UNIVERSITI PUTRA MALAYSIA

EVALUATION OF NEUROBEHAVIORAL AND NEUROTOXICITY EFFECTS OF CHRONIC EMBRYONIC HEAVY METAL EXPOSURE ON ZEBRAFISH (Danio rerio F. HAMILTON, 1822) LARVAE

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By

NORAINI BINTI ABU BAKAR

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the degree of Master of Science

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Master of Science

EVALUATION OF NEUROBEHAVIORAL AND NEUROTOXICITY EFFECTS OF CHRONIC EMBRYONIC HEAVY METAL EXPOSURE ON ZEBRAFISH (*Danio rerio* F. HAMILTON, 1822) LARVAE

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May 2017

Chair: Wan Norhamidah Wan Ibrahim, PhD
Faculty: Science

Occurrence of industrialization without environmental care lead to heavy metals [Mercury chloride ($HgCl_2$), Arsenic trioxide (As_2O_3)] contamination and caused adverse effects to human, especially vulnerable to developing fetus and children. Developmental exposures to heavy metals have been linked to impair motor and cognitive functions. However, the gap of knowledge to link between developmental exposure to heavy metal and neurodevelopmental disorders are still present. Thus, we used zebrafish to demonstrate the neurobehavioral and neurotoxic effects associated with the chronic embryonic exposure to low concentration of mercury and arsenic in a nanomolar to micromolar concentrations. The embryos were exposed to different range of $HgCl_2$ (7.5-250 nM) and As_2O_3 (20-50 µM) starting from 5 hpf until 72 hpf (hatching) in a semi-static condition. The mortality rate was increased in a dose dependent manner for both neurotoxicants. Exposure to 100 nM $HgCl_2$ and 30 µM As_2O_3 decreased the number of tail coilings, heartbeat, and swimming activity. The adverse effects of heavy metals on the development of anxiety-related behavior were assessed in 6 dpf larvae. No changes in thigmotaxis upon $HgCl_2$ and As_2O_3 exposure were found. Yet, $HgCl_2$ exposures reduced swimming speed and elicit resting while As_2O_3 exposure does not elicit any significant changes. Furthermore, aversive stimulation used to provoke anxiety responses also does not elicit any changes in thigmotaxis and avoidance response for both neurotoxicants. Overall, alteration in motor and anxiety responses were also linked with the increased apoptosis assessed at different time points. The peaks were shifted for both neurotoxicants whereby reaching an early peak at 24 hpf as compared to the control (72 hpf). Exposure to both neurotoxicants affects biochemical status (proteins, lipids, carbohydrates and nucleic acids) of the zebrafish larvae. These results showed that $HgCl_2$ and As_2O_3 exert its toxic effects at cellular and biochemical level that leading to alteration at behavioral level.

Keywords : zebrafish; mercury chloride; arsenic trioxide; locomotor; anxiety

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Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
Sebagai memenuhi keperluan untuk ijazah Sarjana Sains

PENILAIAN KESAN TINGKAHLAKU-NEURO DAN NEUROTOKSIK AKIBAT DEDAHAN KRONIK LOGAM BERAT TERHADAP LARVA ZEBRAFISH (*Danio rerio* F. HAMILTON, 1822)

Oleh

NORAINI ABU BAKAR

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Aktiviti perindustrian tanpa menitikberatkan penjagaan alam sekitar menyumbang kepada pencemaran logam berat [Merkuri klorida ($HgCl_2$), Arsenik trioksida (As_2O_3)] dan menyebabkan kesan buruk kepada manusia terutama kepada perkembangan janin dan kanak-kanak. Dedahan jangka panjang kepada logam berat telah dikaitkan dengan kemerosoton fungsi motor dan kognitif. Walau bagaimanapun, jurang pengetahuan untuk menghubungkaitkan antara dedahan logam berat dan gangguan perkembangan-neuro masih lagi wujud. Oleh itu, kami menggunakan zebrafish untuk mengkaji kesan tingkah laku-neuro dan neurotoksik akibat dedahan kepada merkuri dan arsenik pada kepekatan rendah secara kronik dari kepekatan nanomolar sehingga kepekatan mikromolar. Embrio didedahkan kepada kepekatan berbeza $HgCl_2$ (7.5-250 nM) dan As_2O_3 (20-50 µM) bermula dari 5 hpf sehingga 72 hpf (penetasan) dalam keadaan semi-statik. Kadar kematian telah meningkat sejajar dengan peningkatan dos untuk kedua-dua neurotoksikan. Dedahan 100 nM $HgCl_2$ dan 30 µM As_2O_3 mengakibatkan penurunan bilangan pusingan ekor, degupan jantung, dan aktiviti renang. Kesan buruk logam berat kepada tingkah laku kebimbangan dilakukan pada larva berumur 6 dpf. Tiada perubahan dalam thigmotaksis ditemui selepas larva didedahkan dengan $HgCl_2$ dan As_2O_3. Namun, dedahan $HgCl_2$ menyebabkan penurunan kelajuan renang dan peningkatan tingkah laku rehat manakala dedahan As_2O_3 tidak menghasilkan perubahan yang ketara. Tambahan pula, simulasi aversif yang digunakan untuk menguji tindakbalas kebimbangan juga tidak menghasilkan perubahan terhadap thigmotaksis dan tindakbalas mengelak untuk kedua-dua neurotoksikan. Secara keseluruhan, perubahan fungsi motor dan tindakbalas kebimbangan juga dikaitkan dengan peningkatan apoptosis yang dinilai pada masa yang berbeza. Kedua-dua neurotoksikan mengakibatkan perubahan posisi puncak apoptosis di mana puncak apoptosis dicapai lebih awal pada 24 hpf berbanding kawalan yang mencapai puncak apoptosis pada 72 hpf. Dedahan kepada kedua-dua neurotoksikan turut memberi kesan terhadap status biokimia (protein, lipid, karbohidrat dan asid nukleik) larva zebrafish. Penemuan ini membuktikan bahawa $HgCl_2$ dan As_2O_3 memberi kesan toksik pada peringkat selular dan biokimia yang juga membawa kepada perubahan di peringkat tingkah laku.

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Kata kunci: zebrafish; merkuri klorida; arsenic trioksida; lokomotor; kebimbangan

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I certify that a Thesis Examination Committee has met on 4 May 2017 to conduct the final examination of Noraini binti Abu Bakar on her thesis entitled "Evaluation of Neurobehavioral and Neurotoxicity Effects of Chronic Embryonic Heavy Metal Exposure on Zebrafish (*Danio rerio* F. Hamilton, 1822) Larvae" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
As_2O_3	Arsenic trioxide
ADHD	Attention Deficit Hyperactivity Disorder
ASD	Autism spectrum disorder
$CaCl_2$	Calcium chloride
$^{\circ}C$	Celsius
CNS	Central Nervous System
dpf	Day post fertilisation
DNT	Developmental Neurotoxicity Testing
Na_2HPO_4	Disodium phosphate
g/cm^3	Gram per cubic centimetre
g/L	Gram per litre
hr	Hour
hpf	Hour post fertilisation
kg	Kilogram
$HgCl_2$	Mercury (II) chloride
$MgSO_4$	Magnesium sulphate
MeHg	Methylmercury
µg	Microgram
µg/L	Microgram per litre
µm	Micrometer
µM	Micromolar
mg/kg	Milligram per kilogram
mg/L	Milligram per litre
mM	Millimolar
min	Minute
KH_2PO_4	Monopotassium phosphate
ng/g	Nanogram per gram
nM	Nanomolar
PNS	Peripheral nervous system
pM	Picomolar
KBr	Potassium bromide
KCl	Potassium chloride
s	Second
$NaAsO_2$	Sodium arsenite
$NaHCO_3$	Sodium bicarbonate
NaCl	Sodium chloride
SEM	Standard Error Mean
t	Time

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CHAPTER 1

INTRODUCTION

Mental health problems are projected contributing to 16.8% of the global burden diseases (WHO, 2006). Currently, Ministry of Health Malaysia reported that mental health problems keep growing in Malaysia which also affecting children (KKM, 2015), of particular interest anxiety. The prevalence of the anxiety disorders is increasing worldwide, which the etiology is currently unknown. The interference of the normal developmental processes in the central nervous system (CNS) at early stage have been suggested as one of the factors leading to anxiety disorders (Pamphlett, 2014; Ng et al., 2013; Berk et al., 2011; Yorifuji et al., 2011). The developing CNS is exclusively sensitive to environmental pollutants as compared to adults (Lohren et al., 2015; McKean et al., 2015; Ho et al., 2013). Prenatal exposures to heavy metals have been associated with increased risk of aggression, depression and behavioral alterations later in life (Guilarte et al., 2012). Even worst, the emergence of large scale industrial activities over the last decades have introduced massive amounts of new chemicals into the environment which led to greater risks of chemical exposure to human. Apparently, these chemicals and other thousand chemicals available in the commerce are lacking extensive developmental neurotoxicity testing (DNT) data that are crucial for the risk assessment process for the human (Smirnova et al., 2014; Grandjean & Landrigan, 2006).

