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Heavy Metals: From Physiological Basis to Psychological Outcomes

Aida ŞAHMUROVA

Antalya Bilim University, Faculty of Health Sciences, Department of Nursing
Antalya, Türkiye, aida.sahmur@antalya.edu.tr, ORCID ID: https://orcid.org/0009-0004-5287-8701

Mustafa Batuhan DEMİR

Antalya Bilim University, Faculty of Economics and Administrative Sciences, Department of Psychology

Antalya, Türkiye, batuhan.demir@std.antalya.edu.tr, ORCID ID: https://orcid.org/0009-0001-0778-1853

Özet

Bu çalışmada ağır metallerin insan sağlığına olan fizyolojik ve psikolojik etkileri incelenmiştir. Ağır metallerin insan sağlığına eser miktarda faydalı oldukları gibi yüksek konsantrasyonlarda organizmada ciddi sorunlar oluşturmaktadırlar. Oksidatif stres, reaktif oksijen türlerinin (ROS) oluşumu, kanser türleri (göğüs, prostat, akciğer, böbrek, kemik, karaciğer kanseri), çeşitli organ sorunları (karaciğer fibrozis, akciğer inflamasyonu, KOAH), hematopoetik sistem hasarı ve kardiyak hastalıklar buna bir örnektir. Ayrıca konsantrasyonu yüksek olan ağır metaller insan psikolojisini de olumsuz yönden etkilemektedir. Ağır metaller nörotoksik etkilere sahip olup bazı hastalıkları direkt ve indirekt etkilemektedir. Böyle ki, Alzheimer, Parkinson, otizm spektrum bozukluğu veya dikkat eksikliği ve hiperaktivite bozukluğu gibi rahatsızlıkları tetikleyebilmektedirler. Aynı zamanda, depresyon, anksiyete, psikotik semptomlar, uyku bozuklukları veya huzursuzluk ağır metallere maruz kalmış insanlarda görülebilmektedir. Sonuç olarak konsantrasyonu yüksek olan ağır metal birikimi, bireyler üzerinde hem psikolojik hem de fizyolojik olumsuz ve ciddi hasarlara yol açmaktadır.

Anahtar Kelimeler: Ağır Metaller, Fizyolojik Etkiler, Psikolojik Etkiler

Ağır Metaller: Fizyolojik Temelden Psikolojik Sonuçlara

Abstract

In this study we aim to examine physiological and psychological effects of heavy metals on human health. As well as trace elements have beneficial impacts on human health, they present serious problems at high concentrations. Oxidative stress, reactive oxygen species (ROS) generation, cancers (Breast, prostate, lung, kidney, bone, liver cancer), several organ problems (liver fibrosis, lung inflammation, COPD), hematopoietic system damage, cardiac diseases are examples for heavy metal toxicity. Furthermore, heavy metals at elevated concentrations impact human psychology. Alzheimer’s disease, Parkinson’s disease, autism spectrum disorder, or attention deficit and hyperactivity disorder can be manifested by heavy metal toxicity. In addition, depression, anxiety, psychotic symptoms, sleep disorders, or restlessness can be present in individuals with heavy metal toxicity. In conclusion, heavy metal accumulation can lead serious physiologic and psychologic impacts on human beings.

Keywords: Heavy Metals, Physiological Outcomes, Mental Outcomes,

1. Introduction

Heavy metals are characterized as elements which have five or higher density, and by their atomic weight, that have influences on people and environment such as iron (Fe), mercury (Hg), zinc (Zn), arsenic (As), chromium (Cr), cadmium (Cd), copper (Cu), manganese (Mn) (Wang et al., 2021). Heavy metals present in two different resources, which are natural- manifests in nature-, and anthropogenic- influenced by people-, which may be counted as most common polluting aspect of heavy metals due to such human activities, for example, mining, agricultural works, smelting, industrialization, metal-including waste, military works, building materials, smokes (Sahmurova & Balkaya, 2016). Humans are exposed heavy metals through inhalation, ingestion, and skin absorption (Sahmurova et al., 2010). As industrialization has shown rapid increase, such as foundries, oil refineries, petrochemical plants, pesticide manufacturing, or chemical industry danger of exposure have been also increased; furthermore, for example, arsenic-contained industries, such as paper, glass, textile, or wood industries can be considered as examples of heavy metal exposure and heavy metals, as the exposure is common over time, have become major apprehension due to their bio-toxic effects on humans, and polluting effects on environment (Ohigau et al., 2022). Heavy metals may enter into human body through various ways; such metals are crucial and beneficial for human body, for example, Fe, Zn, Cu, and Mn, however, high exposure of these metals also can disrupt overall health (Sahmurova & Shahmurzada, 2016).

