

# 12

## OTHER POPULATIONS SEEN FOR REHABILITATION

### a) HIV

*Michael Perdices*

#### Evolution of an epidemic

In June 1981 the Centers for Disease Control, Atlanta, USA, reported five cases of patients in the Los Angeles area who had *Pneumocystis carinii* pneumonia (CDC, 1981). Further cases were reported soon after. None had a history of immunosuppressive chemotherapy and all showed clinical manifestations and laboratory evidence of an underlying dysfunction of cell-mediated immunity.

Approximately two years later, the Human Immunodeficiency Virus (HIV) was identified as the aetiological agent of a new disease that came to be known as the Acquired Immunodeficiency Syndrome (AIDS). HIV infection was probably already extensive by the late 1970s spreading quickly among populations where high risk behaviours for infection were prevalent (e.g. unprotected sexual intercourse). By the end of 2014, 39.6 million people were living with HIV/AIDS worldwide, the majority (~70 per cent) in sub-Saharan Africa (UNAIDS, 2015).

#### Clinical course of HIV infection

HIV infection is classified into three clinical groups (see Table 12.1) staging infection progression in terms of specified disease symptoms and plasma CD4+ levels. In over 50 per cent of cases initial infection manifests itself as an acute mononucleosis-like illness lasting 3–14 days (Tindall et al., 1988). The early phase (Category A) is relatively asymptomatic but immune function gradually deteriorates.

*Table 12.1* CDC classification system for HIV infection (adapted from CDC, 1992)

<i>Clinical categories</i>			
<i>CD4 cell count categories</i>	<b>A</b> <i>Acute HIV asymptomatic, or PGL</i>	<b>B</b> <i>Symptoms/conditions not in Category A or C</i>	<b>C</b> <i>AIDS-defining conditions</i>
1) ≥500 cells/μL	A1	B1	C1
2) 200–499 cells/μL	A2	B2	C2
3) <200 cells/μL	A3	B3	C3

PGL = persistent generalised lymphadenopathy

The next phases (Categories B and C) are heralded by the onset of specified opportunistic comorbidities. AIDS is the most severe clinical manifestation of HIV infection. Patients with plasma CD4+ counts below 200 cells/ $\mu$ L are considered to have AIDS even in the absence of disease symptoms (Categories A3 and B3).

### Neuropsychological impairment directly attributable to HIV

Neuropsychological impairment directly attributable to HIV is called HIV-Associated Neurocognitive Disorder (HAND). HAND is classified into three diagnostic groups according to severity of impairment and its functional impact on everyday life (see Table 12.2). Subtle/mild, relatively stable cognitive impairment may occur at any stage of infection, and its onset is usually indolent (Grill and Price, 2014). Impairment severity may increase with progression of infection, usually becoming clinically apparent after the onset of systemic disease. Its most severe manifestation is a progressive encephalopathy, initially called the AIDS dementia complex (Navia, Jordan and Price, 1986) and currently referred to as HIV-associated dementia (HAD).

Typically, HAD has a subacute onset and is initially characterised by forgetfulness, loss of concentration and mental slowing. Concurrent behavioural abnormalities (apathy, withdrawal) or motor disturbances (fine motor incoordination, ataxia) are apparent in approximately 50 per cent of cases. Significant impairment of attention/concentration, executive function and memory becomes readily evident over time, eventually evolving into severe global cognitive impairment, mutism, paraplegia, incontinence and myoclonus.

Since the introduction of highly active antiretroviral therapy (HAART) in the mid-1990s, a dramatic reduction has occurred in the incidence (from 6.49 to 0.66/1000 person-years; Bhaskaran et al., 2008) and prevalence of HAD (from 10–15 per cent to 2 per cent). But prevalence of ANI

Table 12.2 Revised criteria for HIV-Associated Neurocognitive Disorder (HAND)

<i>Asymptomatic Neurocognitive Impairment (ANI*)</i>	<i>HIV-Associated Mild Neurocognitive Disorder (MND)</i>	<i>HIV-Associated Dementia (HAD)</i>
1) Performance $\geq$ 1 SD below normal mean on standardised neuropsychological tests in at least two cognitive areas:	1) Performance $\geq$ 1 SD below normal mean on standardised neuropsychological tests in at least two cognitive areas:	1) Performance $\geq$ 2 SD below normal mean on standardised neuropsychological tests in at least two cognitive areas, especially:
<ul style="list-style-type: none"> <li>• attention/information processing</li> <li>• language</li> <li>• abstraction/executive</li> <li>• complex perceptual motor skills</li> <li>• memory (including learning and recall)</li> <li>• simple motor skills (or sensory perceptual abilities)</li> </ul>	<ul style="list-style-type: none"> <li>• verbal/language</li> <li>• attention/working memory</li> <li>• abstraction/executive</li> <li>• memory (learning and recall)</li> <li>• speed of information processing</li> <li>• sensory-perceptual, motor skills</li> </ul>	<ul style="list-style-type: none"> <li>• learning new information</li> <li>• slowed information processing</li> <li>• impaired attention/concentration</li> </ul>
2) Cognitive impairment does not impact on everyday functioning	2) Cognitive impairment has at least mild impact on everyday functioning with at least one of the following:	2) Cognitive impairment has marked impact on everyday functioning in terms of work, home life and social activities
	<ul style="list-style-type: none"> <li>i) self-report of reduced mental acuity, inefficiency in work, homemaking, or social functioning</li> <li>ii) informant report of at least mild decline in mental acuity and inefficiency in functional domains listed in (i)</li> </ul>	

