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Ergonomics and Beyond: Understanding How Chemical and Heat Exposures and Physical Exertions at Work Affect Functional Ability, Injury, and Long-Term Health

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Abstract

Objective: To honor Tom Waters's work on emerging occupational health issues, we review the literature on physical along with chemical exposures and their impact on functional outcomes.

Background: Many occupations present the opportunity for exposure to multiple hazardous exposures, including both physical and chemical factors. However, little is known about how these different factors affect functional ability and injury. The goal of this review is to examine the relationships between these exposures, impairment of the neuromuscular and musculoskeletal systems, functional outcomes, and health problems with a focus on acute injury.

Method: Literature was identified using online databases, including PubMed, Ovid Medline, and Google Scholar. References from included articles were searched for additional relevant articles.

Results: This review documented the limited existing literature that discussed cognitive impairment and functional disorders via neurotoxicity for physical exposures (heat and repetitive loading) and chemical exposures (pesticides, volatile organic compounds [VOCs], and heavy metals).

Conclusion: This review supports that workers are exposed to physical and chemical exposures that are associated with negative health effects, including functional impairment and injury. Innovation in exposure assessment with respect to quantifying the joint exposure to these different exposures is especially needed for developing risk assessment models and, ultimately, preventive measures.

Application: Along with physical exposures, chemical exposures need to be considered, alone and in combination, in assessing functional ability and occupationally related injuries.

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The only potential conflict of interest would be that the bone shock absorption (BSA) device (patent approved in 2014) mentioned in this manuscript is co-invented by Amit Bhattacharya. University of Cincinnati has given the licensing options for this device to a new startup company (OsteoDynamics, Inc.), which was cofounded by Amit Bhattacharya. No monetary compensation is received by Amit Bhattacharya; however, he holds equity shares in the company.

Keywords

occupational; VOCs; metals; pesticides; postural sway

INTRODUCTION

This review is dedicated to the memory and lifetime work of Tom Waters. We present an extension of what Tom Waters had envisioned in a 2004 conference about workplace risk factors experienced by children and adolescents working in agriculture (Waters & Wilkins, 2004). Under Tom's guidance during the conference, a panel of national experts discussed the prevention of workplace musculoskeletal disorders among these vulnerable workers. They identified research needs, including understanding how physical and chemical environmental exposures negatively affect the neuromuscular and skeletal systems and contribute to degenerative disorders. Tom and the panel specifically discussed the need to investigate the role of pesticides and other agricultural chemicals in modifying neuromuscular systems, muscle strength, and neuromotor functions (e.g. balance) and long-term health effects. Two of the authors (AB and ES) of this article were positively influenced by the conference, which directly led to their research efforts.

Keeping in alignment with findings from the conference and Tom's great vision, we discuss how environmental factors (e.g., pesticides, heavy metals, solvents, heat, repetitive loading) affect the neuromuscular and musculoskeletal systems, which collectively endangers functional outcomes (e.g., balance, gait while carrying out tasks). These functional outcomes result in potential injuries and increased risk of developing chronic neurodegenerative and degenerative musculoskeletal disorders later in life. In the long term, having such knowledge would hopefully elicit future collaborations among multidisciplinary experts who would further investigate the relative contributions of workplace physical and chemical exposures in influencing workers' task performance and health status.

Background

Many jobs require working in environments with multiple risk factors of physical and chemical origins. Therefore, it is critical that the impact on worker health of these exposures, alone and combined, is better understood in order to stimulate innovative approaches toward ensuring worker health. Examples of physical risk factors consist of job/task characteristics (e.g., static standing versus dynamic tasks, body segment movement), high temperatures, poor environmental lighting, floor slipperiness, and inclined standing and walking surfaces (e.g., on ramp and roof surface). Examples of chemical risk factors include heavy metals (e.g., lead [Pb], manganese [Mn]), solvents, and pesticides, which are known neurotoxicants. Costa, Giordano, Guizzetti, and Vitalone (2008) define neurotoxicity as "any adverse effect on the central or peripheral nervous system caused by chemical, biological or physical agents" (p. 1241).

Previous studies provide evidence that both physical and chemical exposures affect the neuromuscular and musculoskeletal systems, thus modifying functional abilities. For example, the ability to maintain upright balance in a static posture and/or in dynamic conditions (e.g., reaching, bending, walking with weight on an inclined surface) challenges the neuromuscular and musculoskeletal system and may increase the risk of falls (Bagchee & Bhattacharya, 1998; Kincl, Bhattacharya, Succop, & Bagchee, 2003). For example, roofers are exposed to physical risk factors and often have to maintain postural balance in/on challenging work surfaces (Bhattacharya, Succop, et al., 2007; Kincl et al., 2003). In addition, roofers and other construction workers are exposed to neurotoxic chemicals (e.g., epoxy resins, pitch for cement workers, coal tar pitch and solvents for roofers, and welding fumes and solvents for painters) in addition to these physical exposures (Bhattacharya, Succop, et al., 2007; Kincl et al., 2003). Hunting, Matanoski, Larson, and Wolford (1991) reported an association between solvent exposures and an increased risk of slips, trips, and falls (STFs). In addition, other neurotoxicants (e.g., Pb, Mn, jet fuel, and pesticides) have been reported to affect postural balance and increase the risk of falls (Bhattacharya, Shukla, Bornschein, Dietrich, & Kopke, 1988; Bhattacharya, Shukla, Dietrich, Bornschein, & Berger, 1995; Kincl, Dietrich, & Bhattacharya, 2006; Kuo, Bhattacharya, Succop, & Linz, 1996; Rugless et al., 2014; Sack et al., 1993; Smith et al., 1997; Standridge, Bhattacharya, Succop, Cox, & Haynes, 2008).

Using an interdisciplinary approach, this review presents literature focused on cognitive impairment and neuromuscular and skeletal functional disorders associated with physical (heat and repetitive loading) and chemical (pesticides, volatile organic compounds [VOCs], and heavy metals) exposures. It hopefully will bring attention to the fact that there is a subset of workers who are exposed to both physical and chemical risk factors.

Conceptual Framework

To guide our review, we developed a conceptual model, displayed in Figure 1. This conceptual framework represents how physical and chemical exposures may affect worker health throughout the work life course, which is depicted from adolescence through adulthood. Adolescents are still developing both mentally and physically and may be at an increased risk of health problems due to environmental exposures compared with adults. For example, adolescents (a) have higher rates of respiration, (b) consume more food and fluids per body mass, and (c) have different rates of metabolism, which may increase chemical toxicity (Sly & Carpenter, 2012). For these reasons, it is estimated that environmental factors account for 34% of the global disease burden in children ages 0 to 14 (Pronczuk & Surdu, 2008). Although, adolescence is often defined as a developmental period occurring approximately from the ages of 10 to 19, full brain development may not occur until age 25 (McNeely & Blanchard, 2009). During adolescence, the brain undergoes a process of synaptic pruning that increases efficiency and myelination of axons, which affects how quickly information flows (Spear, 2007). Toxicant exposure during this time could affect not only function but also maturation, leading to both short- and long-term negative health consequences (Golub, 2000).

Chemical, physical, and psychosocial exposures may happen throughout the working life course along with intrinsic factors (e.g., genetics), affecting the worker’s ability to respond to these exposures (Figure 1). Psychosocial exposures, including aspects of work organization, with intrinsic factors are associated with occupational injury and other health outcomes (Hoogendoorn, van Poppel, Bongers, Koes, & Bouter, 2000; Johannessen, Gravseth, & Sterud, 2015; Lesuffleur, Chastang, Sandret, & Niedhammer, 2015). This review focuses on the physical and chemical exposures that, both individually and in combination, could be detrimental to functional abilities, resulting in an increased risk of injury and/or chronic health issues. The functional abilities encompass neuromuscular outcomes (e.g., postural balance, gait, and cognitive abilities).