In the general population, human can be exposed to different forms of mercury and arsenic through the contaminated air inhaled, drinking water, food consumed and cosmetics contaminated with heavy metals (Perez et al., 2017; Ellingson et al., 2014; Holmes et al., 2009; Clarkson et al., 2003). The fact that different forms of mercury and arsenic have the ability to accumulate within the human body, and the developing nervous system is highly sensitive throughout the gestational period, even minute exposure to the inorganic or organic heavy metals can pose persistent harmful effects to the developing nervous system (ATSDR, 2007; WHO, 2003). Noteworthy, the biological barriers (blood brain barrier, placental barrier) are unable to protect the developing nervous system from neurotoxicity effects of heavy metals. Several epidemiological studies showed that embryonic exposure to mercury can produce detrimental effects on cognition and psychomotor functions in the children from infancy to adolescence (Bellinger et al., 2016; Debes et al., 2006) while exposure to arsenic caused deficit in IQ, loss of motor functions and developed neuropsychiatric disorders (Yorifuji et al., 2016; Nahar et al., 2014). Supporting this, experimental evidences in animal models have shown that exposure to mercury (Huo et al., 2015; Teixeira et al., 2014; Smith et al., 2010) and arsenic (Mao et al., 2016; Wu et al., 2016) during developmental stages caused neurocognitive and emotional dysfunctions. However, the adverse effects due to exposure at low concentrations which are more environmentally relevant and associated with the neurodevelopmental dysfunctions are currently scarce. Although rodents have been traditionally used as an animal model for DNT testing,

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though, it is proven laborious, high cost for large scale screening and incompatible to study the effects of chemicals at low concentrations for long term period, thus caused little progress in the DNT testing.

Therefore, there is recognized requirement to use alternatives non-mammalian models to support chemicals screening for DNT testing. Zebrafish started to gain attention as a model of choice for DNT research owing to their special characteristics. High fecundity of the zebrafish is amenable for high throughput toxicity approaches which not feasible in the rodents. Shorter embryonic period (3 days) as compared to the rodents (18-28 days) has put the zebrafish at advantage as it minimizes the use of chemicals, cost of the maintenance and less laborious. Importantly, the high conservation of basic CNS organization with similar key pathway that relevance to human diseases makes the zebrafish a relevant animal model for DNT testing (Patten et al., 2014; Howe et al., 2013; Kalueff et al., 2013; Tsuji & Crofton, 2012; Bal-Price et al., 2010). In this thesis, zebrafish was used as a model organism in order to understand the neurotoxic and neurobehavioral alterations after chronic embryonic exposure to $HgCl_2$ and As_2O_3 at nanomolar and micromolar concentrations.

The objectives of this project are:

a) To identify the toxic effects of embryonic exposure to $HgCl_2$ and As_2O_3 during developmental stages of zebrafish (*Danio rerio*)
b) To examine the alteration in motor function and anxiety-related responses of zebrafish (*Danio rerio*) larvae after embryonic exposure to $HgCl_2$ and As_2O_3
c) To assess apoptosis in the zebrafish embryos and larvae after embryonic exposure to $HgCl_2$ and As_2O_3
d) To evaluate the biochemical changes in the zebrafish embryos and larvae after embryonic exposure to $HgCl_2$ and As_2O_3

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REFERENCES

Abu Bakar, N. (2014). Effect of exposure to mercury (II) chloride ($HgCl_2$) during developmental stages of zebrafish *(Danio rerio)* .(Unpublished undergraduate thesis). Universiti Putra Malaysia, Malaysia.

Acevedo, J., Santana-Almansa, A., Matos-Vergara, N., Marrero-Cordero, L.R., Cabezas- Bou, E., & Díaz-Ríos, M. (2016). Caffeine stimulates locomotor activity in the mammalian spinal cord via adenosine A1 receptor-dopamine D1 receptor interaction and PKA-dependent mechanisms. *Neuropharmacology*, *101*, 490–505.

Agusa, T., Kunito, T., Sudaryanto, A., Monirith, I., Kan-Atireklap, S., Iwata, H., … Tanabe, S. (2007). Exposure assessment for trace elements from consumption of marine fish in Southeast Asia. *Environmental Pollution, 145*(3), 766–777.

Agusa, T., Kunito, T., Yasunaga, G., Iwata, H., Subramanian, A., Ismail, A., and Tanabe, S. (2005). Concentrations of trace elements in marine fish and its risk assessment in Malaysia. In Marine *Pollution Bulletin, 51*, 896–911.

Ahmad, N. I., Noh, M. F. M., Mahiyuddin, W. R. W., Jaafar, H., Ishak, I., Azmi, W. N. F. W., … Hairi, M. H. (2015). Mercury levels of marine fish commonly consumed in Peninsular Malaysia. *Environmental Science and Pollution Research International, 22*(5), 3672–86.

Alava, P., Du Laing, G., Odhiambo, M., Verliefde, A., Tack, F., & Van de Wiele, T. R.(2013). Arsenic bioaccessibility upon gastrointestinal digestion is highly determined by its speciation and lipid-bile salt interactions. *Journal of Environmental Science and Health. Part A, Toxic/hazardous Substances & Environmental Engineering, 48*(6), 656–65.

Alina, M., Azrina, A., Mohd Yunus, A. S., Mohd Zakiuddin, S., Mohd Izuan Effendi, H., & Muhammad Rizal, R. (2012). Heavy metals (mercury, arsenic, cadmium, plumbum) in selected marine fish and shellfish along the straits of malacca. *International Food Research Journal, 19*(1), 135–140.

Al-Saleh, I., Nester, M., Abduljabbar, M., Al-Rouqi, R., Eltabache, C., Al-Rajudi, T., & Elkhatib, R. (2016). Mercury (Hg) exposure and its effects on Saudi breastfed infant's neurodevelopment. *International Journal of Hygiene and Environmental Health, 219*(1), 129–141.

Attina, T. M., & Trasande, L. (2013). Economic Costs of Childhood Lead Exposure in Low- and Middle-Income Countries. *Environmental Health Perspectives*, *121*(9), 1097–1102.

ATSDR. (2007). Toxicological Profile for Arsenic. U.S Public Health Service, Agency for Toxic Substances and Disease Registry. Retrieved from http://doi.org/http://dx.doi.org/10.1155/2013/286524

ATSDR. (2006). Arsenic: potential for human exposure. *Toxicological Profiles*, (Iii), 313–381. Retrieved from https://www.atsdr.cdc.gov/toxprofiles.

Aung, K. H., Kyi-Tha-Thu, C., Sano, K., Nakamura, K., Tanoue, A., Nohara, K., … Maekawa, F. (2016). Prenatal exposure to arsenic impairs behavioral flexibility and cortical structure in mice. *Frontiers in Neuroscience, 10*, 137.

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Baidya, M., Genovez, M., Torres, M., & Chao, M. Y. (2014). Dopamine Modulation of Avoidance Behavior in *Caenorhabditis elegans* Requires the NMDA Receptor NMR-1. *PLoS ONE, 9*(8), e102958.

Baldissarelli, L. A., Capiotti, K. M., Bogo, M. R., Ghisleni, G., & Bonan, C. D.(2012). Arsenic alters behavioral parameters and brain ectonucleotidases activities in zebrafish (*Danio rerio*). *Comparative Biochemistry and Physiology - C Toxicology and Pharmacology, 155*(4), 566–572.

Bailey, K.R. & Crawley, J.N.(2009).Anxiety-Related Behaviors in Mice. *Methods of Behavior Analysis in Neuroscience.2nd edition.* Boca Raton (FL): CRC Press/Taylor & Francis.

Bal-Price, A. K., Hogberg, H. T., Buzanska, L., Lenas, P., van Vliet, E., & Hartung, T.(2010). In vitro developmental neurotoxicity (DNT) testing: Relevant models and endpoints. *NeuroToxicology, 31*(5), 545–554.

Bardullas, U., Limón-Pacheco, J. H., Giordano, M., Carrizales, L., Mendoza-Trejo, M. S., & Rodríguez, V. M. (2009). Chronic low-level arsenic exposure causes gender-specific alterations in locomotor activity, dopaminergic systems, and thioredoxin expression in mice. *Toxicology and Applied Pharmacology, 239*(2), 169–177.

Barros, T. P., Alderton, W. K., Reynolds, H. M., Roach, A. G., & Berghmans, S. (2008). Zebrafish: an emerging technology for in vivo pharmacological assessment to identify potential safety liabilities in early drug discovery. *British Journal of Pharmacology, 154*(7), 1400–13.

Baxter, A. J., Vos, T., Scott, K. M., Norman, R. E., Flaxman, A. D., Blore, J., & Whiteford, H. A. (2014). The regional distribution of anxiety disorders: implications for the Global Burden of Disease Study, 2010. *International Journal of Methods in Psychiatric Research, 23*(4), 422–438.

Bellinger, D.C., O'Leary, K., Rainis, H., & Gibb, H.J.(2016). Country-specific estimates of the incidence of intellectual disability associated with prenatal exposure to methylmercury. *Environmental Research, 147*, 159-63.

Bencan, Z., Sledge, D., & Levin, E. D. (2009). Buspirone, chlordiazepoxide and Diazepam effects in a zebrafish model of anxiety. *Pharmacology Biochemistry and Behavior, 94*(1), 75–80.

Bentley, K. H., Franklin, J. C., Ribeiro, J. D., Kleiman, E. M., Fox, K. R., & Nock, M. K. (2016). Anxiety and its disorders as risk factors for suicidal thoughts and behaviors: A meta-analytic review. *Clinical Psychology Review, 43*, 30–46.

Berk, M., Kapczinski, F., Andreazza, A. C., Dean, O. M., Giorlando, F., Maes, M., … Malhi, G. S. (2011). Pathways underlying neuroprogression in bipolar disorder: Focus on inflammation, oxidative stress and neurotrophic factors. *Neuroscience and Biobehavioral Reviews, 35*(3), 804–817.

