables. Conclusion was that if work design and individual characteristics are not calibrated to match, job enrichment interventions intended to motivate workers might have the opposite effect and lead to an unmotivated workforce.

Similarly to other specific occupations, the military attracts individuals with particular vocational interests. However, field stories and historical writings hint that individuals holding military positions do not belong to an as homogeneous group of people as one could expect [29]. We should recognize that military assignments cover a wide spectrum of different types of jobs attracting people with a high variety of personal needs. It is said that stress is often in the mind of stressed [30]. For each individual there are environments which are less stressful, matching more with the characteristics of their personality. To make use of the versatility of jobs available in the contemporary Armed Forces, the health and performance of military manpower can be enhanced by using the benefits of the Person x Environment approach as a force multiplier in the common military practice.

9.4 REFERENCES

- [1] Kapfhammer, H-P., CS03-04 – Concept of somatoform disorder, European Psychiatry, kd. 26, nr Supplement 1, pp. 1777-1777, 2011.
- [2] Röhrich, F., Gudi, A. and Lewis-Fernandez R., Medically unexplained physical symptoms masking (cenesthopathic) schizophrenia: a case series, Journal Of Psychiatric Practice, kd. 16, nr 4, pp. 258-264, 2010.
- [3] Kanda, J., The Effects of Work-Related Variables on Mental Health of Employees in Manufactory, Journal of US-China Public Administration, kd. 8, nr 5, pp. 577-585, 2011.

- [4] Jonas, W.B., O'Connor, F.G., Deuster, P., Peck, J., Shake, C. and Frost, S.S., Why Total Force Fitness, *Military Medicine*, kd. 175 Supplement, nr 8, pp. 6-13, 2010.
- [5] Bates, M.J., Bowles, S., Hammermeister, J., Stokes, C., Pinder, E., Moore, M., Fritts, M., Vythilingam, M., Yosick, T., Rhodes, J., Myatt, C., Westphal, R., Fautua, D., Hammer, P. and Burbelo G., Psychological fitness: A military demand-resource model, *Military Medicine*, kd. 175 Supplement, nr 8, pp. 21-38, 2010.
- [6] Dickstein, B.D., Suvak, M., Litz, B.T. and Adler, A.B., Heterogeneity in the course of posttraumatic stress disorder: Trajectories of symptomatology, *Journal of Traumatic Stress*, kd. 23, nr 3, pp. 331-339, 2010.
- [7] Meredith, L.S., Sherbourne, C.D., Gailliot, S., Hansell, L., Ritschard, H.V., Parker, A.M. and Wrenn, G., Promoting psychological resilience in the U.S. military, Pittsburgh, PA. USA: RAND Corporation, 2011.
- [8] Hiller, W., Rief, W. and Brähler, E., Somatization in the population: from mild bodily misperceptions to disabling symptoms, *Social Psychiatry Psychiatric Epidemiology*, kd. 41, pp. 704-712, 2006.
- [9] Wakefield, J.C., Misdiagnosing normality: Psychiatry's failure to address the problem of false positive diagnoses of mental disorder in a changing professional environment, *Journal of Mental Health*, kd. 19, nr 4, pp. 337-351, 2010.
- [10] Vyas, L. and Luk, S., Frazzled care for social workers in Hong Kong: Job stress circumstances and consequences, *International Social Work*, kd. 54, nr 6, pp. 832-851, 2011.
- [11] Burton, T., Farley, D. and Rhea, A., Stress-induced somatization in spouses of deployed and nondeployed servicemen, *Journal of the American Academy of Nurse Practitioners*, kd. 21, pp. 332-339, 2009.
- [12] Broesder, W., Soldiers wielding swords and ploughshares, Leuven: W.Broesder, 2011.
- [13] Parmak, M., Should all soldiers be sensation seekers?, The role of personality, Leuven: M.Parmak, 2011.
- [14] Hoedeman, R., Krol, B., Blankenstein, A.H., Koopmans, P.C. and Groothoff, J.W., Sick-listed employees with severe medically unexplained physical symptoms: burden or routine for the occupational health physician? A cross sectional study, *BMC Health Services Research*, kd. 10, pp. 1-8, 2010.
- [15] Wright, T.A. and Cropanzano, R., Psychological Well-Being and Job Satisfaction as Predictors, *Journal of Occupational Health Psychology*, kd. 5, nr 1, pp. 84-94, 2000.
- [16] Cooper, C.L., Mental Capital and Well-Being, *Stress and Health*, kd. 26, pp. 1-2, 2010.
- [17] Lindfors, P. and Lundberg, U., Is low cortisol release an indicator of positive health?, *Stress and Health*, kd. 18, pp. 153-160, 2002.
- [18] Pisarski, A., Bohle, P. and Callan, V.J., Short Communication: Extended shifts in ambulance work: influences on health, *Stress and Health*, kd. 18, pp. 119-126, 2002.
- [19] Gaillard, A.W.K., Concentration, stress and performance, %1 Performance under stress, Hampshire GU, Ashgate Publishing, 2008, pp. 59-75.
- [20] Kavanagh, J., Stress and performance: A review of the literature and its applicability to the military, RAND Corporation, Pittsburgh, PA, USA, 2005.

- [21] Adler, A.B., Brett, T.L. and Bartone, P.T., The nature of peacekeeping stressors, %1 The psychology of the peacekeeper: Lessons from the field, Westport CT, Praeger, 2003, pp. 149-167.
- [22] Delahaij, R., Coping under acute stress: The role of person characteristics, Breda: Roos Delahaij, 2009.
- [23] Diener, E., Subjective Well-Being, Psychological Bulletin, kd. 95, nr 3, pp. 542-575, 1985.
- [24] Lepine, J.A., Podsakoff, N.P. and Lepine, M.A., A meta-analytic test of the challenge stressor – hindrance stressor framework: An explanation for inconsistent relationships among stressors and performance, Academy of Management Journal, kd. 48, nr 5, pp. 764-775, 2005.
- [25] Rademaker, A.R., Personality and adaptation to military trauma, Utrecht: Artur R. Rademaker, 2009.
- [26] Hellriegel, D. and Slocum, J.W.J., Managing individual stress, %1 Organisational behaviour, Mason, Ohio, USA, South-Western, 2004, pp. 166-189.
- [27] Kinman, G. and Griffi, M., Psychosocial factors and gender as predictors of symptoms associated with sick building syndrome, Stress and Health, kd. 24, pp. 165-171, 2008.
- [28] Chung-Yan, G.A. and Butler, A.M., Proactive Personality in the Context of Job Complexity, Canadian Journal of Behavioural Science, kd. 43, nr 4, pp. 279-286, 2011.
- [29] Russell, M., Personality styles of effective soldiers, Military Review, kd. 80, pp. 69-73, 2000.
- [30] Krueger, G.P., Contemporary and future battlefields: Soldier stresses and performance, %1 Performance under stress, Hampshire, GU, Ashgate Publishing, 2008, pp. 19-44.