METHOD

In this review, we focus on the physical exposures—heat and repetitive loading of the musculoskeletal system—and the chemical exposures—Pb, pesticides, and VOCs, particularly solvents—and their potential contribution to cognitive impairment and functional disorders via neurotoxicity. We identified relevant literature published in the English language during the years 1980 to present. Searched databases were CINAHL Complete, Embase, Medline (Ovid), PubMed, Web of Science, SCOPUS, and Google Scholar. Search strategies included combinations of terms and phrases such as *balance, postural sway, injury, neurological, neurotoxicity, motor control, musculoskeletal disorders, occupational, work, Pb, Mn, pesticides, solvents, neurodegeneration, farm, agriculture, farm worker*, and *farmer* within the context of our five main exposure categories: heat, repetitive loading, heavy metals, pesticides, and VOCs. We identified additional articles by manually searching the reference lists of published articles.

RESULTS

Physical Exposures Associated With Functional Impairment, Injury, and Musculoskeletal Health

In this section we review the literature pertaining to the detrimental impact of heat stress on functional outcomes (i.e., postural balance and gait). Such impairment in functional outcomes can trigger fall- and/or near-fall-related acute injuries. In addition, we also review literature on occupational tasks, such as kneeling and squatting, that can lead to chronic joint pain and degenerative bone disorders due to repeated loading of musculoskeletal joints.

Heat stress and its impact on the neuromuscular system and task performance.—Millions of workers in the United States are at increased risk of STFs while performing various job tasks even in normothermic environments. The risk of STFs is further increased when task is performed in hot environments. Sources of heat stress are associated with environmental conditions (temperature, humidity) and physical exertion related to metabolic load. For many, such as firefighters and health care workers, these risks are enhanced due to heat stress associated with wearing encapsulated protective clothing. Physical exertion increases skeletal muscle contractions resulting in metabolic heat production much greater than the resting state (Bernard, 2012; Larranaga & Bernard, 2011). To maintain homeostasis of thermal equilibrium, the heat generated by the muscles (muscle contraction is about 20% efficient; therefore 80% of the energy appears as heat), environmental factors, and clothing must be dissipated so that the body's heat storage is minimal (Bernard, 2012; Goldman, 1994). The most effective mode of heat dissipation in humans is by evaporative cooling. The evaporative potential of the environment is determined by the partial vapor pressure gradient between the sweat on the skin and the surrounding air (Bernard, 2012). Heat strain is described by the physiological responses (e.g., body temperature, heart rate, cardiac output) to the heat stress. Compensable heat stress is defined as heat gained by the body equal to heat loss resulting in a steady-state core/rectal temperature of 38°C. Conversely, uncompensable heat stress occurs when an individual's evaporative cooling demand is not met by the environment's evaporative cooling capacity (e.g., firefighters wearing encapsulated clothing; Mani et al., 2013).

Effect of hot environments on fatigue buildup and task performance.— Literature supports that physical exertion in hot environments affects cardiorespiratory and locomotor systems and brain activities, resulting in central fatigue (Nybo, 2010; Nybo, Rasmussen, & Sawka, 2014). Multiple physiological mechanisms have been associated with central and peripheral fatigue triggered by heat storage at the brain and muscle levels. During physical exertion in heat, central fatigue is potentially affected by elevated heat storage in the brain, dopaminergic neurotransmitters, and nor-adrenaline inhibition (Nybo, 2010, 2012; Nybo & Neilsen, 2001). Mechanistically, hyperthermia-induced fatigue during submaximal intensity exercise is associated with inhibitory signals from thermoreceptors due to increased core and skin temperature and increased feedback from the cardiopulmonary systems, resulting in detrimental impacts on the skeletal metabolism, potentially compromising muscle performance (Sawka, Leon, Montain, & Sonna, 2011). For example, lifting capacity in hot environments is compromised by 13% to 20%, depending on subjects' heat acclimatization status (Hafez & Ayoub, 1991).

Effect of physical exertion with a full-face respirator in normothermic environments and its impact on postural balance.—Physical exertion conducted in normothermic environments generates increased metabolic heat that increases the risk of impairment of workers' gross motor capacity, such as postural balance. Seliga et al. (1991) showed that physical exertion conducted with or without a respirator at room temperature significantly ($p = .007$) impaired the subjects' postural balance (quantified as the total length of postural sway measured by a force platform system) as the workload increased from light (40 watts [W]) to medium (85 W) to heavy (125 W) (Figure 2). Sway area is defined as the total area encompassed by the stabilogram created by the x-y plot of body's center of pressure (CP); an increase in sway area implies poorer balance (Figure 2). Sway length is the total length of the x-y plot of CP; a larger sway length implies reduced postural balance. (Figure 2). Increase in postural imbalance is attributable to workload-induced proprioceptive fatigue effects on the nervous system's inability to adequately process the afferents and deploy appropriate efferent to the postural muscles. This study reported that postural sway was not correlated with heart rate and perceived exertion levels during task performance in normothermic environments. Therefore, measurement of heart rate and perceived exertion during physically demanding tasks do not predict threat to postural balance potentially resulting in a fall. The threat to the postural balance will be even greater when physical exertion is carried out in a hot environment along with other factors, such as firefighting with a full-face respirator.

Effect of physical exertion with a full-face respirator in hot environments and its impact on postural balance.—Using a self-contained breathing apparatus (SCBA) in an encapsulated garment increases heat buildup, which affects gross motor function (e.g., postural stability) among workers, specifically firefighters (Hur, Park, Rosengren, Horn, & Hsiao-Wecksler, 2015; James, Mani, Kincer, & Bhattacharya, 2013; Mani et al., 2013). James et al. (2013) and Mani et al. (2013) studied 26 firefighters' postural balance in a one-legged stance for 30 s with eyes open (EO) and eyes closed (EC) before and after firefighting. After three rounds of firefighting, the sway area and length (defined earlier) were 107.6% and 29.2% higher, respectively, than baseline for the EO test. Shown in Figure 3 is the effect of heat on postural balance for a sample of firefighters. Eight firefighters participated in the EC test. Only one completed the tests without falling (James et al., 2013). In the EO test with all afferents (vision, proprioception, and vestibular systems) intact, the firefighters had difficulty maintaining postural balance; however, with vision removed in the EC test, the remaining two afferents were not sufficient to prevent falls. These findings suggest that feedback from proprioceptors and vestibular systems are compromised in hot environments.

Task performance in hot environments elicits hypohydration, having a negative impact on the neuromuscular system. For example, Distefano et al. (2013) showed the detrimental impact of hypohydration, during task performance in heat, on subjects' neuromuscular control as characterized by poorer postural stability. Fatigue and hypohydration were associated with increased variability of gait patterns, resulting in potential falls. Hypohydration during high-intensity exercise in hot environments could cause dilution of plasma sodium. Low plasma sodium, or hyponatremia, forces water to move from the extracellular compartment into the intracellular compartment, resulting in potential pulmonary congestion, brain swelling, and heat stroke. Under these conditions, degeneration of neurons in the cerebellum and cerebral cortex are associated with impaired central nervous system (CNS) functionality (Sawka et al., 2011; Nybo, 2007). Therefore, it is imperative that electrolyte balance is maintained while working in hot environments.