Bhandiwad, A. A., Zeddies, D. G., Raible, D. W., Rubel, E. W., & Sisneros, J. A. (2013). Auditory sensitivity of larval zebrafish (*Danio rerio*) measured using a behavioral prepulse inhibition assay. *The Journal of Experimental Biology, 216*(Pt 18), 3504–13.

Bianco, I. H., & Engert, F. (2015). Visuomotor Transformations Underlying Hunting Behavior in Zebrafish. *Current Biology, 25*(7), 831–846.

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Biehlmaier, O., Neuhauss, S. C. F., & Kohler, K. (2001). Onset and time course of apoptosis in the developing zebrafish retina. *Cell and Tissue Research, 306*(2), 199–207.

Blaser, R.E. &Vira, D.G.(2014). Experiments on learning in zebrafish (*Danio rerio*): a promising model of neurocognitive function. *Neuroscience and Biobehavioural Reviews*, *42*, 224-31.

Blaser, R.E., Chadwick, L., & McGinnis, G.C. (2010).Behavioral measures of anxiety in zebrafish (*Danio rerio*). *Behavioural Brain Research. 208*(1):56-62.

Bleckmann, H., & Zelick, R. (2009). Lateral line system of fish. *Integrative Zoology,4*(1), 13-25.

Boivin, M. J., Kakooza, A. M., Warf, B. C., Davidson, L. L., & Grigorenko, E. L. (2015). Reducing neurodevelopmental disorders and disability through research and interventions. *Nature, 527*(7578), 155–160.

Bose-O'Reilly, S., McCarty, K. M., Steckling, N., & Lettmeier, B. (2010). Mercury exposure and children's health. *Current Problems in Pediatric and Adolescent Health Care, 40*(8), 186–215.

Brandon, E. F. a, Janssen, P. J. C. M., & de Wit-Bos, L. (2014). Arsenic: bioaccessibility from seaweed and rice, dietary exposure calculations and risk assessment. *Food Additives & Contaminants. Part A, Chemistry, Analysis, Control, Exposure & Risk Assessment, 31*(12), 1993–2003.

Brustein, E., Saint-Amant, L., Buss, R. R., Chong, M., McDearmid, J. R., & Drapeau, P. (2003). Steps during the development of the zebrafish locomotor network. *Journal of Physiology Paris, 97*(1), 77–86.

Budick, S. A., & O'Malley, D. M. (2000). Locomotor repertoire of the larval zebrafish: swimming, turning and prey capture. *The Journal of Experimental Biology, 203*(Pt 17), 2565–79.

Burgos, S., Tenorio, M., Zapata, P., Cáceres, D.D., Klarian, J., Alvarez, N., Oviedo, R., Toro-Campos, R., Claudio, L., & Iglesias, V.(2017). Cognitive performance among cohorts of children exposed to a waste disposal site containing heavy metals in Chile. *International Journal of Environmental Health Research, 27*(2), 117-125.

Buss, R. R., & Drapeau, P. (2001). Synaptic drive to motoneurons during fictive swimming in the developing zebrafish. *Journal of Neurophysiology, 86*(1), 197–210.

Campos, A. C., Fogaça, M. V., Aguiar, D. C., & Guimarães, F. S. (2013). Animal models of anxiety disorders and stress. *Revista Brasileira de Psiquiatria, 35*(Suppl.2), 101-111.

Castoldi, A. F., Johansson, C., Onishchenko, N., Coccini, T., Roda, E., Vahter, M., … Manzo, L. (2008). Human developmental neurotoxicity of methylmercury: Impact of variables and risk modifiers. *Regulatory Toxicology and Pharmacology, 51*(2), 201–214.

Castro-González, M. I., & Méndez-Armenta, M. (2008). Heavy metals: Implications associated to fish consumption. *Environmental Toxicology and Pharmacology, 26*(3), Pages 263-271

Champagne, D.L., Hoefnagels, C.C., de Kloet, R.E., & Richardson, M.K.(2010). Translating rodent behavioral repertoire to zebrafish (*Danio rerio*): relevance for stress research. *Behavioural Brain Research*, *214*(2),332-42.

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Chandravanshi, L. P., Yadav, R. S., Shukla, R. K., Singh, A., Sultana, S., Pant, A. B., … Khanna, V. K. (2014). Reversibility of changes in brain cholinergic receptors and acetylcholinesterase activity in rats following early life arsenic exposure. *International Journal of Developmental Neuroscience, 34*, 60–75.

Chang, C. Y., Guo, H. R., Tsai, W. C., Yang, K. L., Lin, L. C., Cheng, T. J., & Chuu, J. J. (2015). Subchronic arsenic exposure induces anxiety-like behaviors in normal mice and enhances depression-like behaviors in the chemically induced mouse model of depression. *BioMed Research International, 2015*, 159015.

Chaudhari, N., & Roper, S. D. (2010). The cell biology of taste. *Journal of Cell Biology. 190*(3), 285.

Chavan, V. R. (2015). Morphological and Biochemical Profile of Mercury Exposed Fish Kidney, *International Journal of Emerging Technology and Advanced Engineering*, *5*(8), 96–100.

Cheslack-Postava, K., Rantakokko, P. V., Hinkka-Yli-Salomäki, S., Surcel, H. M., McKeague, I. W., Kiviranta, H. A., … Brown, A. S. (2013). Maternal serum persistent organic pollutants in the Finnish Prenatal Study of Autism: A pilot study. *NeuroToxicology and Teratology, 38*, 1–5.

Chhetri, J., Jacobson, G., & Gueven, N. (2014). Zebrafish-on the move towards ophthalmological research. *Eye, 28*(4), 367–80.

Clark, K. J., Boczek, N. J., & Ekker, S. C. (2011). Stressing Zebrafish for Behavioral Genetics. *Reviews in the Neurosciences*, *22*(1), 49–62.

Clarkson, T. W., Magos, L., & Myers, G. J. (2003). The toxicology of mercury—current exposures and clinical manifestations. *The New England Journal of Medicine, 349*, 1731–1737.

Colwill, R. M., & Creton, R. (2011). Imaging escape and avoidance behavior in zebrafish larvae. *Reviews in the Neurosciences, 22*(1), 63–73.

Craske, M. G., Rauch, S. L., Ursano, R., Prenoveau, J., Pine, D. S., & Zinbarg, R. E. (2009). What is an anxiety disorder?. *Depression and Anxiety, 26*(12), 1066–1085.

Crofton, K. M., Mundy, W. R., & Shafer, T. J. (2012). Developmental neurotoxicity testing: A path forward. *Congenital Anomalies, 52*(3), 140–146.

Dakeishi, M., Murata, K., & Grandjean, P. (2006). Long-term consequences of arsenic poisoning during infancy due to contaminated milk powder. *Environmental Health : A Global Access Science Source, 5*(1), 31.

Dash, M., Eid, A., Subaiea, G., Chang, J., Deeb, R., Masoud, A., … Zawia, N. H. (2016). Developmental exposure to lead (Pb) alters the expression of the human tau gene and its products in a transgenic animal model. *NeuroToxicology, 55*, 154–159.

Day, J. J., Reed, M. N., & Newland, M. C. (2005). Neuromotor deficits and mercury concentrations in rats exposed to methyl mercury and fish oil. *Neurotoxicology and Teratology, 27*(4), 629–641.

Debes, F., Budtz-Jørgensen, E., Weihe, P., White, R. F., & Grandjean, P. (2006). Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. *Neurotoxicology and Teratology, 28*(3), 363–375

© COPYRIGHT UPM

Dias, B. G., Banerjee, S. B., Goodman, J. V., & Ressler, K. J. (2013). Towards new approaches to disorders of fear and anxiety. *Current Opinion in Neurobiology*, *23*(3), 346–352.

Dickerson, A. S., Rahbar, M. H., Han, I., Bakian, A. V., Bilder, D. A., Harrington, R. A., … Baio, J. (2015). Autism spectrum disorder prevalence and proximity to industrial facilities releasing arsenic, lead or mercury. *Science of The Total Environment, 536*, 245–251.

Diem, M., Chiriboga, L., & Yee, H. (2000). Infrared spectroscopy of human cells and tissue. VIII. Strategies for analysis of infrared tissue mapping data and applications to liver tissue. *Biopolymers, 57*(5), 282–290.

Dou, Y., Andersson-Lendahl, M., & Arner, A. (2008). Structure and function of skeletal muscle in zebrafish early larvae. *The Journal of General Physiology, 131*(5), 445–453.

Downes, G. B., & Granato, M. (2006). Supraspinal input is dispensable to generate glycine-mediated locomotive behaviors in the zebrafish embryo. *Journal of Neurobiology, 66*(5), 437–451.

Drapeau, P., Saint-Amant, L., Buss, R. R., Chong, M., McDearmid, J. R., & Brustein, E. (2002). Development of the locomotor network in zebrafish. *Progress in Neurobiology, 68*(2), 85–111.

Dridi, I., Leroy, D., Guignard, C., Scholl, G., Bohn, T., Landoulsi, A., … Bouayed, J. (2014). Dietary early-life exposure to contaminated eels does not impair spatial cognitive performances in adult offspring mice as assessed in the Y-maze and the Morris water maze. *Nutrition Research, 34*(12), 1075–1084.

Driscoll, C. T., Mason, R. P., Chan, H. M., Jacob, D. J., & Pirrone, N. (2013). Mercury as a global pollutant—sources, pathways, and effects. *Environmental Science & Technology, 47*(10), 4967–4983.

Egan, R. J., Bergner, C. L., Hart, P. C., Cachat, J. M., Canavello, P. R., Elegante, M. F., … Kalueff, A. V. (2009). Understanding behavioral and physiological phenotypes of stress and anxiety in zebrafish. *Behavioural Brain Research, 205*(1), 38–44.