Chapter 10 – MULTI-DISCIPLINARY TREATMENT OF PERSISTENT SYMPTOMS AFTER GULF WAR SERVICE

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10.1 PERSISTENT POST-DEPLOYMENT PHYSICAL SYMPTOMS: THE NEED FOR INNOVATIVE HEALTH CARE

Service members returning from military deployments often describe disabling symptoms and syndromes [1]. After the Persian Gulf War, concerns of war-related illness have even extended to spouses and children of those deployed [2]. Current evidence suggests that individuals seeking care for Gulf War related health issues suffer from a variety of illnesses, some related and some unrelated to military deployment [3]. Others seeking health care act out of concern over deployment-related exposures, while reporting few physical symptoms at evaluation [3]. One important care-seeking group describes symptom constellations for which no consensus exists regarding underlying disease mechanism. Many of these symptom clusters or syndromes are ultimately given labels based on description (e.g., chronic fatigue syndrome) or putative etiology (e.g., multiple chemical sensitivity) [4].

Frequently, an individual's medical diagnoses fail to sufficiently describe the magnitude, multi-faceted nature, treatment, and prognosis of their health problems. Comprehensive biomedical evaluation may contribute little to understanding the cause of a person's symptoms and associated functional impairment, to choosing an effective treatment, or to delineating the prognosis. For example, a diagnosis of musculoskeletal back pain is often used to describe uncomplicated back pain of recent onset. The same diagnosis may also describe persistent back pain in someone who is overweight, has multiple medical problems or physical symptoms of unclear etiology, lacks psychosocial support, and has pre-existing functional impairment. Under these two circumstances, the cause, treatment, and prognosis of symptoms and related functional impairment are likely to differ markedly, even though the diagnosis is the same. For the second person, efforts to modify physical and psychosocial factors contributing to impairment are essential (Figure 10-1).

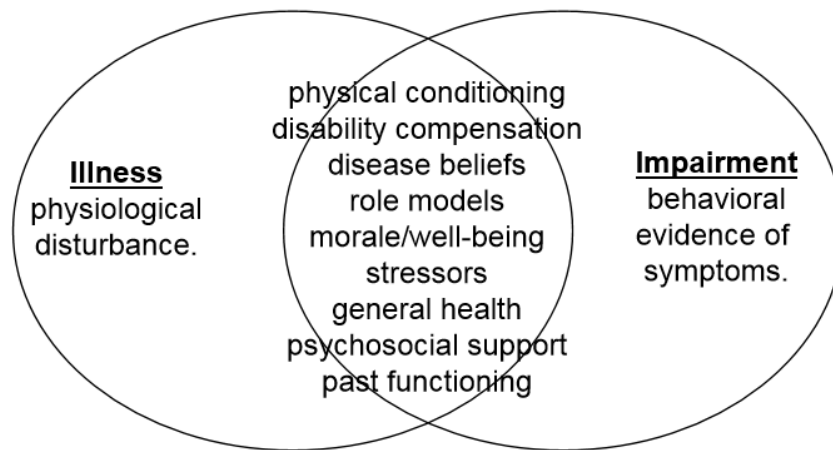


Figure 10-1: The Overlap Between Illness and Impairment Varies Widely Between Individuals with the Same Severity of Illness. A host of modifiable physical and psychosocial factors can reduce or amplify illness-related impairment.

Service-members, friends, family, medical providers, the military, and the general public seek answers regarding the causes of persistent physical symptoms occurring after the Gulf War. Frequently, their concerns focus on unusual environmental exposures or infectious agents for which it may take years, even decades, for sound scientific studies to address. Indeed, the problems associated with establishing cause and effect from observational studies may render definitive determinations elusive if not impossible. When cause-effect relationships can be established with confidence, studies of treatment will also take time. Adequate knowledge, however, currently exists to offer affected individuals a comprehensive, multi-disciplinary intervention aimed at helping them to take control of their symptoms, improve the quality of their lives, and reduce the extent to which symptoms impair their functioning and ability to work. Similar interventions with similar objectives have been implemented successfully for many patients with a wide range of chronic pain problems [5]. A recent meta-analysis of 65 controlled studies of multi-disciplinary interventions for chronic pain patients found that these programs are associated with greater return to work, lasting improvements in pain and mood, and decreases in health care utilization [6].

Successful detection and treatment is important to the Department of Defense and to other employers whose workers may experience persistent work-related symptoms or work-related injuries. Rather than limit care to exhaustive biomedical diagnostic evaluations or implement invasive interventions or treatments targeting a narrow set of symptoms, a comprehensive approach is necessary to reduce chronic disability among those with persistent symptoms.

The purpose of this chapter is to:

- 1) Present the history of the Gulf War Health Center, Walter Reed Army Medical Center's program for evaluating and treating Gulf War related health concerns;
- 2) Describe the Gulf War Health Center's Specialized Care Program (SCP), an intensive outpatient program providing intensive treatment to individuals with persistent, disabling Gulf War related physical symptoms that employs methods used in chronic pain centers internationally; and
- 3) Propose the Deployment Medicine Treatment Center, an extension of the SCP approach to veterans from all future deployments.

10.2 BRIEF HISTORY OF THE GULF WAR HEALTH CENTER'S SPECIALIZED CARE PROGRAM

On August 2, 1990, Iraq launched a surprise invasion of the oil rich neighboring nation of Kuwait. This marked the beginning of a rapid overseas deployment of U.S. and other armed forces. Eventually nearly 697,000 U.S. troops served in the Persian Gulf. Six weeks of U.S. and coalition bombing of Iraq commenced on January 16, 1991 and was followed by a 4-day ground war. Troops faced a range of environmental exposures during the conflict and its aftermath, including:

- Smoke from burned excrement;
- Oil well fires;
- Diesel exhaust;
- Toxic paints;
- Pesticides;
- Sand and other particulates;
- Depleted uranium;
- Infectious agents;
- Chemoprophylactic agents;
- Immunizations; and
- Chemical/biological warfare agents [7], [8].

Subsequent reports suggested that some veterans and their families were experiencing persistent symptoms since returning from the Persian Gulf. Some suggested the emergence of a specific syndrome involving fatigue, aches, pains, rashes, headaches, and dizziness, and concerns were raised regarding congenital anomalies among family members [9]. To investigate further, the Veterans Health Administration and the Department of Defense (DoD) initiated registries of symptomatic Gulf War veterans. In June, 1994 DoD initiated the Comprehensive Clinical Evaluation Program (CCEP), a centrally coordinated and DoD-wide health care program designed to provide rapid, accessible, and expedited clinical assessments for Gulf War veterans with Gulf War related health concerns [10]. The Gulf War Health Center was initiated at Walter Reed Army Medical Center to coordinate CCEP activities among the 23 Army, Navy, and Air Force medical facilities in the Northeast portion of the U.S., to perform tertiary care CCEP evaluations for the region, and to complete primary CCEP assessments for those in the immediate Walter Reed vicinity [10]. CCEP findings were subsequently presented to the Institute of Medicine in a series of reports.