In this study, we aim to investigate physiologic and mental adverse outcomes of 12 heavy metals which are vital heavy metals for human health- iron (Fe), manganese (Mn), copper (Cu), cobalt (Co), and toxic heavy metals- cadmium (Cd), arsenic (As), mercury (Hg), lead (Pb).

2. Beneficial Heavy Metals for Human Health

Some of these metals are vital for physiological functioning for human beings, such as Fe. Fe is considered to be essential for health in order to its benefits on health, first of all, body needs iron for synthesis of oxygen transport proteins, hemoglobin and myoglobin; furthermore, Fe is also crucial for heme and other iron-dependent prosthetic groups' formation (Abbaspour et al., 2014); brain's developmental process, myelination, or metabolism and synthesis of neurotransmitters also are considered to be the role of iron (Sahmurova et al., 2025). Secondly, Mn is also crucial for human health by its role in oxidative stress, anti-oxidant status, mitochondrial function, bone formation, regulation of blood sugar levels, growth and development, and neurotransmitter synthesis; and we can also mention about its role in several biochemical activities, such as, lipid, protein, and carbohydrate metabolism (Obeng et al., 2024). After that, Cu is also required and significant for health. Among the roles of Cu, they can be mentioned as growth and development, respiration, eradication of free radicals, energy production, connective tissue formation, oxygen and iron metabolism, normal metabolic process including amino acids and vitamins, (Chellan & Sadler, 2015). Another vital element is Co which serves as a piece or component of vitamin B12. Strengthening immune response, demonstrating antibacterial activity, DNA synthesis, production of red blood cells, synthesis of amino acids, normal brain and nerve functioning, and production of neurotransmitters can be added as Co role in human body (Batyrova, 2024).

3.Adverse Physiological Effects of Heavy Metals

Even though these metals are required for human body and its functioning, excessive amount of absorption of these heavy metals may cause emergence of several physiological problems. First of all, Excessive Fe accumulation- iron overload can be genetic or acquired- on the body can cause such problems, for example, liver fibrosis, cirrhosis, cardiac issues, impairment in pancreas function, diabetes, cancer, or several neurodegenerative disorders (Wessling-Resnick, 2017). Lönnerdal (2017) posit that iron overload in infants and young children may cause impairment in growth; furthermore, he suggested that iron interactions with copper and zinc also causes several problems, such as decreased developmental functioning and changed gut microflora (Lönnerdal, 2017). Also, Sulais et al. (2020) indicated that iron poisoning, in first 6h, may cause abdominal pain, diarrhea, vomiting, gastrointestinal bleeding, and even can cause, because of blood and fluid loss, hypovolemia. They also mention cytotoxicity that is related with exposure of substantial iron leading diminished mitochondrial function and oxidative phosphorylation that may cause cell death (Sulais et al., 2020). Mn also has negative impacts of human health. It has also adverse effects on individuals when humans are exposed Mn excessively, such as reproductive issues, immunological dysfunction, mutagenicity, carcinogenicity, muscular pain (Das et al., 2014). Thirdly, Cu's impact of human health also mentioned. The benefits of Cu when its level is when it is absorbed trace amount; however, excessive Cu accumulation in human body can cause liver metabolism disorders, increased free radical formation, and development of central nervous system disorders (Claus, 2020). Impacts of Cu poisoning may lead gastrointestinal issues, nausea, vomiting, abdominal pain, red blood cell destruction, liver toxicity, kidney damage (Mahurpawar, 2015). Elevated Cu levels in body have been indicated as risk factor for cardiovascular diseases, cancer, and lymphoma (Bost et al., 2016). Moreover, excessive Co aggregation may cause several health issues. Gregorowicz & Pajchel (2025) suggest that massive amount Co exposure emerges risks of cardiovascular, hematopoietic, and thyroid systems. Elevated levels of cobalt exposure have been investigated; tumors in airways, lung cancer, cardiomyopathy, nervous system problems, and endocrine system problems were indicated as consequences of cobalt exposure (Batyrova, 2024).