Adapted from Antinori et al. (2007).

(\* Asymptomatic = relative absence of functional symptoms in everyday life.)

(33 per cent) and MND (12 per cent) has remained high (Heaton et al., 2010). Treatment with HAART is associated with small improvements in attention, executive function and motor function, but not language, verbal memory, visual memory or visuospatial function (Al-Khindi et al., 2011).

## **Rehabilitation of HAND**

People living with HIV/AIDS experience significant difficulties in a wide range of basic and instrumental activities of daily living. This is evident in the context of ‘minor’ neuropsychological impairment and is not attributable to other comorbidities such as mood disorders and substance dependence (Doyle et al., 2013). However, reports of non-pharmacological neurorehabilitation interventions to specifically address these difficulties are few. Improvement of medication compliance is a focus of attention, and the effectiveness of behavioural, psychotherapeutic and compensatory-based interventions (e.g. electronic prompting device; Andrade et al., 2005) has been demonstrated. At least three studies using a restorative approach have reported some success for computer-delivered cognitive stimulation interventions in improving performance, primarily in processing speed, and attention (Becker et al., 2012; Boivin et al., 2010) and one intervention also improved performance in laboratory measures of everyday functioning (Vance et al., 2012).

HAART dramatically extends longevity, effectively transforming HIV infection into a chronic illness, and slightly improves cognitive function. Prevalence of HAND, however, increases significantly with age (Becker et al., 2004) and there is speculation that as individuals age they are at increased risk for Alzheimer’s disease (Clifford et al., 2009). The interaction of age-related neurocognitive problems and HAND will exacerbate neuropsychological and functional impairment. The investigation by Vance and colleagues (2012) specifically included older individuals living with HIV/AIDS, but only limited attention has been given to issues of ageing in terms of neurorehabilitation.

In summary, HIV/AIDS-related morbidity and mortality have improved dramatically since the infection was identified 35 years ago, particularly since the advent of HAART. Severity and prevalence of HAND have also changed: dementia is rarer nowadays, but milder manifestations of HAND are more prevalent. Consequently, new challenges have emerged in meeting the long-term needs of people living with HIV/AIDS, which highlight the urgent need for non-pharmacological neurorehabilitation interventions.

In the context of the current meagre evidence base of neuropsychological interventions for HAND, Weber and colleagues (2013) suggest that evidence from observational studies examining spontaneous use of compensatory strategies and from investigations using theory-driven experimental approaches to fractionate the specific mechanisms of cognitive impairment can be used to design and implement neurorehabilitation strategies. In addition, evidence-based interventions developed for other neurological populations could be validated for individuals with HIV/AIDS, and provide a good beginning to augment the neurorehabilitation armamentarium.

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## b) Blast injuries

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### **Introduction**

Blast exposure can result in a variety of frequently comorbid chronic injuries, including traumatic brain injury, post-traumatic stress disorder, and pain. Given the nature of these comorbidities, it is not surprising that many individuals with blast exposure experience impairment in cognition and psychosocial functioning. We review the nature and potential causes of these cognitive and functional impairments, with an emphasis on how such understanding can inform a clinician's diagnostic and treatment approach. We then discuss neuropsychological rehabilitation treatment planning in the context of blast injuries.

### **Blast exposure**

The number of people with injuries caused by blast exposure is rising due to the proliferation of improvised explosive devices in contemporary warfare and terrorism. Explosions cause blast waves that can injure the brain and body of an individual through multiple, frequently co-occurring, mechanisms. Rapid over- and under-pressurisation shifts from the blast wind may cause *primary injury* to the brain and other air-fluid interfaces (e.g. ear drums) and air-filled organs (e.g. lungs); *secondary injury* occurs when objects accelerated by the blast wind strike an individual; *tertiary injury* occurs when an individual is displaced by the blast wind, resulting in blunt trauma or other injuries; and *quaternary injury* is caused by fire, explosive materials, and noxious fumes (e.g. burns). These blast injury mechanisms may lead to the development of neurological, mental health and physical conditions that have the potential to impair cognitive and psychosocial functioning.