Ekinci, M., Ceylan, E., Keleş, S., Çağatay, H. H., Apil, A., Tanyıldız, B., & Uludag, G. (2014). Toxic effects of chronic mercury exposure on the retinal nerve fiber layer and macular and choroidal thickness in industrial mercury battery workers. *Medical Science Monitor, 20*, 1284–1290.

El Yacoubi, M., Ledent, C., Parmentier, M., Costentin, J., & Vaugeois, J. M. (2000). The anxiogenic-like effect of caffeine in two experimental procedures measuring anxiety in the mouse is not shared by selective A(2A) adenosine receptor antagonists. *Psychopharmacology, 148*(2), 153–163.

Ellingson, D., Zywicki, R., & Sullivan, D. (2014). Analytical method for the determination of various arsenic species in rice, rice food products, apple juice, and other juices by ion chromatography-inductively coupled plasma/mass spectrometry. *Journal of AOAC International, 97*(6), 1670–1681.

Ellis, L. D., Soo, E. C., Achenbach, J. C., Morash, M. G., & Soanes, K. H. (2014). Use of the zebrafish larvae as a model to study cigarette smoke condensate toxicity. *PLoS ONE, 9*(12), e115305.

© COPYRIGHT UPM

Emmett, P. M., Jones, L. R., & Golding, J. (2015). Pregnancy diet and associated outcomes in the Avon Longitudinal Study of Parents and Children. *Nutrition Reviews, 73*, 154–174.

Ettinger, A. S., Arbuckle, T. E., Fisher, M., Liang, C. L., Davis, K., Cirtiu, C.-M., … Fraser, W. D. (2017). Arsenic levels among pregnant women and newborns in Canada: Results from the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort. *Environmental Research, 153*, 8–16.

Fero, K., Yokogawa, T., & Burgess, H. A. (2011). The behavioral repertoire of larval zebrafish. *Neuromethods, 52*, 249–291.

Fields, S., & Johnston, M. (2005). Cell biology. Whither model organism research?. *Science (New York, N.Y.), 307*(5717), 1885–1886.

Fleisch, V. C., & Neuhauss, S. C. F. (2006). Visual behavior in zebrafish. *Zebrafish, 3*(2), 191–201.

Furieri, L. B., Galán, M., Avendaño, M. S., García-Redondo, A. B., Aguado, A., Martínez, S., … Salaices, M. (2011). Endothelial dysfunction of rat coronary arteries after exposure to low concentrations of mercury is dependent on reactive oxygen species. *British Journal of Pharmacology, 162*(8), 1819–1831.

Gandhi, D.N. & Kumar, R. (2013). Arsenic toxicity and neurobehaviours: A reviews. *Innovation in Pharmaceutical and Pharmacotheraphy, 1*(1), 1-15.

Gerlai, R. (2010). Zebrafish antipredatory responses: A future for translational research?. *Behavioural Brain Research. 207*(2): 223–231.

Ghysen, A., & Dambly-Chaudière, C. (2007). The lateral line microcosmos. *Genes and Development, 21*, 2118-2130

Gillette, R., Reilly, M. P., Topper, V. Y., Thompson, L. M., Crews, D., & Gore, A. C. (2017). Anxiety-like behaviors in adulthood are altered in male but not female rats exposed to low dosages of polychlorinated biphenyls in utero. *Hormones and Behavior, 87*, 8–15.

Giordano, G., & Costa, L. G. (2012). Developmental Neurotoxicity: Some Old and New Issues. *International Scholarly Research Network Toxicology, 2012*, 814795.

Girdhar, K., Gruebele, M., & Chemla, Y. R. (2015). The behavioral space of zebrafish locomotion and its neural network analog. *PLoS ONE, 10*(7). e0128668.

Grandjean, P., & Landrigan, P. J. (2014). Neurobehavioural effects of developmental toxicity. *The Lancet Neurology*, *13*(3), 330-338.

Grandjean, P., Satoh, H., Murata, K., & Eto, K. (2010). Adverse effects of methylmercury: Environmental health research implications. *Environmental Health Perspectives, 118*, 1137-1145.

Grandjean, P., & Landrigan, P. J. (2006). Developmental neurotoxicity of industrial chemicals. *Lancet (London, England), 368*(9553), 2167–78.

Gravielle, M. C. (2015). Activation-induced regulation of GABAA receptors: Is there a link with the molecular basis of benzodiazepine tolerance?. *Pharmacological Research, 109*, 92–100.

Greiling, T. M. S., & Clark, J. I. (2009). Early lens development in the zebrafish: A three-dimensional time-lapse analysis. *Developmental Dynamics, 238*(9), 2254–2265.

© COPYRIGHT UPM

Guilarte, T. R., Opler, M., & Pletnikov, M. (2012). Is lead exposure in early life an environmental risk factor for Schizophrenia?.Neurobiological connections and testable hypotheses. *NeuroToxicology, 33*(3), 560–574.

Gumilar, F., Lencinas, I., Bras, C., Giannuzzi, L., & Minetti, A. (2015). Locomotor activity and sensory–motor developmental alterations in rat offspring exposed to arsenic prenatally and via lactation. *Neurotoxicology and Teratology, 49*, 1–9.

Ha, E., Basu, N., Bose-O'Reilly, S., Dórea, J. G., McSorley, E., Sakamoto, M., & Chan, H. M.(2017). Current progress on understanding the impact of mercury on human health. *Environmental Research, 152*, 419–433.

Hagenaars, A., Stinckens, E., Vergauwen, L., Bervoets, L., & Knapen, D. (2014). PFOS affects posterior swim bladder chamber inflation and swimming performance of zebrafish larvae. *Aquatic Toxicology, 157*, 225–235.

Hajeb, P., Jinap, S., Ismail, A., Fatimah, A. B., Jamilah, B., & Abdul Rahim, M. (2009). Assessment of mercury level in commonly consumed marine fishes in Malaysia. *Food Control*, 20(1), 79–84.

Hallauer, J., Geng, X., Yang, H.C., Shen, J., Tsai, K.J. & Liu, Z.(2016).The effect of chronic arsenic exposure in zebrafish. *Zebrafish, 13*(5), 405-12.

Hamilton, F. (1822). *An Account of the Fishes Found in the River Ganges and its Branches*. Edinburgh and London, Archibald Constable and Co. 321, 390, and 405.

Hanson, M. G., & Landmesser, L. T. (2004). Normal patterns of spontaneous activity are required for correct motor axon guidance and the expression of specific guidance molecules. *Neuron, 43*(5), 687–701.

HSDB—Hazardous Substances Data Bank. Toxicology, Occupational Medicine and Environmental Series. (2004). Mercury. Retrieved from http://toxnet.nlm.nih.gov/.

He, Y., Pedigo, C. E., Lam, B., Cheng, Z. Q., & Zheng, Y. (2012). Bioaccessibility of arsenic in various types of rice in an in vitro gastrointestinal fluid system. *Journal of Environmental Science and Health Part B-Pesticides Food Contaminants and Agricultural Wastes, 47*(2), 74–80.

Helmy, I. M., & Abdel Azim, A. M. (2012). Efficacy of ImageJ in the assessment of apoptosis. *Diagnostic Pathology, 7*, 15.

Heyer, D.B. & Meredith, R.M.(2017).Environmental toxicology: Sensitive periods of development and neurodevelopmental disorders. *Neurotoxicology, 58*, 23-41.

Hill, D.S., Cabrera, R., Wallis Schultz, D., Zhu, H., Lu, W., Finnell, R.H., & Wlodarczyk, B.J. (2015). Autism-like behavior and epigenetic changes associated with autism as consequences of in utero exposure to environmental pollutants in a mouse model. *Behavioural Neurology, 2015*, e426263.

Ho, N. Y., Yang, L., Legradi, J., Armant, O., Takamiya, M., Rastegar, S., & Strähle, U. (2013). Gene responses in the central nervous system of zebrafish embryos exposed to the neurotoxicant methyl mercury. *Environmental Science and Technology, 47*(7), 3316–3325.

Holmes, P., James, K. A. F., & Levy, L. S. (2009). Is low-level environmental Mercury exposure of concern to human health?. *Science of the Total Environment, 408*(2), 171–182.

© COPYRIGHT UPM

Houston, M.C.(2007). The role of mercury and cadmium heavy metals in vascular disease, hypertension, coronary heart disease, and myocardial infarction. *Alternantive Therapy Health Medicine, 13*(2), 128-133.

Howe, K., Clark, M. D., Torroja, C. F., Torrance, J., Berthelot, C., Muffato, M., … Stemple, D. L. (2013). The zebrafish reference genome sequence and its relationship to the human genome. *Nature, 496*(7446), 498–503.

Huang, Y.-Y., & Neuhauss, S. C. F. (2008). The optokinetic response in zebrafish and its applications. *Technology, 13*(January 1), 1899–1916.

Huo, T. G., Li, W. K., Zhang, Y. H., Yuan, J., Gao, L. Y., Yuan, Y., … Sun, G. F. (2015). Excitotoxicity Induced by Realgar in the Rat Hippocampus: the Involvement of Learning Memory Injury, Dysfunction of Glutamate Metabolism and NMDA Receptors. *Molecular Neurobiology, 51*(3), 980–994.

Huq, S. M. I., Joardar, J. C., Parvin, S., Correll, R., & Naidu, R. (2006). Arsenic contamination in food-chain: Transfer of arsenic into food materials through groundwater irrigation. *Journal of Health, Population and Nutrition, 24*(3), 305–316.

IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. (2012). Arsenic, metals, fibres, and dusts. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans / World Health Organization, International Agency for Research on Cancer, 100*(Pt C), 11–465.

Ingebretson, J. J., & Masino, M. A. (2013). Quantification of locomotor activity in larval zebrafish: considerations for the design of high-throughput behavioral studies. *Frontiers in Neural Circuits, 7*(6), 109.

Inoue, A., Nishimura, Y., Matsumoto, N., Umemoto, N., Shimada, Y., Maruyama, …Tanaka, T.(2016).Comparative study of the zebrafish embryonic toxicity test and mouse embryonic stem cell test to screen developmental toxicity of human pharmaceutical drugs. *Fundamental Toxicological Sciences, 3*(2), 79-87.

Irwandi, J., & Farida, O. (2009). Mineral and heavy metal contents of marine fin fish in Langkawi island, Malaysia. *International Food Research Journal, 16*(1), 105-112.

Jaishankar, M., Tseten, T., Anbalagan, N., Mathew, B. B., & Beeregowda, K. N. (2014). Toxicity, mechanism and health effects of some heavy metals. *Interdisciplinary Toxicology, 7*(2), 60–72.

Jakka, N. M., Rao, T. G., & Rao, J. V. (2007). Locomotor behavioral response of mosquitofish (Gambusia affinis) to subacute mercury stress monitored by video tracking system. *Drug and Chemical Toxicology, 30*(4), 383–397.

Jantzen, C. E., Annunziato, K. A., Bugel, S. M., & Cooper, K. R. (2016). PFOS, PFNA, and PFOA sub-lethal exposure to embryonic zebrafish have different toxicity profiles in terms of morphometrics, behavior and gene expression. *Aquatic Toxicology, 175*, 160–170.

Jesuthasan, S. (2012). Fear, anxiety, and control in the zebrafish.*Developemntal Neurobiology, 72*(3), 395–403.

Kalueff, A. V., Stewart, A. M., & Gerlai, R. (2014). Zebrafish as an emerging model for studying complex brain disorders. *Trends in Pharmacological Sciences, 35*(2), 63–75.

© COPYRIGHT UPM

Kalueff, A. V, Gebhardt, M., Stewart, A. M., Cachat, J. M., Brimmer, M., Chawla, J. S., … Schneider, H. (2013). Towards a comprehensive catalog of zebrafish behavior 1.0 and beyond. *Zebrafish, 10*(1), 70–86.

Kamaruzzaman, B. Y., Rina, Z., John, B. A., & Jalal, K. C. A. (2011). Heavy metal accumulation in commercially important fishes of south west malaysian coast. *Research Journal of Environmental Sciences*, *5*(6), 595-602.

Kessler, R. C., Aguilar-Gaxiola, S., Alonso, J., Chatterji, S., Lee, S., Ormel, J., … Wang, P. S. (2011). The global burden of mental disorders: an update from the WHO World Mental Health (WMH) surveys. *Epidemiologia E Psichiatria Sociale, 18*(1), 23–33.

Kim, M. K., & Zoh, K. D. (2012). Fate and transport of mercury in environmental media and human exposure. *Journal of Preventive Medicine and Public Health, 45*(6), 335–343.

Kimmel, C. B., Ballard, W. W., Kimmel, S. R., Ullmann, B. S., & Schilling, T. F. (1995). Stages of embryonic development of the zebrafish. *Developmental Dynamics, 203*(3), 253–310.

Kirk, J. L., Lehnherr, I., Andersson, M., Braune, B. M., Chan, L., Dastoor, A. P., … St. Louis, V. L. (2012). Mercury in Arctic marine ecosystems: Sources, pathways and exposure. *Environmental Research, 119*, 64–87.

Kitambi, S. S., Chandrasekar, G., & Addanki, V. K. (2011). Teleost fish – powerful models for studying development , function and diseases of the human eye. *Current Science, 100*(12), 1815–23.

KKM.(2015). Institute for Public Health National Health and Morbidity Survey 2015 (NHMS 2015) Non-Communicable Diseases. 2015, II, 184-193.

Kleiman, N.J., Quinn, A.M., Fields, K.G., Slavkovich, V. & Graziano, J.H.(2016). Arsenite accumulation in the mouse eye. *Journal of Toxicology and Environmental Health Part A, 79*(8), 339-41.

Knogler, L. D., Ryan, J., Saint-Amant, L., & Drapeau, P. (2014). A Hybrid Electrical/Chemical Circuit in the Spinal Cord Generates a Transient Embryonic Motor Behavior. *Journal of Neuroscience, 34*(29), 9644–9655.

Koch, I., McPherson, K., Smith, P., Easton, L., Doe, K. G., & Reimer, K. J. (2007). Arsenic bioaccessibility and speciation in clams and seaweed from a contaminated marine environment. *Marine Pollution Bulletin, 54*(5), 586–594.

Koerber, A.S. & Kalishman, J.(2009). Preparing for a semiannual IACUC inspection of a satellite zebrafish (*Danio rerio*) facility. *Journal of American Association Laboratory Animal Science, 48*(1), 65-75.

Korbas, M., MacDonald, T. C., Pickering, I. J., George, G. N., & Krone, P. H. (2012). Chemical form matters: Differential accumulation of mercury following inorganic and organic mercury exposures in zebrafish larvae. *ACS Chemical Biology, 7*(2), 411–420.

Korbas, M., Blechinger, S. R., Krone, P. H., Pickering, I. J., & George, G. N. (2008). Localizing organomercury uptake and accumulation in zebrafish larvae at the tissue and cellular level. *Proceeding of National Academy Science,* 105 (34), 12108-12112.

Krauss, A., & Neumeyer, C. (2003). Wavelength dependence of the optomotor response in zebrafish (*Danio rerio*). *Vision Research, 43*(11), 1273–1282.

Kulig, B., Alleva, E., Bignami, G., Cohn, J., Cory-Slechta, D., Landa, V., … Peakall, D.(1996).Animal behavioral methods in neurotoxicity assessment:

© COPYRIGHT UPM

SGOMSEC joint report. *Environmental Health Perspectives, 104*(Suppl 2), 193–204.

Kung, T. S., Richardson, J. R., Cooper, K. R., & White, L. A. (2015). Developmental deltamethrin exposure causes persistent changes in dopaminergic gene expression, neurochemistry, and locomotor activity in zebrafish. *Toxicological Sciences, 146*(2), 235–243.

Lamers, F., van Oppen, P., Comijs, H. C., Smit, J. H., Spinhoven, P., van Balkom, A. J. L. M., … Penninx, B. W. J. H. (2011). Comorbidity patterns of anxiety and depressive disorders in a large cohort study: the Netherlands Study of Depression and Anxiety (NESDA). *The Journal of Clinical Psychiatry, 72*(3), 341–348.

Laparra, J. M., Vélez, D., Barberá, R., Farré, R., & Montoro, R. (2005). Bioavailability of inorganic arsenic in cooked rice: Practical aspects for human health risk assessments. *Journal of Agricultural and Food Chemistry, 53*(22), 8829–8833.

Laparra, J. M., Vélez, D., Montoro, R., Barbera, R., & Farré, R. (2003). Estimation of arsenic bioaccessibility in edible seaweed by an in vitro digestion method. *Journal of Agricultural and Food Chemistry, 51*(20), 6080–6085.

LeDoux, J. (2007). The amygdala. *Current Biology, 17*(20), 868–R874.

Lee, H.M., & Kim, Y. (2016). Drug repurposing is a new opportunity for developing drugs against neuropsychiatric disorders. *Schizophrenia Research and Treatment, 2016*, 1–12.

Lein, P., Locke, P., & Goldberg, A. (2007). Meeting Report: Alternatives for Developmental Neurotoxicity Testing. *Environmental Health Perspectives, 115*(5), 764–768.

Levin, E. D., & Cerutti, D. T. (2009). *Behavioral neuroscience of zebrafish. in: buccafusco jj, editor. Methods of behavior analysis in neuroscience*. 2nd edition. Boca Raton (FL): CRC Press/Taylor & Francis.1–17.

Levin, E. D., Bencan, Z., & Cerutti, D. T. (2007). Anxiolytic effects of nicotine in zebrafish. *Physiology & Behavior, 90*(1), 54–58.

Li, C., Seng, W. L., Park, D., & McGrath, P. (2011). *Methods for assessing neurotoxicity in zebrafish, in zebrafish: Methods for assessing drug safety and toxicity (ed P. McGrath).* John Wiley & Sons, Inc. Hoboken, NJ, USA.

Li, D., Morimoto, K., Takeshita, T., & Lu, Y. (2001). Arsenic induces DNA damage via reactive oxygen species in human cells. *Environmental Health and Preventive Medicine, 6*(1), 27–32.

Liu, J. T., & Bain, L. J. (2014). Arsenic inhibits hedgehog signaling during P19 cell differentiation. *Toxicology and Applied Pharmacology, 281*(3), 243–253.

Liu, X., Lin, J., Zhang, Y., Peng, X., Guo, N., & Li, Q. (2016). Effects of diphenylhydantoin on locomotion and thigmotaxis of larval zebrafish. *Neurotoxicology and Teratology*, *53*, 41–47.

Lohren, H., Blagojevic, L., Fitkau, R., Ebert, F., Schildknecht, S., Leist, M., & Schwerdtle, T. (2015). Toxicity of organic and inorganic mercury species in differentiated human neurons and human astrocytes. *Journal of Trace Elements in Medicine and Biology, 32*, 200–208.