Particular attention focused on a sub-set of about 10 – 15 % (the fraction has fallen over time) of CCEP patients with incompletely explained physical symptoms. In December of 1994, DoD decided that a multi-disciplinary treatment program was needed to help Gulf War veterans with persistent physical symptoms, and in March of 1995 the SCP treated its first patients at the Gulf War Health Center. In May, 1995 the Office of the Assistant Secretary of Defense for Health Affairs (Clinical Services) and Walter Reed Army Medical Center convened a panel of civilian and military academic experts on the multi-disciplinary treatment of individuals with chronic pain, and SP methods were reviewed and refined. Currently, the SCP is the only treatment program of which the authors are aware that offers this multi-disciplinary chronic pain treatment approach for those with persistent Gulf War related physical symptoms.

- 5) Obtain a consistent, primary care-based follow-up plan;
- 6) Address psychosocial contributors to symptom-based disability;
- 7) Improve relationships with health care providers and significant others;
- 8) Reduce excessive and potentially harmful use of the health care system; initiate an program of gradual, paced physical activation that takes into account an individual's unique musculoskeletal limitations; and
- 9) Improve understanding of the known health consequences of Gulf War service.

The SCP emphasizes comprehensive, multi-disciplinary collaboration aimed at reducing persistent symptoms and associated functional impairment. Family involvement is extremely important, and extra efforts are taken to maximize their collaboration with the health care team (e.g., paid travel, long-distance telephone assessment). SCP patients work closely with an internist and a health psychologist. Other members of the health care team include a:

- Psychiatrist;
- Occupational therapist;
- Physical therapist;
- Fitness trainer;
- Wellness coordinator;
- Clinical social worker; and
- Nutritionist.

A range of medical specialists such as occupational medicine, preventive medicine, infectious disease, and others are available for consultation depending on a given patient's estimated medical needs.

The SCP staff can be divided conceptually into three overlapping teams, each oriented to an aspect of the patient's health and rehabilitation needs: the medical team, the physical team, and the psychosocial team (Figure 10-3). The medical team is primarily concerned with evaluating each patient for the presence and severity of diseases and to make certain that patients' are medically appropriate for the SCP. Given the SCP emphasis on chronic symptoms, it is imperative that patients are not suffering from acute or unstable illnesses requiring rapid biomedical intervention. Medical staff thoroughly explain patients' medical status and review completed medical testing with them. The physical team helps patients initiate an exercise program individualized to their unique musculoskeletal and medical limitations and exercise history. Exercise is the cornerstone of treatment for many patients. It allows them to develop a sense of stamina and control over their health concerns and to minimize the impact of symptoms on their functioning. The psychosocial team offers various kinds of support during the treatment process. Typically, bothersome symptoms wear patients down, reduce the quality of their relationships, and diminish morale and mood. Similarly, depressed patients may dwell more on their symptoms, experience more symptoms, and lack energy to function through their symptoms.

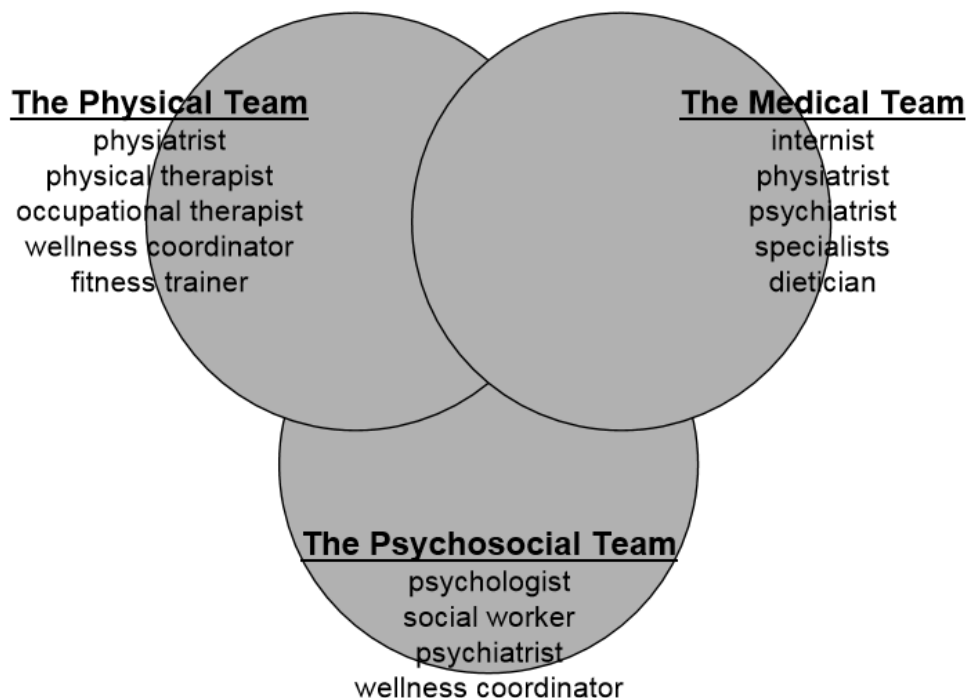


Figure 10-3: The Specialized Care Program is Organized Around 3 Conceptual Rehabilitative Teams with Overlapping Objectives and Staffing.

Psychosocial team staff offer various types of support, therapy, and counseling as patients request and need it. The psychosocial team is also responsible for coordinating the educational portion of the SCP. Participatory seminars (see Table 10-1) encourage education and discussion designed to help patients improve their use of the health care and disability compensation systems, communications with providers, their understanding of persistent symptoms, and their knowledge of what is currently known about Gulf War health issues. Anticipating obstacles to aftercare is also an important task of the psychosocial team.

Table 10-1: Common Seminar Topics Given for Participants in the Specialized Care Program.

- Orientation and overview.
- Illness series:
 - Illness and Impairment;
 - Acute and chronic illness;
 - Illness and emotions; and
 - Gulf War exposures.
- Users' Guide to:
 - Your doctor;
 - Prescription meds;
 - Disability compensation; and
 - Medical labs and tests.

- Learning about your body:
 - Activity and morale;
 - The nervous system;
 - Impact of diet on symptoms; and
 - Review of common symptoms.
- Strategies for coping with illness:
 - Overcome illness flares;
 - P a c i n g ;
 - Sleep hygiene;
 - Goal-setting;
 - Overcoming inactivity;
 - Autonomic Training;
 - Problem-solving; and
 - Communication skills.

10.5 THE ROLES OF PROGRAM PROVIDERS – THE GENERAL INTERNIST

The general internist and the health psychologist lead the SCP's health care team, working together as co-attendees. The general internist leads the medical assessment and decides when medical specialty consultation is necessary. The general internist is responsible for determining whether unresolved medical issues or active medical problems might preclude a candidate from participating in the SCP. Perhaps most importantly, the internist carefully reviews the complete medical evaluation with the patient. Each medical test is collaboratively reviewed with the patient and their questions carefully addressed. Many patients have questions about Gulf War exposures, and these are also addressed according to the best available scientific evidence. Our experience is that most patients have had exhaustive medical evaluations and often misunderstand the meaning of their many test results.