However, several heavy metals are not required for life and have only toxic effects for individuals. Cd is indicated to be mostly accumulated in kidneys; a study conducted by Lech & Sadlik (2017) revealed that lowest Cd accumulation was found to be brain (0.02 µg/g), and highest accumulation was observed in kidneys (16.0 µg/g). Toxic effects of Cd are wide; several studies have posited that Cd is defined as carcinogenic (Kim et al., 2020). Cd may contribute the likelihood of kidney, breast, liver, hematopoietic system, bladder and pancreatic cancers (Derkacz et al., 2024). Li et al. (2019) revealed a link between Cd toxicity and cardiovascular diseases in a study with 4.304 middle-aged males and females, and they suggested the mechanistic link between smoking and cardiovascular pathologies is partially explained by cadmium exposure. Other toxic metal is Hg. One of the ways exposing to Hg is dietary including seafood. It does not always cause high levels of exposure, however, deaths or adverse health outcomes due to ingestion have been mentioned. Inhalation is another way causing tremors, neuromuscular changes, headaches, and kidney thyroid problems (Mahurpawar, 2015). Moreover, low heart rate, inclined myocardial infraction risk, hypertension, atherosclerosis, or other cardiac issues are suggested to be cause of cardiotoxicity as a result of Hg exposure (Genchi et al., 2017). The other vulnerable part of human to Hg is suggested to be pulmonary system, and, in order to mercury vapor inhalation, lung inflammation, difficulty in breath, asthma, or chest pain can be seen in exposed individuals (Bjorklund et al., 2018). Additionally, Pb is defined as a toxic element for environment, animals, and humans. It is suggested that Pb aggregate in bones, liver, and kidneys, and, young people, and pregnant woman are vulnerable population for the adverse effects of Pb. (Wani et al., 2015). One pathology that is mentioned as a result of Pb exposure is atherosclerosis, and it was mentioned to be a stimulator for cardiovascular diseases' development (Ilyas & Shah, 2016). Cancers also suggested to be related with Hg toxicity including brain, kidney, bladder, colon, and rectum cancers (Mahurpawar, 2015). The other toxic element is As which can cause instant toxic effects, for instance, severe vomiting, blood and circulation impairment, nervous system damage, reduction in red blood cell production, liver enlargement, brain damage, renal damage, and death (Mahurpawar, 2015).

4. Psychological Effects of Heavy Metals

As well as there are physiological effects of heavy metal exposure, there are psychological side of the toxicity of these elements. Excess brain Fe is suggested in cognitive impairment especially by catalyzing oxidative stress via Fenton's reaction leading to damage to cellular components causing neuronal death. This process is exacerbated by neuroinflammation, the iron-dependent cell death pathway of ferroptosis, and increased iron uptake due to blood-brain barrier dysfunction in neurodegenerative disease, such as Alzheimer's disease, Parkinson's disease, and prion disease (Spence et al., 2020). Excessive Fe intake was associated with cognitive dysfunction, impaired executive function, and psychomotor retardation which may lead panic disorders, generalized and social anxiety disorders, and depression (Sahmurova et al., 2025). Hypothyroidism, that is caused by excessive Fe uptake, is thought to lead such psychological symptoms, for instance, depression, restlessness, agitation, brain fog, loss of appetite, sleeping problems, or anxiety or anxiety signs which are sweats, tension, or irritability (Samuels & Bernstein, 2022). Sleep problems, due to toxicity, Sahmurova & Bakan Kıraç (2022) mentioned that, can cause such problems, for instance, headache, eating problems, anxiety, anger, overreacting, restlessness.

Equally important, multiple studies indicated a cognitive deficit both adults and pediatric population as a result of low and high Mn absorption by body (Vollet et al., 2016). Several studies also posit the link between Mn toxicity and such diseases, for instance, Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, and prion disease (Martins et al., 2020). Growing evidence indicates that Mn exposure's negative effect impacts, as developing brain is vulnerable to Mn toxicity, intellectual function, cognition (e.g., memory impairment, lower intelligence quotient), and behavior- including anxiety and depression- of developing children (Iyare, 2019; Lucchini et al., 2017).

Moreover, the contribution of Cu on psychological well-being were several times indicated. As a result of Cu poisoning, fatigue can be seen in individuals due to impaired neurotransmitters in nervous system (Faazal et al., 2023). In addition, depression was also linked with high levels of Cu in the body; and also, due to Cu's ability to reduce tissue manganese levels, can cause depression in highly exposed individuals (Anant et al., 2018). Psychiatric manifestations in Cu poisoning were reported to be wide; personality change, anti-sociality, aggression, sleep problems, depression, anxiety, and psychotic symptoms are examples of psychological impact of elevated Cu exposure (Manchia et al., 2024). In a study conducted in Bangladesh with male and female adults revealed that, individuals with generalized anxiety disorder have elevated levels of serum copper (Islam et al., 2013).