Effect of repeated/chronic exposure to physical exertion in hot environments.—Firefighters and construction and agricultural workers are among those repeatedly exposed to hot environments. Chronic exposure may result in heat acclimation and potential gene–environment interactions. During recent years, significant advances have been made in understanding the role of gene–environment interactions involving physical exertion in hot environments and heat acclimation (Sawka et al., 2011). Exposure to hot environments and/or high-intensity aerobic exercise stimulates gene expression (in skeletal muscles and any cells that reside in the skeletal muscle capillary beds) known as heat shock proteins (HSP), which could trigger anti-inflammatory response to enhance tolerance to subsequent hyperthermia-induced cell damage (Sonna, Sawka, & Lilly, 2007). Repeated exposure to hyperthermia caused by physical exertion stimulates enhanced thermal tolerance due to increased expression of HSP basal levels and altered HSP expression patterns. This change in HSP levels could potentially improve functional abilities (such as postural balance and gait function) while working in hot environments (Connolly et al., 2004; Sonna et al., 2010). Recent studies also report cellular malfunctions and maladaptation associated with exposure to acute high heat levels and cumulative heat exposures. Heat-associated cellular malfunctions are not completely understood but include a myriad of outcomes (e.g., protein denaturation, translational inhibition, ribosomal bio-genesis arrest, and cytoskeletal damage; Mizzen & Welch, 1988; Sonna et al., 2004; Welch & Mizzen, 1988).

Repetitive physical loading of joints and its detrimental impact on musculoskeletal health.—Previous studies provide strong evidence in adult populations for an association between chronic exposure to heavy lifting (10 to 20 kg weight for up to 20 years) and hip osteoarthritis (OA; Andersen, Thygesen, Davidsen, & Helweg-Larsen, 2012; Jensen, 2008). The risk of hip OA in farmers doubled after 10 years of work involving lifting. In addition, sustained static kneeling positions commonly found in agriculture and construction tasks impair knee joint stability, resulting in detrimental loading of the subchondral bone, affecting the integrity of the cartilage (Kajaks & Costigan, 2015). Studies have reported osteoarthritic/arthritic and other types of musculoskeletal conditions in carpet layers, ballet dancers, housemaids, miners, and construction workers (Bhattacharya, Habes, & Dewees, 2007; Bhattacharya, Mueller, & Putz-Anderson, 1985). Data indicate that carpet installers experience more than 10 times the lower-extremity disorders expected, possibly because their knee joint is overtraumatized due to combination of kneeling and use of knee kicker that delivers, on average, an impact force of 3,000 newtons (N) at a repetition rate of 140 kicks per hour (Bhattacharya et al., 1985; Bhattacharya, Ramakrishanan, & Habes, 1986). Since adult workers' knee joints are mature, their response to work-related excessive knee/hip loading is much less traumatic than in adolescent agriculture workers, whose skeleton is still developing. Therefore, adolescent workers with excessive loading of their joints due to cumulative repetitive kneeling, squatting, and heavy lifting will be predisposed to the development of musculoskeletal disorders, for example, OA (Bhattacharya, Watts, et al., 2007).

Mechanistic studies by several investigators have identified that stiffening of subchondral bone is a precursor to cartilage damage, eventually resulting in OA (Brandt, Radin, Dieppe, & van de Putte, 2006). Although stiffening of subchondral bone appears to be a preclinical marker of OA, it cannot be detected in traditional X-rays. It is a challenge to identify individuals at risk of developing OA at a preclinical stage. Studies have reported the early development of decreasing damping capacity (associated with stiffening of subchondral bone) of the musculoskeletal system in adolescent workers involved in farming activities, including repetitive kneeling, squatting, and heavy lifting, in tasks such as feeding and watering livestock, shoveling grain or silage, using a pitchfork, and scraping manure (Bhattacharya, Watts et al., 2007; Marlenga, Pickett, & Berg, 2001). The damping capacity of their musculoskeletal system was noninvasively assessed with a bone shock absorption (BSA) method (Bhattacharya, Watts, et al., 2007; Bhattacharya et al., 2016). The results showed that youth who repeatedly performed farm-related physically demanding tasks had decreased bone-damping properties. This condition could trigger OA later in life by further exposing the cartilage to increased loading and the release of biochemicals (e.g., cytokines and enzymes), thus damaging the matrix.

Chemical Exposure Associated With Functional Impairment and Injury

Several studies have reported that the long-term health effects of exposure to certain neurotoxicants in the workplace predispose workers to the development of Parkinsonism, osteoporosis, OA, mild cognitive impairment, and Alzheimer's disease (Holz et al., 2012; Potula & Kaye, 2006; Potula, Kleinbaum, & Kaye, 2006; van Wijngaarden, Campell, & Cory-Slechta, 2009; Weisskopf et al., 2010; Weisskopf & Myers, 2006). Evidence also supports that they negatively affect motor control, including postural balance and gait function (Atchison, 1988; Goldstein, 1990; Kamel et al., 2007; Kamel & Hoppin, 2004; Sack et al. 1993). In the following section, we focus on the neurotoxic effects of chemical exposures, specifically pesticides, VOCs, and metals, and their ability to modify functional outcomes (e.g., postural balance) and increase susceptibility to acute injury. More information is presented on pesticides because fewer data on VOCs and metals exist.

Exposure to pesticide: Mechanisms of neurotoxicity and impact on functional outcome and injury.—Studies demonstrate that pesticides can impair the CNS and peripheral nervous system (PNS) via three ways: (a) by directly targeting the nervous system, (b) by disrupting cellular mechanisms affecting the nervous system, and (c) by interfering with chemical neurotransmission or ion channels (Costa et al., 2008; Igho & Afoke, 2014; Kimura et al., 2005; Yokoyama, 2007). Organophosphate (OP) and carbamate subgroups have the most documented neurotoxic mechanism for insecticides. Although the prevalence of OP use is declining, it remains one of the most widely used classes of insecticides, particularly in agriculture (Grube, Donaldson, Kiely, & Wu, 2011).

Both OPs and carbamates can inhibit the enzyme acetylcholinesterase (AChE). This enzyme breaks down the neurotransmitter acetylcholine (Ach). Without AChE, ACh accumulates in synaptic clefts, eventually resulting in overstimulation of the nervous system (Costa, 2012), which can potentially influence muscular contraction patterns, thereby detrimentally modifying postural balance and gait functions. Short- and long-term effects following high-dose exposure can include sweating and salivation, profound bronchial secretion, bronchoconstriction, miosis, increased gastrointestinal motility, diarrhea, tremors, fasciculation, tingling in hands and feet, muscle weakness, neuropsychological deficits, and other CNS effects (Costa et al., 2008). Carbamates are believed to have lower toxicity and less long-term complications compared with OPs (Costa et al., 2008). Given the summary of neurotoxicity of OP exposure associated with muscle weakness and tremors, it is reasonable to expect OPs will affect functional outcomes, such as postural balance (Sack et al., 1993; Yokoyama, 2007).

The occupational groups most commonly exposed to pesticides are agricultural workers and pest control applicators. Although the short-and long-term effects of an acute, high-dose exposure to pesticides (e.g., poisonings) are known for most subclasses, the impact of chronic exposure to lower doses leading to chronic neurotoxicity is a topic of debate. The literature includes inconsistent findings (Ismail, Bodner, & Rohlman, 2012; Kamel & Hoppin, 2004; Meyer-Baron, Knapp, Schäper, & van Thriel, 2015). Understanding the extent to which lower-level exposures influence health is of particular importance for adolescent workers, because these workers are still developing. One mechanism for increased acute injury risk is via decrements in postural stability, which may predispose these workers to STFs (Figure 4). In studies with agricultural populations, a sizeable proportion of acute occupational injuries involves a fall from elevation, STF, or loss of balance (McCurdy, Xiao, & Kwan, 2012; Rautiainen, Lange, Hodne, Schneiders, & Donham, 2004; Xiang et al., 2000).