### **Conditions caused by blast exposure**

Prevalence estimates of traumatic brain injury (TBI) in deployed US military personnel range from 8 to 23 percent (Roebuck-Spencer et al., 2012), and blast exposure is the predominant cause of TBI in this group (Terrio et al., 2009). As such, while not all blast exposures result in TBI, the former clearly is a risk factor for the latter. How primary blast waves affect the brain is a topic of ongoing research, but secondary and tertiary injuries contribute to many blast TBIs. Findings from studies of US military

personnel have revealed that while the vast majority of blast TBIs are mild in severity (Hoge et al., 2008), it is not uncommon for people in combat zones to sustain multiple blast TBIs in a single tour of duty (Vanderploeg et al., 2012). In line with the characteristics of blast TBI, this chapter section will focus on the neuropsychological impact of mild blast TBI. However, given that prior research has not found robust differences in neuropsychological profiles of blast and non-blast TBI (Belanger et al., 2009), the reader is referred to Chapter 6(A) for a review of moderate to severe TBI.

Post-traumatic stress disorder (PTSD) is a second condition that is highly prevalent in blast-exposed individuals in combat intense areas. Interestingly, PTSD is more common among blast-exposed individuals who have suffered mild TBI than those who have not (Hoge et al., 2008). This has led to the suggestion that TBI may facilitate the development and persistence of PTSD (Vasterling et al., 2009). For instance, temporary disruption to medial temporal lobe functioning from blast TBI may cause abnormal consolidation of traumatic events surrounding the blast. Moreover, TBI-induced disruption to limbic and prefrontal regions may affect emotional reactions and their cognitive regulation in the aftermath of a blast.

A third condition that is closely associated with blast exposure is pain. Blast exposure has been identified as a common source of pain in active duty soldiers receiving treatment in military pain clinics (Cohen et al., 2005), and pain is highly prevalent in blast-exposed veterans in inpatient rehabilitation (i.e. 96 per cent of cases in one setting; Clark et al., 2007). Moreover, complex injury mechanisms of blast exposure often lead to multiple musculoskeletal injuries (Otis et al., 2011). Many blast-exposed individuals suffer from 'chronic' pain, which refers to pain that persists for more than three months after the initial injury. Headache is a common chronic pain symptom of blast TBI (Ruff et al., 2008), but location of pain varies and can be in multiple sites. Moreover, emotional distress can complicate the experience of pain. For instance, blast-related pain is more common in individuals who report higher re-experiencing PTSD symptoms and more severe depression symptomatology (Stratton et al., 2014).

Blast exposure can result in additional conditions that are associated with TBI, PTSD, and/or pain and may exacerbate negative cognitive and psychosocial outcomes. For example, hearing loss and tinnitus, which are highly comorbid with blast TBI in particular, have been found in approximately 20 per cent of US military service members one year after blast exposure (Dougherty et al., 2013). Depression also is highly comorbid with PTSD in blast TBI (Verfaellie et al., 2013), and there is a high rate of substance abuse in the population of US veterans returning from recent conflicts (e.g. alcohol and opioid) (Lippa et al., 2015; Seal et al., 2012). Moreover, blast exposure may interfere with sleep, as complaints of poor sleep quality and diagnosed sleep disorders are common in this population (Vanderploeg et al., 2012).

### **Cognitive and psychosocial impairments**

Prior research has shown that blast-exposed individuals often complain about (Lippa et al., 2010; Verfaellie et al., 2013) and demonstrate (Nelson et al., 2012; Verfaellie et al., 2014) impairment in cognition, most frequently in memory, executive functioning, and complex attention. Blast-exposed individuals also commonly report experiencing difficulties in their everyday functioning, with missed workdays (Hoge et al., 2008) and social problems being more prominent than physical setbacks (Verfaellie et al., 2013). Marital and family discord also may be common psychosocial issues in blast-exposed populations, based on findings from research on non-blast veteran populations with similar comorbidities (Vanderploeg et al., 2007; Vasterling et al., 2015). Much of the research on the cause of cognitive and psychosocial impairments in the chronic stage of blast exposure has focused on uncovering the contributions of mild TBI and mental health factors. The vast majority of studies to do so have shown that cognitive and functional impairments are primarily associated with mental health factors, including PTSD and depression (Verfaellie et al., 2013, 2014). These results are

consistent with neuropsychological research on uncomplicated mild non-blast TBI recovery, and they are in line with the broader literature demonstrating mild impairments in processing speed, memory, and executive functioning associated with PTSD and depression.