Furthermore, there is growing evidence suggesting that Co exposure may affect brain directly, such as neurotoxicity; tremors, coordination problems, mood disturbances, cognitive impairment, hearing and visual issues are thought to be neurological symptoms that individuals experience due to cobalt toxicity (Catalani et al., 2012). In addition, in studies conducted with hip arthroplasty patients revealed that failure in these operations can cause cobalt toxicity resulting in mood disorders, anxiety, sleep disorders, hallucinations, and cognitive decline (Pallavi et al., 2024). Furthermore, Tudoise et al. (2017) indicated that Co may manifest psychological and neurobehavioral symptoms and can present ADHD like symptoms.

Besides the psychological impacts of vital elements, toxic heavy metals may contribute the emergence of several psychological problems. Neurological and psychological impacts of Cd exposure have been investigated; besides damaging nervous system, Cd can go through blood-brain barrier (BBB), accumulate in brain, and may impair brain health directly (Lata & Mishra, 2019). In addition to neurologic issues, Liu et al. (2019) posited that huge numbers of children cannot complete their neurologic development due to several problems suggesting that one of them is Cd exposure. Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, olfactory dysfunction, parkinsonian-like symptoms, impaired vasomotor functioning, mental retardation, learning disabilities, dyslexia, and peripheral neuropathy are some of the mentioned problems due to Cd-induced neurotoxicity (Liu et al., 2019; Wang & Du, 2013). Depression is one of the highly linked mental issues with Cd exposure. Scinicariello et al. (2015) found that elevated blood Cd levels increase likelihood of developing depressive symptoms; Nguyen et al. (2022) revealed that 2-fold increase in serum Cd levels linked with 21% incline in likelihood of depression.

In addition, psychological side of Hg toxicity have been proposed multiple times; Santos-Lima et al. (2020) performed a Hg exposure analysis in children with hair samples, and, revealed that elevated levels of HgH associated with diminished neuropsychological performance on Estimated and Verbal IQ assessed by WASI; another study correlated high Hg levels with ASD (Sulaiman et al., 2020); and there is growing evidence suggesting that there is a link between Hg exposure and ADHD (Huang et al., 2016). Yoshimasu et al. (2014) posited that there is an incline in ASD risk by 1.7 times, and, there is also incline in ADHD risk by 1.6 times due to Hg exposure. Hg toxicity can lead prolonged damage to fatal neurodevelopment; through utero or breast milk has been linked with impairments in learning, lower IQ, ADHD, mental retardation, and ASD (Oliveira et al., 2018). In some studies, furthermore, Hg exposure associated with depression and anxiety; in a study conducted by Kim et al. (2020) revealed that depression in Korean women positively correlated with elevated levels of blood mercury.

Furthermore, Pb exposure, even at low levels, as a result of its capability of crossing placenta and blood-brain barrier, shows neurotoxic qualifications, affects nervous system, may disrupt neurodevelopment, can negatively alter neurobehavioral functions, may cause neurodegenerative diseases such as Alzheimer’s disease, or Parkinson’s disease, and impairs cognition and neurobehaviors for example, in children, problems in motor skills, impaired executive functions, decreased learning, or attention can be seen (Charkiewicz et al., 2023). Psychiatric pathologies are also connected with Pb levels; Pb exposure is mentioned to cause harm for brain and cause several psychological manifestations; blood Hg levels are positively associated with development of depression and anxiety (Buser & Scinicariello, 2017). Pb exposure in children, or prenatal and postnatal exposure to Pb, is associated with ADHD (Gari et al., 2022). Due to brain and nervous system effects, and cognitive adverse outcomes of some intellectual disorders, such as dyslexia, lower intelligence quotient, and specific learning disorders, are associated with Pb toxicity (Ebadi et al., 2025). Implicitly, a newborn who has special needs may cause family to experience severe stress and anxiety leading several psychologic problems (İşbilir & Sahmurova, 2024).

Over the years, mental impacts of As exposure have been investigated. As is suggested to be having neurotoxic effects causing, cognitive decline, neurodevelopmental issues (e.g., cognitive impairment, learning problems. Furthermore, due to its triggering effect on brain inflammation and oxidative stress, it can damage brain cells. Neurodegenerative disorders, Alzheimer’s disease, or Parkinson’s disease, are also suggested to be caused by As toxicity (Tian et al., 2025). Furthermore, it is indicated that As can be a risk factor for ADHD (Roy et al., 2011). In addition to ADHD, Ding et al. (2023) observed elevated levels of As and Hg in the urine test of ASD group comparing the healthy group, suggesting that heavy metals may play different role in ASD emergence or progression. Sharma & Kumar (2019) mentioned that exposure to As may lead impairment in both central nervous system and peripheral nervous system leading depression, memory decline, problem solving difficulty, and difficulty in body coordination. Moreover, Wu et al. (2017) reported that, in a study about As-induced acute psychosis, individuals have had severe symptoms, which were obsessive compulsive symptoms, psychosis, and hallucinations.