Despite the publication over 50 years ago of a landmark study of apple farmers and chronic effects of pesticide exposure, including disturbances of equilibrium (Davignon, St.-Pierre, Charest, & Tourangeau, 1965), only a few studies of pesticide exposure include an assessment of postural stability, either by direct measure or via self-report. Kamel et al. (2003) measured postural stability in a group of farmworkers from Florida. For the condition that challenges vestibular and proprioception the greatest, EC standing on foam, observed patterns suggested that those with more years of experience doing farm work had larger sway length, implying compromised postural balance. Associations with conditions that allowed participants to rely on visual afferents were not significant or as great in magnitude. Using a comparable sway protocol, Sack et al. (1993) reported similar findings with pesticide applicators. These males had an average sway length that was larger than controls under the most challenging test condition. Given the difference in sway length, as opposed to area, this finding suggests that a proprioceptive impairment may be more prominent than a disturbance in vestibular function (Yasuda, Nakagawa, Inoue, Iwamoto, & Inokuchi, 1999). A deficit in proprioception as well as vestibular function is biologically plausible given that pesticides, such as OPs, target structures in the cerebellum, the area of the brain that coordinates information needed to control balance (Fonnum & Lock, 2000; Watson & Black, 2008).

Additional studies yielded increased sway parameters among pesticide applicators compared with control groups (Kimura et al., 2005; Steen-land et al., 2000). This association between pesticide exposure and increased sway parameters was not found among pesticide applicators in the Agricultural Health Study, but associations were reported for abnormal toe proprioception (Starks et al., 2012).

Pesticide exposure associated with acute injury.—If pesticide-related neurotoxicity manifests as diminished cognitive function or motor control, the risk of acute occupational injury could increase due to decreased reaction times, stability, and cognitive-processing speeds, among other causes (Figure 4). Authors of only a few studies examined this issue in agricultural populations. Exposure definitions and other methods vary widely, complicating comparison. With respect to self-reported symptoms of neurotoxicity, Atrubin, Wilkins, Crawford, and Bean (2005) conducted a case-control study of nonfatal, acute injury (past 12 months) with principal operators (n = 1,510) involved in cash-grain operations in Ohio. Significant associations were detected for difficulty moving fingers or grasping things, feeling lightheaded or dizzy, trouble remembering things, difficulty driving after work, feeling irritable, sleeping more, and headaches at least once per week. The strongest association was for being bothered by lack of coordination or loss of balance (adjusted odd ratio [OR] = 3.12; 95% confidence interval [CI] = [1.68, 5.81]). Park et al. (2001) reported a slightly elevated, but not significant, unadjusted association (OR_{unadj} = 1.33; 90% CI =

[0.50, 3.56]) between seven or more neurotoxicity symptoms and injury (prior year) for farmers in Iowa.

In a similar analysis, Whitworth, Shipp, Cooper, and del Junco (2010) conducted a cross-sectional analysis of 96 adolescent farmworkers along the Texas-Mexico border. They examined self-reported symptoms of neurotoxicity and acute injury (past 9 months). The associations for those reporting two to four symptoms (OR_{unadj} = 3.28; 95% CI = [0.91, 11.89]) and five or more symptoms (OR_{unadj} = 8.75; 95% CI = [1.89, 40.54]) strengthened with increasing symptom category, compared with those reporting no symptoms or only one symptom.

A handful of additional studies on acute occupational injuries in adolescent and adult farmworkers included an assessment of pesticide exposure rather than symptoms of neurotoxicity. Studies of farmers in Iowa, Alabama, and Colorado showed that associations between exposure to pesticides and injury were indicative of a one-and-a-half- to twofold increase in risk (Rautiainen et al., 2004; Stallones, Keefe, & Xiang, 1997; Xiang, Stallones, Chiu, & Epperson, 1998; Zhou & Roseman, 1994). The exception is a study of farmers in China, where the adjusted OR for farmers applying pesticide four or more times per week (compared with those applying less) was 16.75 (95% CI = [4.70, 59.70]; Xiang et al., 2000).

Waggoner et al. (2013) conducted an analysis of fatal injury among 51,035 male farmers from North Carolina and Iowa in the Agricultural Health Study. From 1993 to 2008, 338 fatal injuries were observed. After adjusting for age and state, associated factors included 60+ days of pesticide application per year (adjusted hazard ratio = 1.87; 95% CI = [1.10, 3.18]). Ever use of five herbicides, including 2,4,5,-T, paraquat, alachlor, metribuzin, or butylate; the fumigant carbon tetrachloride/carbon disulfide; and the fungicide Ziram was associated with fatal injury. Having at least one high-pesticide-exposure event was not significant, indicating that findings cannot be attributed to a single pesticide. Associations with herbicides were unexpected, given the research with stronger associations between insecticides and neurotoxicity. The authors concluded that the results were not due to confounding by high-risk farm activities (driving a combine) but urged caution while interpreting findings due to uncertainty on the timing of the exposure.

A couple of studies pertain to adolescent farmworkers and self-reported exposure to pesticides or chemicals and acute injury within the prior 12 months. Among youth in China, Shen et al. (2013) reported an adjusted OR of 1.18 (95% CI = [1.03, 1.36]) for exposure to pesticides, and McCurdy and Kwan (2012) reported an adjusted OR of 1.86 (95% CI = [1.15, 3.03]) for youth in California who were mixing chemicals. A study from Texas yielded an unadjusted estimate (OR_{unadj} = 1.83; 95% CI = [1.05, 3.19]) within this range, but the variable was not retained in a final model (Shipp, Cooper, del Junco, Cooper, & Whitworth, 2013). For adolescents, we found no studies based on exposure to specific pesticides or studies of fatal injury.

Exposure to VOCs and metals: Mechanisms of neurotoxicity and impact on functional outcome and injury.—This section includes a brief discussion of occupational exposure to VOCs and metals affecting the neuromuscular system and predisposing workers to STFs. Workers at risk of exposure to VOCs include pilots and others working in transportation, welders, and, painters. Heavy metal exposure is a concern specifically among battery factory workers, smelter workers, and metal miners as well as painters, welders, and construction workers.

Exposure to VOCs.—Occupational VOC exposure has been correlated with STFs and neurological diseases, with exposure variability being an important predictor. Both increases and decreases in exposure were correlated with increases in STFs, with a stronger correlation for increases in exposure (Hunting et al., 1991). Hunting et al. (1991) suggested two possible ways for variability in exposure to be impactful: (a) a mechanism of solvent toxicity tolerance and (b) a behavioral tolerance in which the workers would find ways to work with the impairment effects of the VOCs. Studies have utilized hand tremor and postural sway techniques to study the health effects of VOCs (Iwata, Mori, Dakeishi, Onozaki, & Murata, 2005; Kilburn, Warshaw, & Hanscom, 1994; Kuo et al., 1996; Park, Lee, Lee, & Lim, 2009; Smith et al., 1997; Yokoyama et al., 1997). These methods are both more objective and more sensitive than the batteries of neurobehavioral assessments (Laine, Seppäläinen, Savolainen, & Riihimäki, 1996; Ruijten, Verberk, & Sallé, 1991).

A postural sway and hand tremor study showed workers with detectable trichloroethylene in their urine had greater postural instability and dominant-hand tremor than those not exposed (Murata, Inoue, Akutsu, & Iwata, 2010). Araki, Sato, Yokoyama, and Murata (2000) showed a correlation between solvent exposure and vestibular, cerebellar, and spinocerebellar lesions among Pb workers. These lesions could be a mechanism for causing STFs and other injuries in VOC-exposed workers.