From a clinical perspective, these findings suggest that, while concern about TBI is often a primary factor that brings individuals exposed to blast in for neuropsychological assessment, it is important to consider the contribution of mental health factors, as cognitive and functional impairments typically are driven primarily by the latter. One potentially important exception is when an individual has experienced multiple mild blast TBIs, as repeated injury can have a cumulative effect on memory and executive functioning (Belanger et al., 2010). Moreover, prior research has shown that mild blast TBI with loss of consciousness adds to the negative impact of mental health factors on psychosocial functioning (Verfaellie et al., 2013). It also is noteworthy that mild blast TBI has been shown to result in diffuse white matter damage (Hayes, Bigler and Verfaellie, 2016; MacDonald et al., 2011), and to influence memory through its effect on white matter integrity (Hayes et al., 2015). In addition, white matter damage from mTBI (mild TBI) also has been associated with executive dysfunction (Sorg et al., 2014). Therefore, neuroimaging findings are revealing a more complex picture of the neuropsychological effects of blast TBI than diagnostic classification alone.

Less is known about the unique contributions of pain and other blast exposure comorbidities to cognitive and functional impairments. Nevertheless, chronic pain in non-blast populations has been associated with impaired processing speed in particular (Hart et al., 2000). Recent research has revealed that self-reported sleep disturbance in blast-exposed individuals is associated with worse objective performance in multiple cognitive domains (Verfaellie et al., 2016). There is considerable evidence to show that substance abuse, including alcohol and opioid use disorders, can lead to dysfunctional learning and memory and executive functioning, as well as other cognitive deficits (Ersche and Sahakian, 2007; Oscar-Berman and Marinkovic, 2007). Moreover, hearing loss and tinnitus are likely to have a general effect on cognition that may be overlooked given that such conditions are relatively uncommon in young and middle-aged individuals. Clinically, these findings suggest that blast-exposed individuals with these comorbidities may have more severe cognitive and functional impairments.

Importantly, because prior research has focused on understanding how blast-exposure affects cognitive and functional outcome in relatively young and middle-age adults, it is not clear how blast exposure affects cognition across the life span. Trotter and colleagues (2015) recently reported cross-sectional evidence to suggest that age-related white matter integrity loss may be accelerated in blast-exposed individuals in comparison to individuals without a history of blast exposure. Whether such changes to brain structure integrity result in abnormal cognitive ageing needs to be elucidated through future research. If it is found that blast exposure per se leads to age-related cognitive impairment, perhaps mild blast TBI takes on greater importance in the cognitive performance of older adults.

### **Treatment considerations**

In treatment of blast-exposed individuals, the challenge for neuropsychological rehabilitation is to (1) assess for blast conditions and cognitive and psychosocial impairment, and (2) implement a treatment plan that can effectively help a blast-exposed individual improve cognition and functional status. Here we outline two approaches to this challenge.

One approach to this challenge is to treat cognitive impairment directly through cognitive training. The idea behind this approach is that boosting cognitive functioning may have a positive impact not only on functional status (e.g. better performance in school), but also more generally on cognitive control of emotional reactions and behaviour (Twamley et al., 2014). Based on what is known about cognitive impairment in blast-exposed individuals, memory, executive functioning,

and complex attention are likely candidates for such cognitive training. Cognitive training of external memory strategies (e.g. using a calendar or notebook) and internal memory strategies (e.g. mental imagery and rehearsal), while effort intensive, has revealed promising results in many populations with mild memory impairments. However, additional research is needed to determine which memory strategies are most practical and effective. Goal Management Training (Levine et al., 2000), a theory-based intervention for problem solving, may be particularly useful for blast-exposed individuals with executive dysfunction. For instance, Goal Management Training could be adapted to facilitate return to school or work or to deal with relationship issues in this population. When appropriate, cognitive training could be coupled with other mental health treatments to, for example, enhance implementation of cognitive strategies for managing stress.

A second approach to this challenge can be characterised as a stepped-care treatment model. In this approach, the initial focus is not on cognitive impairment but rather on blast conditions that may be causing an individual's cognitive impairment. The expectation of this approach is that to the extent that these blast conditions are successfully treated, cognition may improve as a result. In such a stepped-care treatment model, treatment could begin with psychoeducation about conditions that are associated with blast exposure. Indeed, while many blast-exposed individuals are concerned about the impact of blast TBI, they often have not considered the role of other conditions on cognition and functional status. Then common sources of *reversible* cognitive impairment could be assessed for and treated when necessary (e.g. sleep hygiene intervention). In support of this approach, treatment of PTSD has been associated with improved cognition (Kent et al., 2011; Walter, Palmieri and Gunstad, 2010). In this approach, more effort-intensive cognitive training could be deferred until these conditions have been managed, if cognitive impairment persists.

While we do not see one approach as inherently better than the other, nor are they mutually exclusive (Twamley et al., 2014), one may be more feasible than the other depending on clinical setting and resources.

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