© COPYRIGHT UPM

Lovato, A. K., Creton, R., & Colwill, R. M. (2016). Effects of embryonic exposure to polychlorinated biphenyls (PCBs) on larval zebrafish behavior. *Neurotoxicology and Teratology, 53*, 1–10.

Lu, Z., & Desmidt, A. A. (2013). Early development of hearing in zebrafish. *JARO - Journal of the Association for Research in Otolaryngology, 14*(4), 509–521.

Lynch, H.N., Greenberg, G.I., Pollock, M.C. & Lewis, A.S.(2014). A comprehensive evaluation of inorganic arsenic in food and considerations for dietary intake analyses. *The Science Total Environment, 496*, 299-313.

Maaswinkel, H., Zhu, L., & Weng, W. (2012). The immediate and the delayed effects of buspirone on zebrafish (*Danio rerio*) in an open field test: A 3-D approach. *Behavioural Brain Research, 234*(2), 365–374.

MacDonald, T. C., Nehzati, S., Sylvain, N. J., James, A. K., Korbas, M., Caine, S., … Krone, P. H. (2015). Phenylthiourea alters toxicity of mercury compounds in zebrafish larvae. *Journal of Inorganic Biochemistry, 151*, 10–17.

Manaf, R.A., Aljunid, S.M., & Rahman, H.A. (2009). Economic burden of three common psychiatric disorders in Malaysia. *Proceeding from 12th World Congress on Public Health.*

Mao, G., Zhou, Z., Chen, Y., Wang, W., Wu, X., Feng, W., … Wu, X. (2016). Neurological toxicity of individual and mixtures of low dose arsenic, mono and di (n-butyl) phthalates on sub-chronic exposure to mice. *Biological Trace Element Research, 170*(1), 183–193.

Markowski, V. P., Reeve, E. A., Onos, K., Assadollahzadeh, M., & McKay, N. (2012). Effects of prenatal exposure to sodium arsenite on motor and food-motivated behaviors from birth to adulthood in C57BL6/J mice. *Neurotoxicology and Teratology, 34*(2), 221–231.

Matthews, M., Trevarrow, B., & Matthews, J.(2002).A virtual tour of the guide for zebrafish users. *Laboratory Animal (NY), 31*, 34–40.

Maximino, C., da Silva, A.W.B., Araújo, J., Lima, M.G., Miranda, V., Puty, B., … Herculano, A.M. (2014) Fingerprinting of Psychoactive Drugs in Zebrafish Anxiety-Like Behaviors. *PLoS ONE, 9*(7), e103943.

Maximino, C., de Brito, T. M., da Silva Batista, A. W., Herculano, A. M., Morato, S., & Gouveia, A. (2010). Measuring anxiety in zebrafish: A critical review. *Behavioural Brain Research, 214*(2), 157–171.

Meredith, R.M.(2015).Sensitive and critical periods during neurotypical and aberrant neurodevelopment: a framework for neurodevelopmental disorders *Neuroscience and Biobehavioral Reviews*, *50*, 180-188.

McCollum, C.W., Ducharme, N.A., Bondesson, M., & Gustafsson, J.A.(2011). Developmental toxicity screening in zebrafish. *Birth Defects Research Part C, Embryo Today : reviews, 93*(2), 67-114.

McKean, S. J., Bartell, S. M., Hansen, R. L., Barfod, G. H., Green, P. G., & Hertz-Picciotto, I. (2015). Prenatal mercury exposure, autism, and developmental delay, using pharmacokinetic combination of newborn blood concentrations and questionnaire data: A case control study. *Environmental Health: A Global Access Science Source, 14*, 62.

McEvoy, P. M., Grove, R., & Slade, T. (2011). Epidemiology of anxiety disorders in the Australian general population: findings of the 2007 Australian

© COPYRIGHT UPM

National Survey of Mental Health and Wellbeing. Australian and New Zealand. *Journal of Psychiatry, 45*, 957–67.

Mohd Sata, S.A., Abu Bakar, N., Ramlan, N.F. & Wan Ibrahim, W. N. (2015). Developmental neurotoxicity: evaluation of zebrafish larvae anxiety behavior after chronic embryonic exposure to arsenic. *Proceeding 2nd International Conference on Environmental Systems Research (ICESR 2015)*, Phuket 25-26 December 2015., 91(2016). Retrieved from http://doi.org/10.7763/IPCBEE.

Mohammad, F., Aryal, S., Ho, J., Stewart, J. C., Norman, N. A., Tan, T. L., … Claridge-Chang, A. (2016). Ancient Anxiety Pathways Influence *Drosophila* Defense Behaviors. *Current Biology*, *26*(7), 981–986.

Mok, W. J., Senoo, S., Itoh, T., Tsukamasa, Y., Kawasaki, K., & Ando, M. (2012). Assessment of concentrations of toxic elements in aquaculture food products in Malaysia. *Food Chemistry, 133*(4), 1326–1332.

Monroe, J. D., Manning, D. P., Uribe, P. M., Bhandiwad, A., Sisneros, J. A., Smith, M. E., & Coffin, A. B. (2016). Hearing sensitivity differs between zebrafish lines used in auditory research. *Hearing Research, 341*, 220–231.

Morgano, M. A., Rabonato, L. C., Milani, R. F., Miyagusku, L., & Balian, S. C. (2011). Assessment of trace elements in fishes of Japanese foods marketed in São Paulo (Brazil). *Food Control, 22*(5), 778–785.

Moorman, S. J. (2001). Development of Sensory Systems in Zebrafish (*Danio rerio*). *Institute of Laboratory Animal Research Journal, 42*(2), 292-298.

Moser, V. C. (2011). Functional assays for neurotoxicity testing. *Toxicologic Pathology, 39*(1), 36–45

Myers, C. P., Lewcock, J. W., Hanson, M. G., Gosgnach, S., Aimone, J. B., Gage, F. H., … Pfaff, S. L. (2005). Cholinergic input is required during embryonic development to mediate proper assembly of spinal locomotor circuits. *Neuron, 46*(1), 37–49

Nahar, M. N., Inaoka, T., & Fujimura, M. (2014). A consecutive study on arsenic exposure and intelligence quotient (IQ) of children in Bangladesh. *Environmental Health and Preventive Medicine, 19*(3), 194–199.

Nasiadka, A. & Clark, M.D. (2012). Zebrafish breeding in the laboratory environment. *Institute of Laboratory Animal Research Journal, 53*, 161–168

National Research Council.(2000).*Chemistry, Exposure, Toxicokinetics, and Toxicodynamics: Toxicological Effects of Methylmercury*. Washington, DC: The National Academies Press.

Németi, B., & Gregus, Z. (2005). Reduction of arsenate to arsenite by human erythrocyte lysate and rat liver cytosol - Characterization of a glutathione- and NAD- dependent arsenate reduction linked to glycolysis. *Toxicological Sciences, 85*(2), 847–858.

Ng, T. H. H., Mossey, J. M., & Lee, B. K. (2013). Total blood mercury levels and depression among adults in the United States: National Health and Nutrition Examination Survey 2005-2008. *PLoS ONE, 8*(11), e79339.

Ng, S., Lin, C.C., Jeng, S.F., Hwang, Y.H., Hsieh, W.S., & Chen, P.C. (2015). Mercury, APOE, and child behavior. *Chemosphere, 120*, 123–130.

Nichols, C. D., Becnel, J., & Pandey, U. B. (2012). Methods to Assay Drosophila Behavior. *Journal of Visualized Experiments : JoVE*, *61*, 3795.

© COPYRIGHT UPM

Nusslein-Volhard, C. & Dahm, R. (2002). *Zebrafish: A Practical Approach. The Practical Approach Series (Vol. Book 261).* New York, NY: Oxford University Press.

OECD. (2013). Test No. 236: *Fish Embryo Acute Toxicity (FET) Test. OECD Guidelines for the Testing of Chemicals, Section 2*. Paris: OECD Publishing.

Olesen, J., Gustavsson, A., Svensson, M., Wittchen, H. U., & Jönsson, B. (2012). The economic cost of brain disorders in Europe. *European Journal of Neurology, 19*(1), 155–162.

Olivares, C. I., Field, J. A., Simonich, M., Tanguay, R. L., & Sierra-Alvarez, R. (2016). Arsenic (III, V), indium (III), and gallium (III) toxicity to zebrafish embryos using a high-throughput multi-endpoint in vivo developmental and behavioral assay. *Chemosphere, 148*, 361–368.

Onishchenko, N., Fischer, C., Wan Ibrahim, W. N., Negri, S., Spulber, S., Cottica, D., & Ceccatelli, S. (2011). Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. *Neurotoxicity Research, 19*(3), 452–461

Ophuis, R. H., Lokkerbol, J., Heemskerk, S. C. M., van Balkom, A. J. L. M., Hiligsmann, M., & Evers, S. M. A. A. (2017). Cost-effectiveness of interventions for treating anxiety disorders: A systematic review. *Journal of Affective Disorders, 210*, 1–13.

Orger, M. B., Gahtan, E., Muto, A., Page-McCaw, P., Smear, M. C., & Baier, H. (2004). Behavioral Screening Assays in Zebrafish. *Methods in Cell Biology, 77*, 53–68.

Orisakwe, O. E. (2014). The role of lead and cadmium in psychiatry. *North American Journal of Medical Sciences, 6*(8), 370-376.

Padilla, S., Corum, D., Padnos, B., Hunter, D. L., Beam, A., Houck, K. A., … Reif, D. M. (2012). Zebrafish developmental screening of the ToxCast™ Phase I chemical library. *Reproductive Toxicology, 33*(2), 174–187.