Exposure to metals.—Exposure to heavy metals, such as Pb, detrimentally affects multiple organs, such as CNS, PNS, and skeletal, renal, and visual systems. As Pb competes with calcium, it affects neurotransmitter release necessary for muscle contraction (Atchison, 1988; Goldstein, 1990), thereby disturbing motor functions. Mansouri and Cauli (2009) and Weisskopf et al. (2010) provide evidence of Pb exposure–associated motor dysfunctions (postural imbalance and gait impairment) comparable to those found in Parkinson’s disease. Pb is associated with disrupting the dopaminergic function, which is one of the mechanisms of etiology for Parkinson’s disease (Jenner, 2003; Jenner & Olanow, 2006). Van Wijngaarden et al. (2009) reports that lifelong burden of Pb exposure measured in the bone is associated with memory impairment in older adults, a marker of potential development of Alzheimer’s disease. Racette et al. (2012) reports increased risk of Parkinsonism associated with welding exposure, which contains another heavy metal, Mn.

In addition, studies report chronic exposure to Pb is associated with impact on bone health, potentially predisposing workers to early development of osteoporosis. For example, Pb-associated inhibition of parathyroid hormone–related peptide causes premature maturation of chondrocytes (Zuscik et al., 2002). This premature maturation may result in a higher bone density and a transiently lower accumulation of bone mass during early life, predisposing to development of osteoporosis (Campbell & Auinger, 2007; Cooper et al., 2002; Javaid & Cooper, 2002; Schlüssel, Vas, & Kac, 2010). A growing literature exists regarding the body burden of heavy metals in adults and bone health, including osteoporosis, bone mineral density, and bone fractures, specifically of the hip. Findings illustrate that cadmium (Cd) and Pb exposures, including those from environmental and food sources, may be contributing to fractures, especially in older adults and those who smoke (Dahl et al., 2014; Engström et al., 2012; Staessen et al., 1999). Similar associations have been found between increased Pb exposure and impairments in postural sway or balance (Dick et al., 1999; Iwata, Yano, Karita, Dakeishi, & Murata, 2005; Pawlas, Broberg, Skerfving, & Pawlas, 2014).

With respect to the potential for an increased risk for STFs, limited data are available regarding assessments of postural sway or balance, particularly among workers and beyond examining Pb exposures. For the general population, among adults 40 years of age and older who participated in the National Health and Nutrition Examination Survey, those with higher blood Cd, as well as Pb, concentrations had poorer performance on balance tests. Among those with concentrations in the fifth compared with the first quintile, the adjusted ORs were 1.27 (95% CI = [1.10, 1.60]) and 1.42 (95% CI = [1.07, 1.89]) for Cd and Pb, respectively (Campbell & Auinger, 2007).

Increased Mn levels are associated with impaired cognitive and psychomotor development (Claus Henn et al., 2010; Takser, Mergler, Hellier, Sahuquillo, & Huel, 2003). A systematic review showed Mn exposure resulted in decreased cognitive function and decreased motor neuron conduction velocities (Mergler & Baldwin, 1997). Mergler et al. (1994) suggested that Mn exposure impairs the ability to perform bilaterally transposed (mirror image) motor movements. Mn exposure's effect on balance has been studied in occupational and non-occupational populations (Rugless et al., 2014; Standridge et al., 2008; Takser et al., 2003). Welders may be the largest occupational group exposed to Mn. Studies yield evidence for a relationship, but findings are inconclusive (Bowler et al., 2007; Ellingsen et al., 2008; Kim et al., 2007). Data from a research study of a community near to a ferromanganese refinery provide further evidence of a relationship. Among children, mean Mn levels in blood and hair were both significantly associated with poorer postural balance (Rugless et al., 2014). A similar pattern was also observed among adults (Standridge et al., 2008). With respect to studies on workers exposed to Hg, findings are less supportive of an association (Frumkin et al., 2001; Iwata et al., 2007).

Minimal studies of the impact of metals exposure on injury risk are available. Kincl et al. (2006) found evidence that early-childhood Pb exposure increased the risk of acute unintentional injury later in adolescence. The average blood lead level (BLL) among those reporting an injury (14.23 μg/dL) was higher compared with those reporting no injury (12.2 μg/dL) during the follow-up period. A considerable proportion (46%) of reported injuries was due to falls. The average BLL for a subgroup of those experiencing falls was 15.5 μg/dL. This cohort study is particularly of interest because it yielded evidence that early Pb exposure influenced postural stability later in life, even at low to moderate BLL (Bhattacharya, Shukla, Dietrich, & Bornschein, 2006).

DISCUSSION AND CONCLUSION

Integration of the Effects of Physical and Chemical Exposures on Injury Risk

This review highlights the importance of considering the different types of risk factors that are present in the workplace to improve injury prevention. In this context, physical exposures often are identified as points for intervention without also acknowledging the contribution of other types of risk factors, namely, chemical exposures, alone or in combination with other chemical or physical exposures. The lack of information on combinations of chemical and physical exposures is a limitation to the current literature; however, we hope this literature review and Tom Waters's work inspire researchers to address combined chemical and physical exposures.

There are many occupations in which workers encounter both chemical and physical exposures. In some of these professions, physical exertion exacerbates the effects of these exposures. As an example, agricultural workers are exposed often simultaneously to high-heat environments, high physical exertion, and neurotoxins, such as pesticides. Under these circumstances, these workers' functional outcome, as characterized by postural balance and gait function, could be seriously affected by all exposures, thereby increasing their susceptibility to STFs and other injuries. Consider another example of jet fuel mechanics exposed to VOCs, including solvent-based jet fuels, during daily maintenance of aircraft. Jet fuel mechanics' tasks requires wearing whole-body protective clothing with respirators while carrying out physically demanding tasks, such as crawling inside and out of the fuel tank and walking on the wings under slippery conditions. In the jet fuel mechanics work scenario, multiple exposures consist of heat, physical exertion, and jet fuel, all of which individually have been associated with increased postural imbalance (Distefano et al., 2013; Hafez & Ayoub, 1991; Seliga et al., 1991; Smith et al., 1997). Therefore, the risk of STFs is likely to be significantly enhanced due to these coinciding physical and chemical exposures.

Another occupation that is chronically exposed to multiple physical and chemical risk factors is firefighters. They are exposed to toxic chemicals, heat, and physical exertion. Under high temperature and heavy exertion, exposure penetration of toxic chemicals into the skin and deep tissue is significantly increased, resulting in higher toxicity. Other occupations that encounter physical and chemical exposures simultaneously are welders, painters, and construction workers. Such multiple exposure agents experienced by the worker will seriously jeopardize his or her functional abilities and safety. However, more comprehensive and prospective data will have to be obtained to quantify the relative contributions of each of the exposure types (i.e., heat, physical exertion, and chemicals) in predisposing workers to injury. Having such information will permit development of data-driven predictive models that can take into account the roles of various risk factors in modifying workers' functional outcomes and the resulting impact on the risk of injury.

Physical Exposures: Future Research Needs

Due to individual susceptibility to acquired thermal tolerance and molecular adaptations varying from person to person, there is a need for biomarkers to identify susceptible populations (e.g., adolescents, older individuals, first responders). In this manner, individualized interventions could be developed. In particular, first responders are at increased risk of exposure to cumulative hyperthermia, which detrimentally affects thermal adaptation at the molecular level and potentially compromises their neuromuscular performance because of fatigue (Sobeih, Davis, Succop, Jetter, & Bhattacharya, 2006; Figure 5). Therefore, early biomarkers and/or predictive model(s) for identifying hyperthermia are important areas of future research to minimize heat-associated injuries and fatality among workers of all ages. Literature provides two models for predicting hyperthermia (core temperature >100.4°F): (a) one based on physiology of heat stress (Yokota, Berglund, Santee, Butler, & Hoyt, 2005; Yokota, Berglund, & Bathalon, 2012; Yokota, Berglund, Santee, et al., 2012) and (b) data-driven decision trees (Mani, Rao, James, & Bhattacharya, 2015). Use of such predictive modeling has a critical role in designing and developing innovative interventions to minimize heat stress in the working population of all ages in hot environments (Mani et al., 2013, 2015), such as firefighters and agricultural and construction workers.