Frequently, they do not know the results of important medical tests or that a particular test was performed. Sometimes patients feel that certain medical tests need to be performed and specifically request them. The internist assesses the patient's understanding of their medical testing, works with them to improve that understanding, and collaborates with the patient and the health care team to determine the utility of new or repeat tests. The added information obtained from medical testing is weighed against drawbacks. Common drawbacks are the increased likelihood of false positives resulting from repeat or marginally indicated testing and the tendency for continued testing to place patients in a passive 'watch and wait for a diagnosis and cure' approach to wellness. The emphasis of the SCP is treatment rather than extensive medical evaluation, and a conservative approach is taken to ordering further medical testing.

The internist attends the Medical Systems Review Group, a daily meeting of SCP patients, the internist, and the health psychologist. In the Medical Systems Review Group, patients recount their symptoms, exposures, completed medical tests, diagnoses, and treatments in detail. Patients describe the longitudinal course of their symptoms. Most patients have many symptoms without an easily identifiable pattern, and this often confuses providers in the context of a brief office visit. The Medical Systems Review Group provides patients and providers a less pressured forum for making sense of these complex symptoms presentations.

10.5.1 The Health Psychologist

As previously mentioned, the health psychologist and the internist serve as co-attendees on the health care team. Many patients are particularly defensive regarding psychological labeling and resist or refuse meetings with a psychologist. Often, doctors have told patients or implied to them that their symptoms were not “real” or are “in your head”. During the initial phases of the program, it is essential to validate patients’ concerns. Simultaneously, patients must be taught the utility of psychologists for those with persistent symptoms. Impairment can be viewed as a behavioral manifestation of illness. Reducing such ‘impairment behaviors’ is a critical role of the health psychologist.

The psychologist completes the psychosocial assessment, coordinates the psychosocial treatment plan, rounds daily with the internist, attends the Medical Systems Group, and tracks patient progress in activation efforts such as exercise. A careful psychosocial assessment is done at the start of the program. Symptoms and signs of depression are assessed, since it can reduce functioning, motivation, and tolerance of bothersome physical symptoms. Post-traumatic stress disorder, the emotional sequela of severe psychological trauma is assessed since patients are typically veterans of the Gulf War and expected to be at elevated risk for this disorder. The psychosocial assessment includes a careful look at the family, both the current family (or other key support systems) and the family of origin. For example, many patients inadvertently learn problematic responses to illness from others they know with chronic illness who then serve as a model for them. ‘Disability models’ can have a potent influence on how people with symptoms respond to those symptoms. Similarly, overly solicitous friends, co-workers, or families may unintentionally reward functional impairment by relieving the patient of key undesirable responsibilities. In the latter instance, the psychologist can help these all parties understand the impact of their behavior. The psychologist also addresses patients’ behavioral responses to treatment. For example, patients track their own progress in physical and occupational therapy by graphing the number of repetitions of key exercises. The psychologist tracks patients’ progress using these graphs and looks for ways to create incentives and reinforce gains in functioning.

10.5.2 Medical Specialists

The SCP, in conjunction with the Gulf War Health Center has access to a range of medical specialists as the internist and psychologist deem necessary. A list of specialists commonly consulted includes:

- Rheumatology;
- Neurology;
- Occupational medicine;
- Infectious disease;
- Cardiology;
- Pulmonology;
- Orthopedics; and
- Psychiatry.

Specialists also present seminars to SCP patients on common symptoms. For example, a neurologist may talk to the patients about headaches.

10.5.3 The Physiatrist

The physiatrist heads the SCP's physical team. The physiatrist is responsible for performing a thorough musculoskeletal evaluation for each program patient and formulating the physical therapy treatment plan in collaboration with the physical therapist. A thorough musculoskeletal examination is imperative to insure that physical training is properly individualized to patients' unique physical limitations and abilities. As already noted, a conservative approach is taken with regard to medical testing during the program. Common reasons for new testing are acute or classic symptomatology or objective examination findings that are new or previously unrecognized.

10.5.4 The Physical Therapist

The physical therapist works in close collaboration with the physiatrist and the fitness trainer and is a key member of the physical rehabilitation team. The physical therapist corroborates the physiatrist's musculoskeletal examination, supervises the fitness trainer, and, implements the physical rehabilitation treatment plan in conjunction with the fitness trainer. The physical therapist designs and implements physical therapy circuit training. While all patients use the same circuit, the stations of the circuit are individualized according to each person's unique physical therapy needs. The physical therapist is responsible for prescribing, monitoring, and helping patients graph their progress in the physical therapy circuit. Patient's progress on the circuit offers useful information regarding their progress toward taking active control of their health, an important objective of the SCP.

10.5.5 The Occupational Therapist

The occupational therapist, also a key member of the physical rehabilitation team, assesses the work functioning of each patient and develops an individualized approach to rehabilitation of identified deficits. The occupational therapist supervises this work conditioning program. The program, similar to the physical therapy program, involves the use of circuit training. The occupational therapist prescribes the components of the occupational therapy circuit as indicated. As in physical therapy, the extent that patients take an active role in the occupational rehabilitation process provides useful information regarding their movement from a passive approach to their health issues to a more active one.

10.5.6 The Fitness Trainer

The fitness trainer is, in effect, an extension of the physical therapist and has the responsibility of safely implementing individualized programs. Emphasis is on gradually increasing physical demands within the ability and conditioning of each patient. Physical conditioning that progresses too rapidly can exacerbate physical symptoms and cause patients to question prematurely the utility of exercise as a useful treatment. Another pitfall is to underestimate patients' exercise capacity. Most SCP patients are currently in the military and already exercise regularly. Patients may become disillusioned with this portion of the intervention if they feel the amount of exercise is trivial compared to their usual regimen.

10.5.7 The Clinical Social Worker

The social worker assists in the arrangement of primary care follow-up, assesses patients' social and occupational circumstances, provides them information on military and civilian services potentially helpful to them, and helps to coordinate with patients' military units. Primary care follow-up is arguably the most important SCP task. Patients have many physical symptoms and diagnoses. Centralizing their care around a primary care provider ensures that one provider coordinates the overall health care plan and talks with

participating specialists. In the absence of a primary care provider, several specialists may treat the patient without any knowledge of what the others are doing, leading to patient and provider confusion. Assessment of patients' social situation entails learning about the quality of supportive relationships from the patient. Given the patient's permission, family, partners, or friends are involved directly in the program. Since patients are referred from all over the world, this may require the use of conference telephone calls or other methods coordinated by the clinical social worker.

10.5.8 The Wellness Coordinator

The wellness coordinator is the provider responsible for coordinating and implementing strategies of care such as art therapy, recreation therapy, biofeedback, autonomic response ('relaxation') training, and other 'mind-body' or lifestyle modalities. Most patients are unaware of the many available alternative modalities and tend to underestimate the relief they can obtain from their use. The wellness coordinator arranges sessions in which patients can practice relaxation techniques, biofeedback, problem-solving, and other modalities to ensure they can perform them with confidence.