Palaniappan Dr., P. L. R. M., & Vijayasundaram, V. (2009). Arsenic-induced biochemical changes in Labeo rohita kidney: An FTIR study. *Spectroscopy Letters, 42*(5), 213–218.

Palaniappan, P.L. & Pramod, K.S.(2010). FTIR study of the effect of nTiO2 on the biochemical constituents of gill tissues of Zebrafish (*Danio rerio*). *Food and Chemical Toxicology, 48*(8-9), 2337-43.

Pamphlett, R. (2014). Uptake of environmental toxicants by the locus ceruleus: A potential trigger for neurodegenerative, demyelinating and psychiatric disorders. *Medical Hypotheses, 82*(1), 97–104.

Pamphlett, R., & Jew, S. K. (2013). Uptake of inorganic mercury by human locus ceruleus and corticomotor neurons: implications for amyotrophic lateral sclerosis. *Acta Neuropathologica Communications, 1*(1), 1–11.

Pandey, U. B. & Nichols, C. D. (2011). Human disease models in *Drosophila melanogaster* and the role of the fly in therapeutic drug discovery. *Drug Delivery, 63*(2), 411–436.

Parichy, D. M., Elizondo, M. R., Mills, M. G., Gordon, T. N., & Engeszer, R. E. (2009). Normal table of postembryonic zebrafish development: Staging by externally visible anatomy of the living fish. *Developmental Dynamics, 238*(12), 2975–3015.

© COPYRIGHT UPM

Park, J.D. & Zheng, W. (2012). Human exposure and health effects of inorganic and elemental mercury. *Journal of Preventive Medicine and Public Health, 45*(6), 344–352.

Patten, A. R., Fontaine, C. J., & Christie, B. R. (2014). A Comparison of the Different Animal Models of Fetal Alcohol Spectrum Disorders and Their Use in Studying Complex Behaviors. *Frontiers in Pediatrics*, *2*, 93.

Pelkowski, S. D., Kapoor, M., Richendrfer, H. A., Wang, X., Colwill, R. M., & Creton, R. (2011). A novel high-throughput imaging system for automated analyses of avoidance behavior in zebrafish larvae. *Behavioural Brain Research, 223*(1), 135–144.

Perez, A. L., Nembhard, M., Monnot, A., Bator, D., Madonick, E., & Gaffney, S. H. (2017). Child and adult exposure and health risk evaluation following the use of metal- and metalloid-containing costume cosmetics sold in the United States. *Regulatory Toxicology and Pharmacology, 84*, 54–63.

Perry, W., Minassian, A., Paulus, M. P., Young, J. W., Kincaid, M. J., Ferguson, E. J., … Geyer, M. A. (2009). A reverse-translational study of dysfunctional exploration in psychiatric disorders: From mice to men. *Archives General Psychiatry, 66*(10), 1072–1080.

Perusini, J. N., & Fanselow, M. S. (2015). Neurobehavioral perspectives on the distinction between fear and anxiety. *Learning & Memory (Cold Spring Harbor, N.Y.), 22*(9), 417–25.

Pichery, C., Bellanger, M., Zmirou-Navier, D., Fréry, N., Cordier, S., Roue-LeGall, A., … Grandjean, P. (2012). Economic evaluation of health consequences of prenatal methylmercury exposure in France. *Environmental Health*, *11*, 53.

Pohlmann, K., Grasso, F. W., & Breithaupt, T. (2001). Tracking wakes: the nocturnal predatory strategy of piscivorous catfish. *Proceedings of the National Academy of Sciences of the United States of America, 98*(13), 7371–4.

Porazinski, S.R., Wang, H., & Furutani-Seiki, M.(2011). Essential techniques for introducing medaka to a zebrafish laboratory-towards the combined use of medaka and zebrafish for further genetic dissection of the function of the vertebrate genome. *Methods in Molecular Biology*, 770, 21-241.

Pujol-Martí, J., & López-Schier, H. (2013). Developmental and architectural principles of the lateral-line neural map. *Frontiers in Neural Circuits, 7*(3), 47.

Pylatiuk, C., Sanchez, D., Mikut, R., Alshut, R., Reischl, M., Hirth, S., … Just, S. (2014). Automatic zebrafish heartbeat detection and analysis for zebrafish embryos. *Zebrafish, 11*(4), 379–383.

Rachman, S. (2004). *Anxiety 2nd Edition*. New York, N.Y.: Psychology Press.

Rahbar, M. H., Samms-Vaughan, M., Ardjomand-Hessabi, M., Loveland, K. A., Dickerson, A. S., Chen, Z., … Boerwinkle, E. (2012). The role of drinking water sources, consumption of vegetables and seafood in relation to blood arsenic concentrations of Jamaican children with and without Autism Spectrum Disorders. *Science of the Total Environment, 433*, 362–370.

Rankin, C.H., Abrams, T., Barry, R.J., Bhatnagar, S., Clayton, D.F., Colombo, J., Coppola, G., Geyer, M.A., Glanzman, D.L., Marsland, S., McSweeney, F.K., Wilson, D.A., Wu, C.F. & Thompson, R.F. (2009). Habituation

© COPYRIGHT UPM

revisited: an updated and revised description of the behavioral characteristics of habituation. *Neurobiology of Learning and Memory, 92*(2), 135-8.

Rawson, D. M., Zhang, T., Kalicharan, D., & Jongebloed, W. L. (2000). Field emission scanning electron microscopy and transmission electron microscopy studies of the chorion, plasma membrane and syncytial layers of the gastrula-stage embryo of the zebrafish Brachydanio rerio: a consideration of the structural and functional. *Aquaculture Research, 31*(3), 325–336.

Redei, E.E. Ahmadiayah, N., Baum, A.E., Sasso, D.A., Slone, J.L., Solberg, L.C.,…Volenec, A. (2001), Novel animal models of affective disorders. *Seminar Clinical Neuropsychiatry*,*6*,43-67.

Rice, K. M., Walker, E. M., Wu, M., Gillette, C., & Blough, E. R. (2014). Environmental mercury and its toxic effects. *Journal of Preventive Medicine and Public Health, 47*(2), 74–83.

Richendrfer, H., & Créton, R. (2013). Automated high-throughput behavioral analyses in zebrafish larvae. *Journal of Visualized Experiments : JoVE*, (77), e50622.

Richendrfer, H., Pelkowski, S. D., Colwill, R. M., & Creton, R. (2012). On the edge: Pharmacological evidence for anxiety-related behavior in zebrafish larvae. *Behavioural Brain Research, 228*(1), 99–106.

Roberts, A. C., Bill, B. R., & Glanzman, D. L. (2013). Learning and memory in zebrafish larvae. *Frontiers in Neural Circuits, 7*(August), 126.

Rodríguez, V. M., Limón-Pacheco, J. H., Del Razo, L. M., & Giordano, M. (2016). Effects of inorganic arsenic exposure on glucose transporters and insulin receptor in the hippocampus of C57BL/6 male mice. *Neurotoxicology and Teratology, 54*, 68–77.

Rodríguez-Barranco, M., Gil, F., Hernández, A. F., Alguacil, J., Lorca, A., Mendoza, R., … Lacasaña, M. (2016). Postnatal arsenic exposure and attention impairment in school children. *Cortex, 74*, 370–382.

Rothenberg, S.E., Yu, X., Liu, J., Biasini, F.J., Hong, C., Jiang, X., Nong, Y., Cheng, Y., Korrick, S.A.(2016). Maternal methylmercury exposure through rice ingestion and offspring neurodevelopment: A prospective cohort study. *International Journal of Hygiene Environmental Health, 219*(8), 832-842.

Rustagi, N., & Singh, R. (2010). Mercury and health care. *Indian Journal of Occupational and Environmental Medicine, 14*(2), 45–48.

Saint-Amant, L., & Drapeau, P. (2001). Synchronization of an embryonic network of identified spinal interneurons solely by electrical coupling. *Neuron, 31*(6), 1035–1046.

Saint-Amant, L., & Drapeau, P. (1998). Time course of the development of motor behaviors in the zebrafish embryo. *Journal of Neurobiology, 37*(4), 622–632.

Samson, J. C., Goodridge, R., Olobatuyi, F., & Weis, J. S. (2001). Delayed effects of embryonic exposure of zebrafish (*Danio rerio*) to methylmercury (MeHg). *Aquatic Toxicology, 51*(4), 369–376.

Samson, J. C., & Shenker, J. (2000). The teratogenic effects of methylmercury on early development of the zebrafish, *Danio rerio*. *Aquatic Toxicology, 48*(2-3), 343–354.

© COPYRIGHT UPM

Samuel, S., Kathirvel, R., Jayavelu, T., & Chinnakkannu, P. (2005). Protein oxidative damage in arsenic induced rat brain: influence of DL-alpha-lipoic acid. *Toxicology Letters, 155*(1), 27–34.

Sanders, A. P., Claus Henn, B., & Wright, R. O. (2015). Perinatal and childhood exposure to cadmium, manganese, and metal mixtures and effects on cognition and behavior: A review of recent literature. *Current Environmental Health Reports, 2*(3), 284–294.

Schnörr, S. J., Steenbergen, P. J., Richardson, M. K., & Champagne, D. L. (2012). Measuring thigmotaxis in larval zebrafish. *Behavioural Brain Research, 228*(2), 367–374.

Selderslaghs, I. W. T., Hooyberghs, J., Blust, R., & Witters, H. E. (2013). Assessment of the developmental neurotoxicity of compounds by measuring locomotor activity in zebrafish embryos and larvae. *Neurotoxicology and Teratology, 37*, 44–56.