There are limitations when studying repetitive physical loading. Findings of the BSA method indicate that it could form the basis of an early-detection tool that identifies individuals with an increased risk of developing OA later in life. However, larger prospective cohort studies are needed to confirm the findings in the existing literature with adolescents doing farm work (Bhattacharya, Watts, et al., 2007).

Chemical Exposures: Future Research for VOCs, Pesticides, and Metals

There are large gaps in the literature regarding chemical exposures. Many of these gaps result from difficulties with exposure assessment that can lead to misclassification and information bias. Specific challenges include accurately estimating the type, source, dose, and duration of exposure (Kamel & Hoppin, 2004), which is especially problematic for both short- and long-term exposures and repeated exposures and chemical mixtures. Chemical half-lives further complicate assessment. Chemicals often have short half-lives in tissues, which requires their measurement very close to the time of exposure. Additional concerns include correctly assessing the purity and composition of chemicals, isolating different routes of exposure, and understanding variability in work practices and area ventilation, which all influence the dose and duration of exposure. Further, workers rarely are exposed to a single potential toxicant, with the bulk of solvents being mixtures. The impact of many of these issues would be ameliorated by better, noninvasive measures of exposure or new biomarkers, similar to the needs pointed out for heat exposure. Improved exposure assessment would dramatically further our knowledge of the chronic effects of low dose and cumulative toxicant exposures, particularly for VOCs and pesticides (Chin-Chan, Navarro-Yepes, & Quintanilla-Vega, 2015).

Prospective studies are particularly needed for establishing the temporal sequence between the exposure and the onset of neurobehavioral or neuromuscular outcomes. There is a need for studies of long-term, low-dose exposures (Wu, Bhanegaoankar, & Flowers, 2006) that could also be examined with such large prospective studies. Since many chemicals used at work are also prevalent in the nonwork environment, large population-based prospective studies also would enable differentiating chemical exposures that are occupational versus non-occupational and their joint contribution to health effects (Liu & Jia, 2015).

Authors of future work should carefully address potential sources of bias, including selection bias and potential confounding, especially for the chemical exposures. Many current studies have the limitation of bias due to selection of the control group. Depending on the choice of control groups (working populations, similarity of tasks, where the group lives), association between exposures and outcomes may be masked or attenuated. Poor adjustment for or poor measurement of potential confounders needs to be considered in the design and analysis phases of future studies (e.g., alcohol use; Baker et al., 1988; Liu & Jia, 2015; Wu et al., 2006). For example, educational attainment, gender, genetic susceptibility, and age should be considered as confounding characteristics in studies on chemical exposures (Meyer-Baron et al., 2015). Age is of particular interest because duration and accumulation of exposure may correlate to age or years of work (Meyer-Baron et al., 2015). In addition, aging is correlated with neuromotor dysfunction and neurodegeneration (Lucchini et al., 2014). Although the neurotoxicity and pathways of chemical exposures may be different in children and adolescents than in adults, the exposures lead to the same long-term impairments. Gender and adolescence may also be important confounders, but there is a lack of data at this time (Meyer-Baron et al., 2015). Genetic susceptibility studies are becoming more common, but more work is needed for some classes of pesticides, metals, and VOCs.

The mechanisms of neurotoxicity are similar between some classes of pesticides, metals, and VOCs, as seen in Figure 4. Exposure to VOCs, metals, and pesticides may cause neuron demyelination or inhibit neurotransmitters (also caused by heat stress), resulting in neuropathy. Other pesticides inhibit gated ion channels in neurons. Inhibition of both gated ion channels and neurotransmitters can lead to repetitive nerve firing. Neuropathy may progress to musculoskeletal disorders and neurodegenerative diseases. VOCs and metals can cause demyelination in the temporal lobe or structural changes in the prefrontal cortex. These changes to the brain may result in cognitive or executive function impairment and may contribute to neurodegeneration. Consequently, repetitive nerve firing, neuropathy, structural changes in the brain, and neurodegeneration may all lead to injuries in the workplace. Of great concern, toxicants produce neurobehavioral impairment and structural changes in the brain before this toxicity can be detected clinically. Therefore, it is crucial to develop methods to detect preclinical levels of toxicity early. Methods like postural sway and exposure assessments are important in early detection and prevention of further toxicity.

A significant amount of research is needed to elucidate the precise mechanism by which VOC exposure leads to neurotoxic health effects. Research is needed to understand how VOC exposures lead to STFs and other injuries. For metals other than Mn, more work is needed on the association of metal toxicity and injury. There is also a great need for work on the effects of pesticides on female and adolescent workers. Women and adolescents may be more susceptible to pesticide exposure, but the data are not sufficient to support this claim. Research distinguishing pathways of chemical exposures and neuromuscular outcomes throughout the life course is needed to protect the workforce prior to the development of workplace musculoskeletal disorders. Although there is literature on visuospatial, olfactory, and motor control impairments due to metal exposures, there is almost no research linking these impairments to injury. There is a need for studies on mixtures of chemicals, not just mixtures of metals or pesticides but the combination of all potential sources of exposure in the workplace (Chin-Chan et al., 2015). For example, farmworkers may be co-exposed to metals and pesticides (e.g., Mn in fungicides; Quandt et al., 2010).

In the long term, there is a need for the development of comprehensive risk assessment modeling that is based on population-based studies and includes parameters for both physical and chemical exposures. Such data-driven predictive models could be based on regression methods and classification trees. These tools can then be used to investigate the relative contributions of individual exposure types (physical and/or chemical) in modifying functional outcomes that lead to injury.

In summary, there are certain environments where workers have to carry out their tasks during both physical and chemical exposures. This combination affects their functional outcomes, thereby increasing their injury risk. Through this review, we presented the need for a comprehensive and multidisciplinary approach to occupational injury research that goes beyond the assessment of traditional ergonomic physical exposures by also considering the role of chemical exposures.

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KEY POINTS

- Both physical and chemical exposures, alone and in combination, may impair functional outcomes, thereby increasing the risk of occupational injury, such as those resulting from slips, trips, and falls.
- To understand combined exposures and health effects, there are multiple research needs, such as better understanding mechanisms and identifying highly susceptible groups,
- To prevent further exposures or toxicity and associated negative health effects, it is important that methods (e.g., postural sway and comprehensive exposure assessments) are used for early detection.