10.5.9 The Nutritionist

Many patients are chronically deactivated due to the impact of persistent and bothersome physical symptoms. For some, deactivation leads to weight gain. Weight gain can exacerbate symptoms and lead to a sedentary lifestyle and passive mindset. A nutritionist sees each SCP patient and assesses the impact of diet on their health. The nutritionist advises patients on the impact of diet on health.

10.6 EVOLUTION OF EACH CYCLE OVER TIME

Each week of an SCP cycle has a slightly different emphasis. The first week emphasizes medical reassessment and trust and rapport-building between staff and patients. Many patients enter the program concerned that a conspiracy may exist aiming to invalidate the physical reality of their health concerns.

Other patients feel that providers have minimized their concerns, blamed them for their problems, or suggested their symptoms are psychological. In the SCP, patients' health concerns are repeatedly validated so as to reduce mistrust and enhance provider-patient treatment collaboration. By week two, patients are feeling more comfortable discussing the ways their physical symptoms limit their lives and cause them emotional discomfort. Week three emphasizes behavioral coping, goal setting, and discharge planning.

Table 10-2 displays the patient schedule for a typical SCP day. The day begins with individualized physical training followed by shower and breakfast. After breakfast, patients meet together with one or more of the staff for the morning meeting and participatory seminar. Patients can use this forum to address any pressing issues. The rest of the morning and the early part of the afternoon are scheduled with various providers according to each patient's treatment needs. The afternoon session closes with Medical Systems Review group followed by an hour with the wellness coordinator for practicing wellness strategies such as relaxation techniques.

**Table 10-2: An Example of Patient's Daily Schedule
in the Specialized Care Program.**

0600	Individualized Fitness Training
0700	Hygiene and Breakfast
0800	Medical System Review Group
0900	Occupational Therapy Individual Therapy / Physical Therapy Physician
1130	Team Rounds
1200	Lunch
1300	Wellness Activities / Medical Tests / PRN / Physical Therapy Nutrition Therapy
1500	Participatory Seminar
1630	End of Day

Morning and afternoon is broken by rounds and lunch. The basic purpose of rounds is to develop patients' treatment plans, to track patient progress, and to keep the multi-disciplinary staff in tune with what one another are doing for each patients. A multi-disciplinary program can undermine itself if providers from different disciplines do not respect each other's' clinical input. Most days, rounds last 30 minutes and entail brief 'housekeeping' visits between staff and patients, followed by staff treatment planning and coordination. Once weekly, rounds last for an hour without patient participation.

10.7 A PATIENT EXAMPLE

Sergeant L is a 36-year old active duty Army woman with 10 years' time in service. She described persistent symptoms and extreme worry that she was suffering from a serious undiagnosed medical condition. Among her symptoms were cyclic bouts of weight gain and self-reported vertical growth, itchy scalp and mucous membranes, sores in the mouth, rashes on areas exposed to air, shooting back and rib pains, excessive hair growth on her legs, gastrointestinal problems, shortness of breath, intermittent numbness, and frequent headaches. SGT L's descriptions of her symptoms were often detailed and belied her concerns about an undiagnosed illness. She described stiffness with inactivity as "rigor mortis" and told of her ribs being "pushed out by my heart." She also talked of "blood rushing to my head at the same time my stomach swells up." Additionally, SGT and Mr. L noticed their two children born after the Gulf were oversized and lethargic compared to their other two.

Review of the SGT L's health record showed she tended to use medical care regularly (8 – 16 visits per year prior to the Gulf, 25 visits in the 9 months prior to deployment in 1990, 15 – 20 visits per year subsequent to the Gulf, and 53 CCEP-related visits in 1995). Her CCEP work-up was extensive, including 14 specialist consultations and over 100 diagnostic tests. None of the tests were clearly abnormal, though many were equivocal. On completion of the CCEP, SGT L was diagnosed with fibromyalgia, costochondritis, recurrent low back pain, mild obesity, anxiety attacks, lentigo simplex, and idiopathic fatigue. SGT and Mr. L were not particularly reassured by the findings, and she often pressed for more tests. Once, Mr. L asked the doctor, "why are you ordering more tests, if you really think there is nothing to worry about?" The SCP team felt that SGT L had persistent symptoms that, in spite of her many diagnoses, offered an incomplete medical explanation for her symptoms. She was given a spot in the SCP, and she accepted.

On medical reassessment at the start of SCP, the general internist found no objective signs or classic symptom constellations requiring of further medical testing. The internist found SGT L was concerned that her weight gain and perceived height increase was a sign of acromegaly. SGT L also thought she might have porphyria, because urinary porphobilinogens done during the CCEP had been mildly elevated at 2.8 (normal was recorded on the lab slip as 0 – 2.0). The health psychologist noted that several maladaptive beliefs were obstacles to SGT L's recovery from symptoms:

- She was mistrustful of the military, believing that the government was hiding secrets about veterans' illnesses, causing her to become confrontational with the military providers trying to assist her;*
- She believed that any physical activity would exacerbate her illness, so she was avoiding strenuous activities including important household chores and acts of interpersonal closeness such as lifting her children; and*
- She believed that her illness might be infectious, causing her to avoid intimacy with her husband and close contact with her children such as meal preparation.*

The physiatrist and physical therapist noted that SGT L was de-conditioned and overweight as a consequence of chronic, symptom-induced inactivity. The social worker noted that Mr. L was frightened about SGT L's illness and was resentful of what he thought was a lackadaisical response of the military health care system to her problems and systematic attempts by military providers to minimize her illness and blame it on psychological factors.

At the SCP treatment planning conference held after initial clinical assessments were completed, several collaborative decisions were made. At first, the internist suggested that we order growth hormone levels to investigate the unlikely diagnosis of acromegaly and some other porphyrin levels to investigate for porphyria. The psychologist urged that we consider a conservative approach, since ordering the test might strengthen SGT L's improbable belief that these diagnoses were present. The internist agreed and noted further that since these diagnoses were unlikely on clinical grounds, any positive tests would probably be false and misleading. Instead, the team decided to consult an endocrinologist. The physiatrist and physical therapist concurred that she could exercise without an unacceptable risk of injury. They urged that her fitness program progress slowly so as to introduce activity but avoid exacerbation of fatigue and other physical symptoms from new use of de-conditioned muscles. The psychologist agreed, since an exacerbation of symptoms after exercise would strengthen SGT L's current belief that activity was harmful and decrease the probability she would continue to exercise on her own. The fitness trainer confirmed that she currently ran 3 miles and did push-ups and sit-ups once weekly after which she was fatigued, symptomatic, and disabled for a day or two. The social worker suggested we invite Mr. L to participate in SCP with SGT L, otherwise any gains during SCP might be rapidly undone when the two were reunited at home.

Mr. L agreed to bring their 4 children and join SGT L at the guest house on the Walter Reed post.