5. Conclusion

In this study we aimed to investigate the physiological and psychological impacts of heavy metals (Fe, Mn, Cu, Co, Cd, Hg, Pb, As,). Our findings revealed that while certain metals are essential micronutrients necessary for fundamental life processes, such as oxygen transport (Fe), enzyme activity (Mn, Cu), and nervous system function (Co), their beneficial effects are dose-dependent and limited to trace amount. Physiologically, heavy metal toxicity is mediated by their ability to induce oxidative stress and generate Reactive Oxygen Species (ROS). This results in direct damage to DNA, proteins, and lipids, leading to cellular dysfunction and death. Key physiological manifestations include organ damage. Sever toxicity is consistently linked to dysfunction in major organs, for example, liver (fibrosis, hepatotoxicity), kidneys (nephrotoxicity, chronic kidney disease), and cardiovascular system (hypertension, atherosclerosis, cardiomyopathy). Moreover, many heavy metals, notably Cd, Hg, Pb, and As are classified as carcinogens, increasing the risk for cancers in the lung, bladder, liver, and prostate. Furthermore, considering systemic disruption, heavy metals interfere with the hematopoietic system (e.g., anemia due to Pb and Cd exposure), reproductive health (fertility issues, developmental delays), and endocrine balance (e.g., thyroid dysfunction from Fe and Hg). In addition, the psychological adverse outcomes are particular profound, stemming from the heavy metals' ability to penetrate the blood-brain barrier (BBB) and exert neurotoxic effects. The mechanisms include direct neuronal damage, disruption of neurotransmitter systems (cholinergic, dopaminergic, serotoninergic), neuroinflammation, and acceleration of pathological processes characteristic of neurodegenerative diseases. In addition, strong associations were found between heavy metal exposure and pathogenesis of Alzheimer's disease, Parkinson's disease, and other neurodegenerative disorder (e.g., excess Fe, Mn, Cd). Concomitantly, heavy metal exposure, particularly prenatal and early-life, is a recognized risk factor for autism spectrum disorder (ASD) and attention deficit and hyperactivity disorder (ADHD) (e.g., Hg, Pb, As, Tl). Additionally, elevated heavy metal levels are repeatedly correlated with a spectrum of mental health issues, including depression, anxiety, psychotic symptoms, sleep disorders, and cognitive impairment. In conclusion, the cumulative evidence suggests that heavy metal toxicity is a significant public health concern with widespread implications for both physical and mental well-being. Their pervasive presence in the environment and occupational settings, coupled with the body's limited capacity to safely manage excess levels, results in a devastating impact on human health, both physiologically and psychologically.

6. Suggestions

As a matter of environment pollution, heavy metals are one of the factors that affect human health negatively. As suggestions, for future studies and prevention strategies;

(1) future researches should focus on delineate accurate, uniformly applicable threshold levels for vital heavy metals in various biological metrices;

(2) furthermore, subsequent investigations also should implement advanced multi-omics approaches to fully map the molecular pathways by which heavy metals, particularly those with neurotoxic characteristics, breach the blood-brain barrier and cause neurodegenerative and psychiatric manifestations. This will promote the identification of novel biomarkers for early detection and clinical intervention;

(3) additionally, considering the strong relations established between heavy metal toxicity and various neuropsychiatric symptoms, clinical studies are necessitated to evaluate the effectiveness and safety of targeted chelation therapies or nutritional interventions aimed at mitigating internal load of toxic metals as an complementary therapy for these conditions;

(4) moreover, practitioners, especially in primary care and specialized fields (e.g., pediatrics, neurology, psychiatry), ought to evaluate heavy metal surveillance as part of the clinical evaluation for patients exhibiting idiopathic neurodevelopmental delays, complex neuropsychiatric symptoms, or occupational/environmental risk factors. This mandates enhanced professional development for healthcare providers on the varied presentations of heavy metal poisoning;

(5) then, legislators should utilize the evidence of adverse psychological and physiological outcomes to establish and stringently apply stricter regulations on heavy metal effluents from industrial sectors (e.g., mining, smelting) and common consumer products. Population health

initiatives should prioritize decreasing common pathways of exposure, such as contaminated water and particular food sources;

(6) lastly, prospective cohort studies are required to follow the enduring psychological and well-being sequelae for individuals who have been subjected long-term exposure to heavy metals, even at low concentrations. Studies should investigate determinants that foster psychological resilience in impacted communities, which could inform mental health interventions.

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