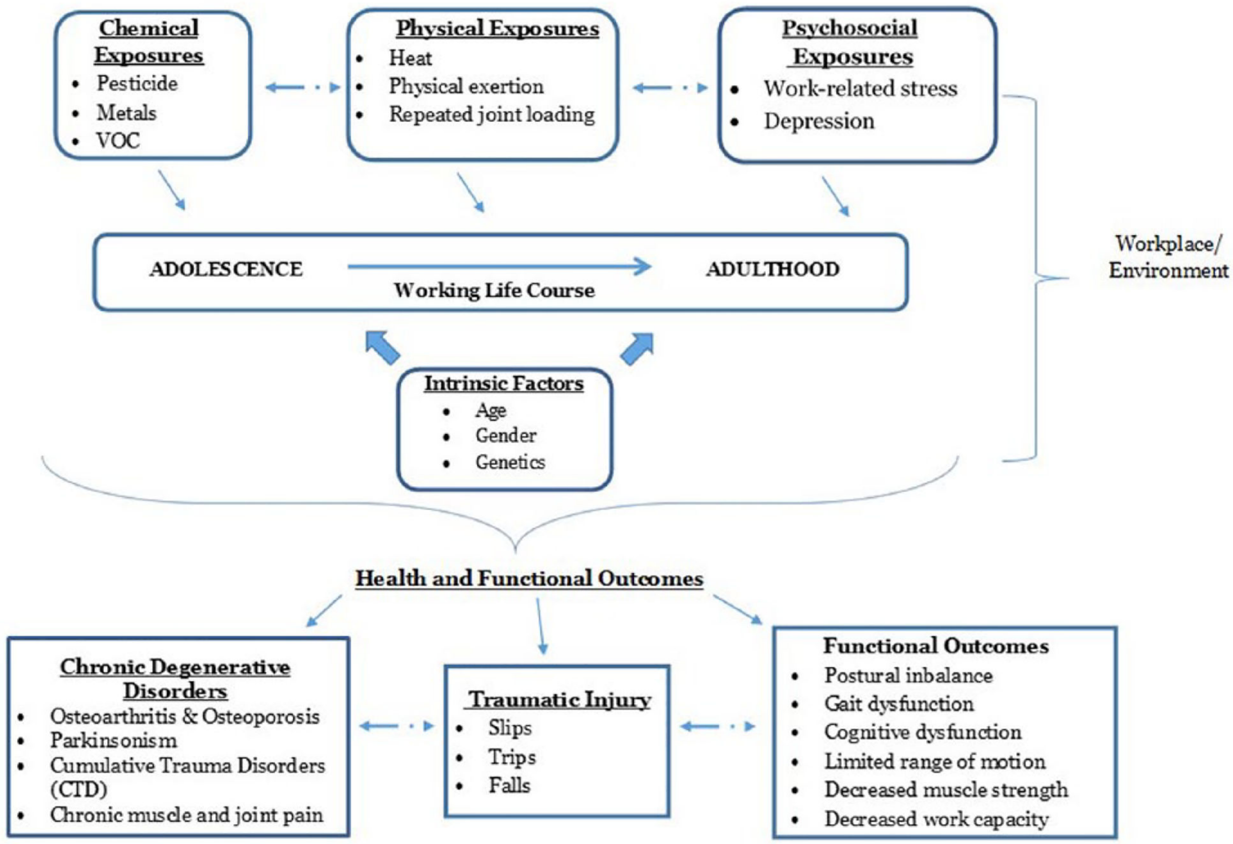

Figure 1.

Neurotoxic and physical exposures throughout the life course and their contribution to traumatic injury and degenerative disorders.

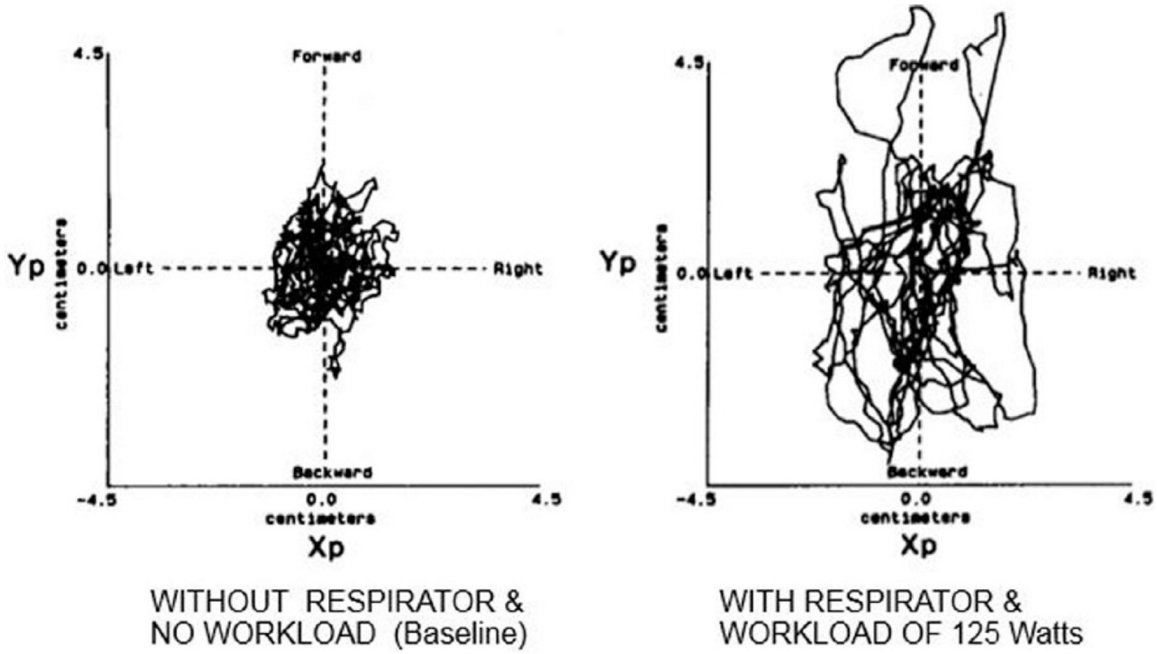

Figure 2.
Effect of full-face respirator under baseline and workload on postural balance (adapted from Seliga et al., 1991).

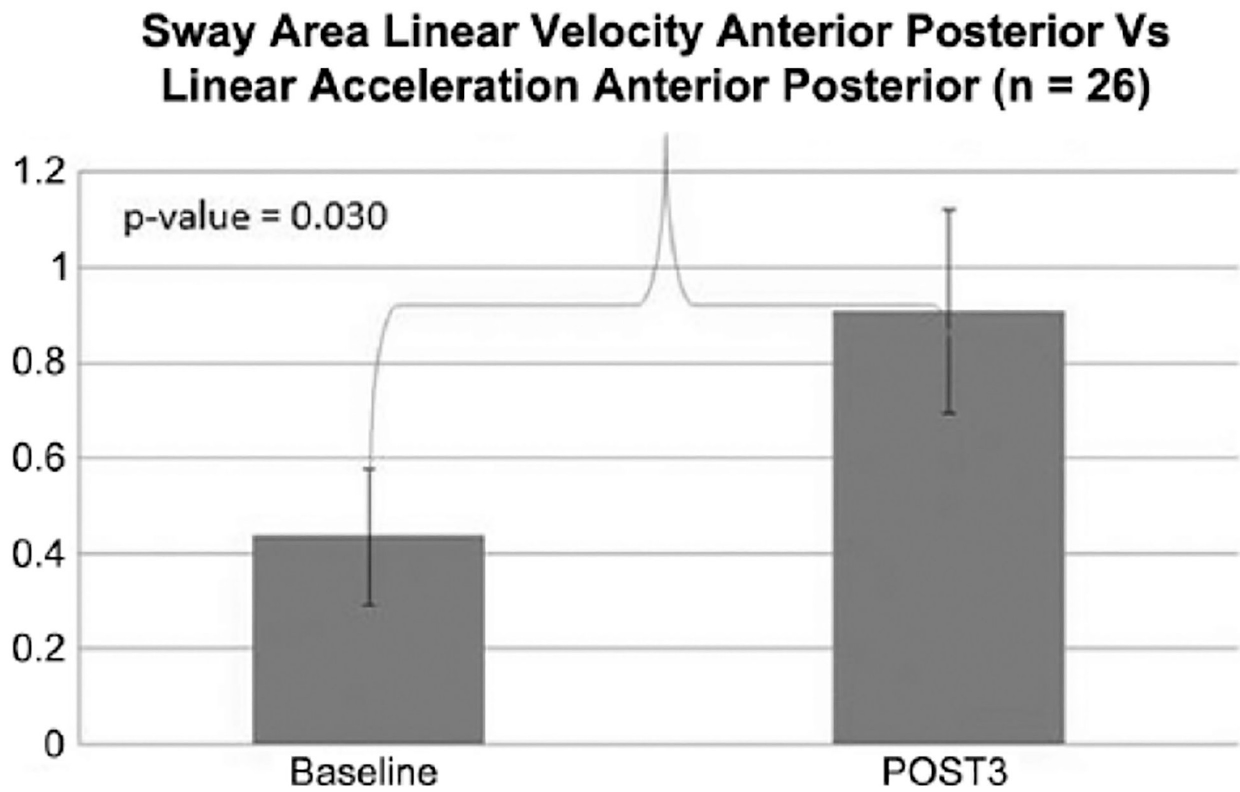

Figure 3.
Sway area plot of baseline (before firefighting) and after Scenario 3 (at the end of firefighting) (adapted from James, Mani, Kincer, & Bhattacharya, 2013).