The social worker helped them arrange for local child care so Mr. L would be able to attend SCP activities. During participatory seminars, the couple learned that physical symptoms commonly remain unexplained after careful medical evaluation; that treatable or progressive medical diseases were unlikely after such an extensive and negative medical evaluation; that the absence of a clear diagnosis did not mean that symptoms are "psychogenic"; and that invasive medical testing or noxious medications were more likely to cause harm than benefit. They learned how to prepare to see their doctor so as to make best use of the doctor's brief presence each visit. The fitness trainer helped SGT L develop a graph showing her physical activity goals during and after SCP. Mr. L thought her goals were too easy; he felt sure she already got more exercise than that.

The endocrinologist met with the internist, psychologist, and SGT and Mr. L, explaining that acromegaly would not cause new growth at her age because epiphyseal closure had occurred. The endocrinologist showed them pictures of the characteristics of acromegaly, and they were able to appreciate that she did not look like someone with acromegaly. The endocrinologist told the couple that porphyria is unlikely unless urinary porphyrins are elevated several-fold. The endocrinologist explained to the team and the L's that laboratory norms were based only on a statistical bell curve. SGT L had a value that was relatively high compared to the general population, but not nearly high enough to have porphyria. They reluctantly accepted this explanation, and the internist agreed to copy some pages from a medicine text for their perusal. During fitness training, SGT L appeared to want to show she was motivated by initial vigorous attempts at exercise. Unfortunately, she became symptomatic and staff had to remind her to pace herself and stay within her goals. Over time, she was able to see gradual physical progress on her daily graphs and connected this with an improving sense of well-being.

At first, the Ls openly questioned what use a psychologist could be to them. A breakthrough occurred during the second week, however, when SGT and Mr. L cried openly about their concern that a chronic infection might be the source of her symptoms. Together they lamented the loss of the closeness they had before the fear of spreading infection robbed them of sexual intimacy. During a subsequent communication skills class, Mr. L realized that he often misinterpreted her symptom-related irritability as anger toward him. SGT L learned that her reluctance to complain about her symptoms often left him unsure as to the source of her emotions. Gradually, the Ls realized the psychologist was not there to label them, but to help them deal with the impact of SGT L's symptoms.

After 3 weeks of SCP, SGT L's morale was much improved and she left motivated to continue her activation program. She and Mr. L said they were grateful to the SCP staff for giving them new options besides waiting for doctors to come up with a diagnosis. The social worker and internist had helped them to arrange a primary care provider at her post. At six month follow-up, SGT L was still exercising and had passed the physical training test for the first time in 2 years. She noted her symptoms were decreased though still present, and she felt better able to function on the job and at home during symptomatic periods. Her primary care doctor was moving to a new duty station, so our social worker helped her to arrange a new provider to coordinate her care. Mr. L noted that they were sleeping in the same bed now, and for the first time in years, the L's were optimistic about their sexual relationship. At one year follow-up, SGT L remained on full active duty.

10.8 PROPOSAL FOR THE FUTURE – THE DEPLOYMENT MEDICINE TREATMENT CENTER

History suggests that the Persian Gulf War is just one of many conflicts leading to the occurrence of persistent, unexplained symptoms or syndromes [1]. We live in an age in which people scrutinize their health and the health implications of the workplace to an unprecedented degree [11]. An organization routinely providing health care for people deploying to unpredictable, traumatic, and potentially toxic environments must prepare to implement coordinated, multi-disciplinary medical evaluations for those requesting care on their return. Likewise, an analogue to the SCP is needed to provide timely, innovative, and effective health care to those with persistent post-deployment physical symptoms.

In response to these needs, we propose the Deployment Medicine Treatment Center, an institutionalized version of the Gulf War Health Center open to any eligible beneficiary with post-deployment health concerns. Currently, the Department of Defense is constructing a pre-deployment and post-deployment medical surveillance program. Surveillance efforts can be used to identify groups at particular risk of post-deployment health issues and to identify those with health care needs. Once those with needs are identified, there should be one or more

Deployment Medicine Treatment Centers available for the provision of specialized post-deployment medical care.

Deployment Medicine Treatment Centers may even have specific utility during periods of infrequent deployment. Primary care research suggests that 25 – 40 % of patients present with physical symptoms that remain incompletely explained after careful medical assessment. Four Clinical research has consistently suggested that pain patients derive lasting medical and occupational benefits from multi-disciplinary interventions like SCP. During peacetime, Deployment Medicine Treatment Centers might play a critical role providing intensive, multi-disciplinary treatment for patients using extensive services for persistent, incompletely explained physical symptoms. This training mission is analogous to the surgeon providing peacetime care to civilian trauma victims, developing and maintaining skills necessary during war in the process. By helping high utilizers of hospital-based care, peacetime Deployment Medicine Treatment Centers might play a critical ‘demand management’ role during a time when military health care is emphasizing managed care and resource utilization review.

10.9 ACKNOWLEDGEMENT

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10.10 REFERENCES

- [1] Hyams, K.C., Wignall, F.S. and Roswell, R., War syndromes and their evaluation: from the U.S. Civil War to the Persian Gulf War, *Annals of Internal Medicine* 1996; 125(5):398-405.
- [2] Horton, R., Persian Gulf syndrome puzzle, *Lancet* 1994; 343:1150-1.
- [3] Comprehensive Clinical Evaluation Program for Gulf War veterans: report on 18,598 patients, Washington, DC, USA: Department of Defense, 1996.
- [4] Kroenke, K., Symptoms in the Comprehensive Clinical Evaluation Program: Similarities and differences compared to the general population in the United States, Meeting of the Institute of Medicine Committee to Review the Health Consequences of Service during the Persian Gulf War, Washington, DC, USA; 1996.
- [5] Loeser, J.D. and Egan, K.J., editors, *Managing the chronic pain patient: Theory and practice at the University of Washington Multidisciplinary Pain Center*, New York, NY, USA, Raven Press, 1989.
- [6] Flor, H., Fydrich, T. and Turk, D.C., Efficacy of multidisciplinary pain treatment centers: a meta-analytic review, *Pain* 1992; 49(2):221-30.
- [7] Institute of Medicine Committee to review the health consequences of service during the Persian Gulf War: Health consequences of service during the Persian Gulf War: recommendations for research and information systems, Washington, DC, USA, National Academy Press, 1996.
- [8] National Institutes of Health Technology Assessment Workshop Panel, The Persian Gulf experience and health, *JAMA* 1994; 272:391-6.
- [9] Brown, D., Diagnosis unknown: Gulf War syndrome, *Washington Post*, July 24, 1994.

- [10] Roy, M.J., Chung, R.C.Y., Huntley, D.E. and Blanck, R.R., Evaluating the symptoms of Persian Gulf War veterans, *Federal Practitioner* 1994; 11(10): 13-22.
- [11] Barsky, A.J., *Worried sick: our troubled quest for wellness*, Boston, MA, USA, Little, Brown, 1988.



Chapter 11 – SUMMARY AND FUTURE DIRECTIONS

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11.1 SUMMARY

The somatic consequences of exposure to the threat and horror of war have been documented across the millennium. The continued emergence of post-deployment syndromes has continued to dominate the discussions about the veterans of recent wars such as the Gulf War, the Vietnam War and the most recent Middle East conflicts. A longstanding issue which has never been resolved in psychiatry is the extent to which somatic distress is a distinct but inescapable dimension of psychiatric disorder [1]. One of the difficulties is that different diagnostic categories depend upon symptoms being able to separate disorders.

In Chapter 2, the different conceptual approaches has been reviewed which have been taken in the past to explore the nature of post-deployment syndromes and propose a method of approaching the emerging data from the studies conducted of veterans from the most recent conflicts in Iraq and Afghanistan.

Chapter 3 discussed allostatic load; this refers to the consequences of sustained or repeated action by physiological systems in order to deal with either or both physical and/or psychological stress. In turn, continuous wear and tear across these multiple physiological systems contributes to overall health risk. By measuring an individual's allostatic load, it is possible to estimate not only their current health status but also the probability of future morbidity or mortality.

An increasing body of evidence demonstrates how the increased allostatic load associated with PTSD is associated with a significant body of physical morbidity in the form of chronic musculoskeletal pain, hypertension, hyperlipidaemia, obesity and cardiovascular disease. Chapter 4 discussed the intertwined physical and psychological consequences, psychosomatic syndromes, hypertension, hyperlipidaemia, obesity, coronary heart disease, as well as clinical treatment implications. This emphasizes that PTSD is not simply a psychosocial disorder, but one underpinned by a major neurobiological disruption.

Chapter 5 deals with a number of considerations for researchers and clinicians when assessing suspected concussion/mTBI in military personnel. The issues discussed in this review are highly relevant to health care professionals working with individuals returning from deployment. Considerations for clinical management of those presenting with concerns related to concussion/mTBI are proposed.

The lack of specificity of the symptoms of the different disorders used to describe widespread musculoskeletal pain may be explained by their shared aetiology, including neural sensitisation and alterations of the HPA-axis due to stress. This is addressed in Chapter 6. Fear avoidance is a central stress, related perceptual characteristic and behavioural dimension in these disorders. Treatment depends on thorough assessment, including psychiatric diagnosis, avoiding simplistic attributions and implementing evidence-based treatments that are well-documented.

Explanatory trials tend to examine causal mechanisms and questions of efficacy and value internal validity (creating optimal study conditions) over generalizability (using study results to understand treatment effects in real-life patient populations). Chapter 7 draws inspiration from the contrasting explanatory and pragmatic perspectives and develops them for clinical and research pertaining to idiopathic physical symptoms and related

SUMMARY AND FUTURE DIRECTIONS

syndromes (e.g., somatization disorder, chronic fatigue syndrome, multiple chemical sensitivities, irritable bowel syndrome).

In Chapter 8, a blended care program for medical unexplained physical symptoms is presented. This offers a more holistic and preventive approach that focuses on allostatic load awareness contributes to a reduction of unnecessary medical consumption and increases job participation. It is recommended that the development of guidelines for diagnoses and treatment of these complaints in military setting will improve the quality of patient care, reduce disability, facilitate reintegration and encourage scientific research.

Chapter 9 states that to make use of the versatility of jobs available in the contemporary Armed Forces, the health and performance of military manpower can be enhanced by using the benefits of the Person x Environment approach as a force multiplier in the common military practice.

Finally, Chapter 10 presented:

- 1) The history of the Gulf War Health Center, Walter Reed Army Medical Center's program for evaluating and treating Gulf War related health concerns;
- 2) The Gulf War Health Center's Specialized Care Program (SCP), an intensive outpatient program providing intensive treatment to individuals with persistent, disabling Gulf War related physical symptoms that employs methods used in chronic pain centers internationally; and
- 3) The Deployment Medicine Treatment Center, an extension of the SCP approach to veterans from all future deployments.

11.2 FUTURE DIRECTIONS

About 2/3 of people experience one or more painful or distressing symptoms in the average month, and studies show that in routine practice 25 – 30% of symptoms remain unexplained. Scientific and clinical investigations are limited in their capacity to provide timely answers to the complex causal questions that arise in defining and responding to these common persistent symptoms. There is a need to provide an operational definition of MUPS. This is an area that is a challenge for military, occupational and general medical settings. At the same time caution is needed to prevent widespread socialization of a cause in the absence of conclusive scientific evidence.

MUPS is a persistent pattern of chronic symptoms that last 3 months or longer. The presentation is typically characterized by pain, fatigue, mood, memory and concentration problems that cause significant distress or functional impairment. There is absence of disease or clear cause (no objective clinical findings) after appropriate and directed clinical assessment. A frequent associated feature includes preoccupation with symptom severity, precipitating events or presumed exposures and causes.

MUPS is neither a disease nor a specific diagnostic category. These non-specific symptoms have a variety of potential causes. We offer a MUPS as a pragmatic clinical definition that will enable early identification and treatment of patients. MUPS can be considered a spectrum of symptoms. Chronicity is often accompanied with co-morbidity (anxiety and depression). MUPS adds to a significant burden on delivery of health care and is generally poorly dealt with. All specialties have created specific functional syndromes that fall into the category of MUPS that appear to deserve their own specific treatment.

MUPS adds to a significant burden on delivery of health care and is generally poorly dealt with. Factors encompassing the challenge include:

- The ability to prevent chronic morbidity is far greater if this group of patients are managed effectively early in their presentations (management message).
- Identification of common elements that help patients get better.
- Developing an awareness of recurrent patterns of presentation. (Sustaining the intervention).
- This is a group of patients that easily are neglected by the system, and fail to attract attention of clinicians. They easily fall in a vacuum. (Continuity of care).
- Manage prejudicial attitudes of some health providers to this group of patients.
- Teaching health providers recognize MUPS.
- Development of an IT system that enables registries to identify and treat patient at specific stages of MUPS progression.

The assessment needs to consist of a team:

- 1) General practitioner: assessment of medical chart, integrating all generated reports, consider additional diagnostic tests; and
- 2) Specialized care in MUPS clinic: review of records, motivational assessment, team evaluation and review with patient.

A provider attitude is oriented to acknowledgement of suffering and orientation to change (hopeful expectancy).

Essential ingredients for treatment are:

- Multi-disciplinary approach (preferably group wise long-term rehabilitative functioning);
- Focus not on elimination of specific symptoms, focus on restoration, taking responsibility for health return to work; and
- Positive attitude of patient to change (positive expectancy).

New symptoms in the course of treatment always need to be evaluated through careful history taking in combination with physical examination.