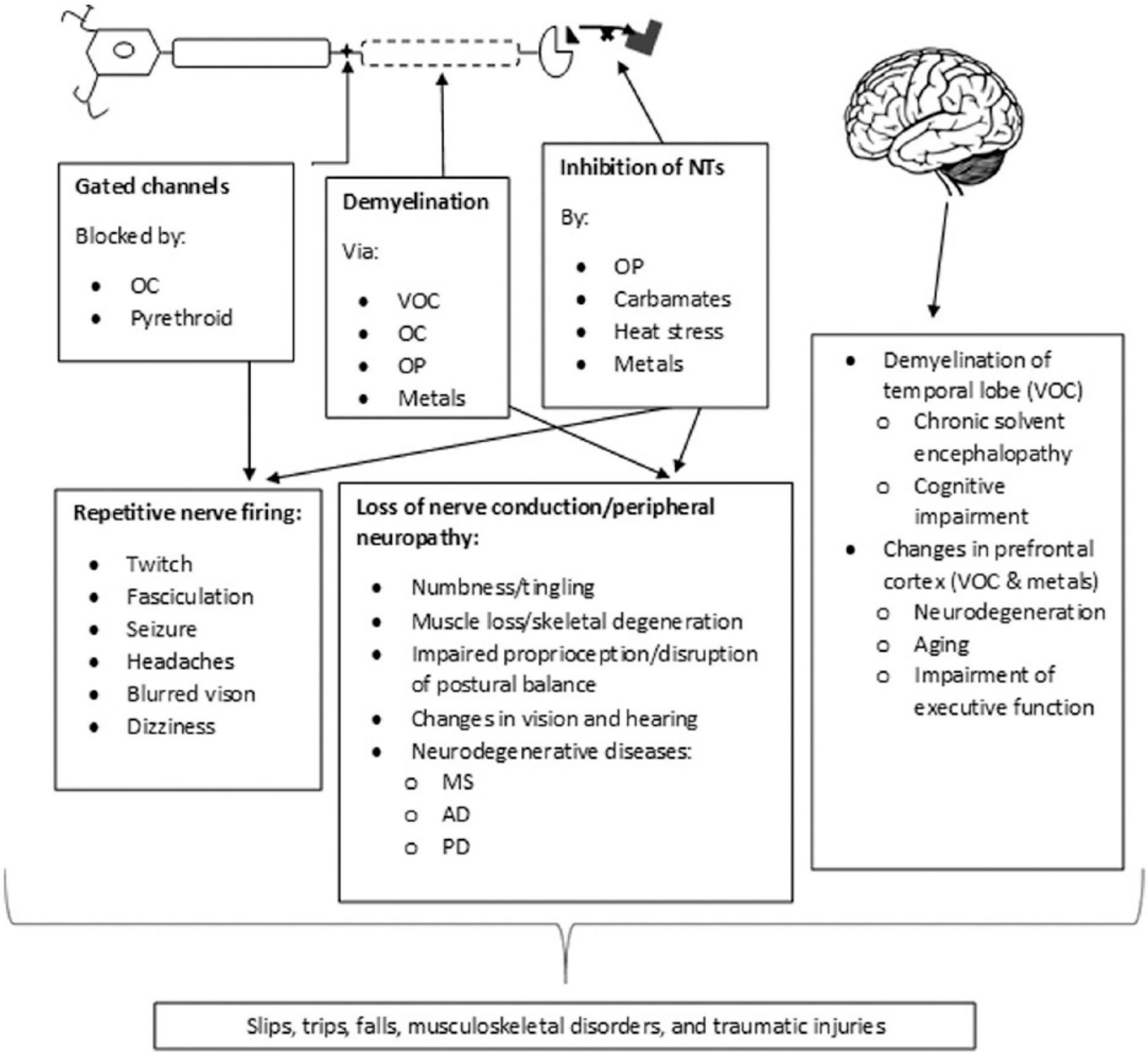

Figure 4.

Comparison of the mechanisms of neurotoxicity for pesticides, volatile organic compounds, metals, and heat stress.

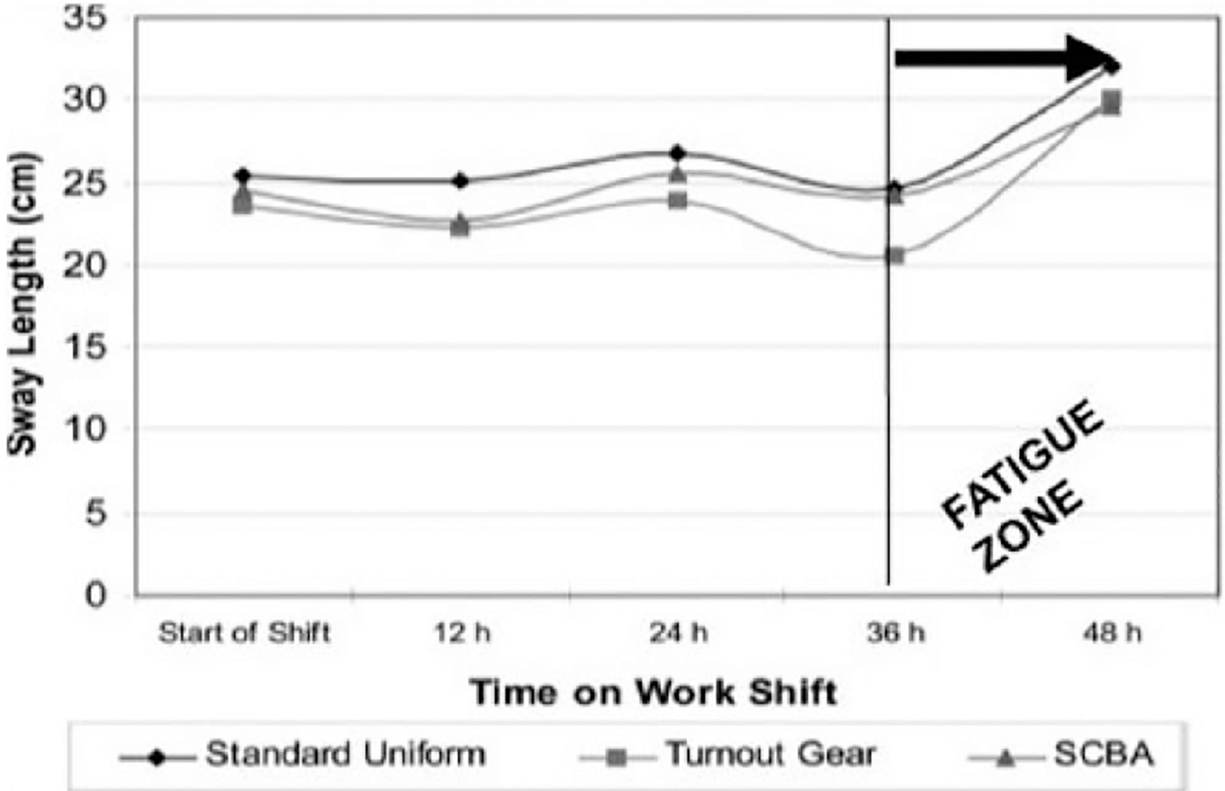

Figure 5.
Effect of long working hours on postural balance of firefighters and a solution. The figure shows association between long work hours and postural imbalance as fatigue builds up (adapted from Sobeih, Davis, Succop, Jetter, & Bhattacharya, 2006).