Finally, construction of medical surveillance programs aiming at identification of groups at particular risk of post-deployment health issues and to identify those with health care needs. This needs to be branded as 'Multi-Disciplinary Treatment Center' for provision of specialized medical care for persistent, incompletely explained physical symptoms. In this construction there needs to be identification of novel outcome parameters beyond a symptom-focused approach, e.g., health-related quality of life. For this way ahead it is also important to organizing treatment teams, blended care programs; assessment and follow-up of groups, as well as organization with insurance companies around a business plan within health care providers.

11.3 REFERENCE

- [1] Goldberg, D. (1996), A dimensional model for common mental disorders. Br J Psychiatry Suppl(30), pp. 44-49.



Annex A – NATO DEFINITION OF MEDICALLY UNEXPLAINED PHYSICAL SYMPTOMS

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A.1 PURPOSE

To define Medically Unexplained Physical Symptoms (MUPS) and Post-Deployment Syndromes (PDS).

A.2 THE CHALLENGE

About 2/3 of people experience one or more painful or distressing symptoms in the average month, and studies show that in routine practice 25 – 30 % of symptoms remain unexplained. Scientific and clinical investigations are limited in their capacity to provide timely answers to the complex causal questions that arise in defining and responding to these common persistent symptoms. There is a need to provide an operational definition of MUPS. This is an area that is a challenge for military, occupational and general medical settings. At the same time caution is needed to prevent widespread socialization of a cause in the absence of conclusive scientific evidence.

A.3 DEFINITIONS

MUPS is a persistent pattern of chronic symptoms that last 3 months or longer. The presentation is typically characterized by:

- Pain, fatigue, mood, memory and concentration problems;
- Cause significant distress or functional impairment; and
- Absence of disease or clear cause (no objective clinical findings) after appropriate and directed clinical assessment.

A frequent associated feature includes:

- Preoccupation with symptom severity;
- Precipitating events; or
- Presumed exposures and causes.

MUPS is neither a disease nor a specific diagnostic category. These non-specific symptoms have a variety of potential causes. We offer a MUPS as a pragmatic clinical definition that will enable early identification and treatment of patients.

PDS is the occurrence of MUPS in the context of a recent military deployment wherein affected individuals may develop concerns regarding toxic battlefield exposures and injuries (e.g., insecticides, nerve agents, depleted uranium, blasts, immunizations).

A.4 RELEVANCE FOR NATO

The definition allows for common understanding and standardization across NATO Nations. An agreed upon definition can also help to coordinate other strategies such as health and environmental surveillance, and the evaluation of deployment health outcomes.

Annex B – NATO ORGANISATIONAL RESPONSE STRATEGIES TO MUPS/PDS

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B.1 BACKGROUND

Every major war is followed by controversy around Post-Deployment Syndrome (PDS). In this setting there has often been overstated certainty about possible causes of these symptoms in the absence of clear scientific evidence and this leads to a debate that contributed to distrust and disability. Examples are Shell Shock, Agent Orange, Gulf War syndrome. This has in many cases led to mistrust and loss of faith in military leadership and government and medical establishment. The current conflicts in the Iraq and Afghanistan is intendant with the same risks of oversimplification of causality of symptoms to blast exposure.

B.2 PURPOSE

- To manage the potentially harmful health concerns and psychosocial effects associated with the perceived threat of CBRN weapons and countermeasures.
- Mitigate the adverse organisational effects related to MUPS (e.g., cost of disability, operational readiness, attrition, distrust of leaders' government and health care, disruption of cohesion, morale).

B.3 WAY AHEAD

To develop mitigation strategies to minimize the psychosocial and organisational hazards of exposures and countermeasures (e.g., CBRN, blast exposure, environmental toxins):

- Proactive environmental health and hazard surveillance strategy before, during and after deployment.
- Develop a transparent and efficient communication strategy (e.g., messages for family members).
- Explore, anticipate and address population health and exposure concerns.
- Conduct systematic ongoing longitudinal population health surveillance.



Annex C – MUPS HEALTH SERVICES RESPONSE STRATEGIES

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C.1 BACKGROUND

Two-thirds of people experience one or more painful or distressing symptoms in the average month, and 25 – 30 % of symptoms remain unexplained. Clinicians are limited in their capacity to provide timely answers to the complex causal questions that arise in defining and responding to these common persistent symptoms. Given the ubiquitous nature MUPS the supporting force health systems require a population strategy.

C.2 THE CHALLENGE

MUPS adds to a significant burden on delivery of health care and is generally poorly dealt with. Factors encompassing the challenge include:

- The ability to prevent chronic morbidity is far greater if this group of patients are managed effectively early in their presentations (management message).
- Identification of common elements that help patients get better.
- Developing an awareness of recurrent patterns of presentation. (Sustaining the intervention).
- This is a group of patients that easily are neglected by the system, and fail to attract attention of clinicians. They easily fall in a vacuum. (Continuity of care).
- Manage prejudicial attitudes of some health providers to this group of patients.
- Teaching health providers recognize MUPS.
- Development of an IT system that enables registries to identify and treat patient at specific stages of MUPS progression.

C.3 CURRENT PRACTICES

One of the main drivers of current clinical practice is that it is a sub-specialty based system. What it fails to do is the non-specific presentation.

C.4 WAY AHEAD

- Development of a NATO-wide clinical framework for MUPS.
- Construction of medical surveillance programs aiming at identification of groups at particular risk of post-deployment health issues and to identify those with health care needs. This needs to be branded as ‘Multi-Disciplinary Treatment Center’ for provision of specialized medical care for persistent, incompletely explained physical symptoms.
- Identification of novel outcome parameters beyond symptom-focused approach, e.g., health-related quality of life.

Annex D – MUPS BEST PRACTICES

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D.1 BACKGROUND

MUPS can be considered a spectrum of symptoms. Chronicity is often accompanied with comorbidity (anxiety and depression). MUPS adds to a significant burden on delivery of health care and is generally poorly dealt with. All specialties have created specific functional syndromes that fall into the category of MUPS that appear to deserve their own specific treatment. Often used ICD codes for these presentations are:

- Psychological conditions (290 – 319);
- Musculoskeletal conditions, (710 – 739); and
- Signs, symptoms and ill-defined conditions (780 – 799).

D.2 ASSESSMENT

General practitioner:

- Assessment of medical chart;
- Integrating all generated reports; and
- Consider additional diagnostic tests.

Specialised care in MUPS clinic:

- Review of records;
- Motivational assessment;
- Team evaluation; and
- Review with patient.

Provider attitude is oriented to acknowledgement of suffering and orientation to change (*hopeful expectancy*).

D.3 TREATMENT

Essential ingredients for treatment are:

ANNEX D – MUPS BEST PRACTICES

- Multi-disciplinary approach (preferably group wise long-term rehabilitative functioning).
- Focus **not** on elimination of specific symptoms.
- Focus on restoration, taking responsibility for health return to work.
- Positive attitude of patient to change (*positive expectancy*).

New symptoms in the course of treatment always need to be evaluated through careful history taking in combination with physical examination.

D.4 WAY AHEAD

- Organizing treatment teams, blended care programs.
- Assessment and follow up of groups.
- Organization with insurance companies around a business plan within health care providers.

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