Selin, N. E. (2009). Global biogeochemical cycling of mercury: A review. *Annual Review of Environment and Resources, 34*(1), 43–63.

Selin, N. E., Javob, D. J., Park, R. J., Yantosca, R. M., Strode, S., Jaeglé, L., & Jaffe, D. (2007). Chemical cycling and deposition of atmospheric mercury: Global constraints from observations. *Journal of Geophysical Research Atmospheres, 112*(2). 2156-2202.

Selvendiran, P., Driscoll, C. T., Bushey, J. T., & Montesdeoca, M. R. (2008). Wetland influence on mercury fate and transport in a temperate forested watershed. *Environmental Pollution, 154*(1), 46–55.

Smirnova, L., Anderson, P., Smirnova, L., Hogberg, H. T., Leist, M., & Hartung, T. (2014). Developmental neurotoxicity – Challenges in the 21 st century and in vitro opportunities. *Altex, 31*(2), 129–156.

Smith, L. E., Carvan, M. J., Dellinger, J. A., Ghorai, J. K., White, D. B., Williams, F. E., & Weber, D. N. (2010). Developmental selenomethionine and methylmercury exposures affect zebrafish learning. *Neurotoxicology and Teratology, 32*(2), 246–255.

Smith, A. (2002). Effects of caffeine on human behavior. *Food and Chemical Toxicology, 40*(9), 1243–1255.

Solnica-Krezel, L. (2006). Gastrulation in zebrafish - all just about adhesion?. *Current Opinion in Genetic and Development, 16*(4), 433-41.

Spence, R., Gerlach, G., Lawrence, C., & Smith, C. (2008). The behaviour and ecology of the zebrafish, *Danio rerio*. *Biological Reviews, 83*(1), 13–34.

Spulber, S., Kilian, P., Ibrahim, W. N. W., Onishchenko, N., Ulhaq, M., Norrgren, L., … Ceccatelli, S. (2014). PFOS induces behavioral alterations, including spontaneous hyperactivity that is corrected by dexamfetamine in zebrafish larvae. *PLoS ONE, 9*(4). e94227.

Steimer, T. (2002). The biology of fear- and anxiety-related behaviors. *Dialogues in Clinical Neuroscience, 4*(3), 231–249.

Stewart, A., Gaikwad, S., Kyzar, E., Green, J., Roth, A., & Kalueff, A. V. (2012). Modeling anxiety using adult zebrafish: A conceptual review. *Neuropharmacology, 62*(1), 135–143.

Suzuki, H., Terasaki, T., & Sugiyama, Y. (1997). Role of efflux transport across the blood-brain barrier and blood-cerebrospinal fluid barrier on the disposition of xenobiotics in the central nervous system. *Advanced Drug Delivery Reviews, 25*(2-3), 257–285.

© COPYRIGHT UPM

Tasneem, S., Farrell, K., Lee, M. Y., & Kothapalli, C. R. (2016). Sensitivity of neural stem cell survival, differentiation and neurite outgrowth within 3D hydrogels to environmental heavy metals. *Toxicology Letters, 242*, 9–22.

Tchounwou, P. B., Yedjou, C. G., Patlolla, A. K., & Sutton, D. J. (2012). Heavy metals toxicity and the environment. *In Molecular, Clinical and Environmental Toxicology, 101*,133–164.

Teixeira, F. B., Fernandes, R. M., Farias-Junior, P. M. A., Costa, N. M. M., Fernandes, L. M. P., Santana, L. N. S., … Lima, R. R. (2014). Evaluation of the effects of chronic intoxication with inorganic mercury on memory and motor control in rats. *International Journal of Environmental Research and Public Health, 11*(9), 9171–9185.

Telonis, A. G., & Margarity, M. (2015). Phobos: A novel software for recording rodents' behavior during the thigmotaxis and the elevated plus-maze test. *Neuroscience Letters*, *599*, 81-85.

Tierney, K. B. (2011). Behavioural assessments of neurotoxic effects and neurodegeneration in zebrafish. *Biochimica et Biophysica Acta - Molecular Basis of Disease, 1812*(3), 381–389.

Tong, H., & McDearmid, J. R. (2012). Pacemaker and plateau potentials shape output of a developing locomotor network. *Current Biology, 22*(24), 2285–2293.

Topper, S.M., Aguilar, S.C., Topper, V.Y., Elbel, E. & Pierce-Shimomura, J.T. (2014). Alcohol Disinhibition of Behaviors in *C. elegans*. *PLoS ONE, 9*(3), e92965.

Tovote, P., Fadok, J. P. & Lüthi, A. (2015). Neuronal circuits for fear and anxiety. *Nature Reviews Neuroscience, 16*, 317–33.

Tran, S., Fulcher, N., Nowicki, M., Desai, P., Tsang, B., Facciol, A., … Gerlai, R. (2017). Time-dependent interacting effects of caffeine, diazepam, and ethanol on zebrafish behaviour. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 75*, 16–27.

Tran, S., & Gerlai, R. (2013). Time-course of behavioural changes induced by ethanol in zebrafish (*Danio rerio*). *Behavioural Brain Research, 252*, 204–213.

Tsuji, R., & Crofton, K. M. (2012). Developmental neurotoxicity guideline study: Issues with methodology, evaluation and regulation. *Congenital Anomalies, 52*(3), 122–128.

Tyler, C. R., & Allan, A. M. (2014). The effects of arsenic exposure on neurological and cognitive dysfunction in human and rodent studies: A review. *Current Environmental Health Report, 1*, 132–147.

Ung, C. Y., Lam, S. H., Hlaing, M. M., Winata, C. L., Korzh, S., Mathavan, S., & Gong, Z. (2010). Mercury-induced hepatotoxicity in zebrafish: in vivo mechanistic insights from transcriptome analysis, phenotype anchoring and targeted gene expression validation. *BMC Genomics, 11*(1), 212.

van Wijngaarden, E., Davidson, P. W., Smith, T. H., Evans, K., Yost, K., Love, T., … Myers, G. J. (2013). Autism spectrum disorder phenotypes and prenatal exposure to methylmercury. *Epidemiology (Cambridge, Mass), 24*(5), 651–9.

Vrijheid, M., Casas, M., Gascon, M., Valvi, D., & Nieuwenhuijsen, M. (2016). Environmental pollutants and child health—A review of recent concerns.

© COPYRIGHT UPM

International Journal of Hygiene and Environmental Health, 219(4), 331–342.

Walf, A. A., & Frye, C. A. (2007). The use of the elevated plus maze as an assay of anxiety-related behavior in rodents. *Nature Protocols, 2*(2), 322–328.

Walz, N., Mühlberger, A., & Pauli, P. (2016). A human open field test reveals thigmotaxis related to agoraphobic fear. *Biological Psychiatry*, *80*(5), 390–397.

Wang, H., Mu, S., Zhang, F., Wang, H., Liu, H., Zhang, H., & Kang, X. (2015)a. Effects of atrazine on the development of neural system of zebrafish , *Danio rerio. Biomed Research International, 2015*, 10.

Wang, J., Song, Q., Yu, D., Yang, G., Xia, L., Su, K., … Yin, S. (2015)b. Ontogenetic development of the auditory sensory organ in zebrafish (*Danio rerio*): changes in hearing sensitivity and related morphology. *Scientific Reports, 5*(4), 15943

Wang, P., Sun, G., Jia, Y., Meharg, A. A., & Zhu, Y. (2014)c. A review on completing arsenic biogeochemical cycle: Microbial volatilization of arsines in environment. *Journal of Environmental Sciences, 26*(2), 371–381.

Weiser, D. C., Pyati, U. J., & Kimelman, D. (2007). Gravin regulates mesodermal cell behavior changes required for axis elongation during zebrafish gastrulation. *Genes and Development, 21*(12), 1559–1571.

Westphal, R. E., & O'Malley, D. M. (2013). Fusion of locomotor maneuvers, and improving sensory capabilities, give rise to the flexible homing strikes of juvenile zebrafish. *Frontier Neural Circuits, 7*(6), 108.

WHO.(2006).*Neurological Disorders: Public Health Challenges*.Switzerland: World Health Organization Press.

WHO. (2003). Elemental mercury and inorganic mercury compounds: human health aspects. Concise International Chemical Assessment Document 50. *World Health Organisation International Programme on Chemical Safety*. Retrieved from http://www.who.int/iris/handle/10665/42607

WHO. (2001). Arsenic and arsenic compounds. Environmental Health Criteria 224. *Environmental Health,13*.

Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., … Steinhausen, H.C. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European Neuropsychopharmacology : The Journal of the European College of Neuropsychopharmacology, 21*(9), 655–79.

Wu, J., Cheng, G., Lu, Z., Wang, M., Tian, J., & Bi, Y. (2016). Effects of methyl mercury chloride on rat hippocampus structure. *Biological Trace Element Research, 171*(1), 124–130.

Xu, X., Mathieu, C., Boitard, S. E., Dairou, J., Dupret, J. M., Agbulut, O., & Rodrigues-Lima, F. (2014). Skeletal muscle glycogen phosphorylase is irreversibly inhibited by mercury: Molecular, cellular and kinetic aspects. *FEBS Letters, 588*(1), 138–142.

Xu, X., Weber, D., Carvan, M. J., Coppens, R., Lamb, C., Goetz, S., & Schaefer, L. A. (2012). Comparison of neurobehavioral effects of methylmercury exposure in older and younger adult zebrafish (*Danio rerio*). *NeuroToxicology, 33*(5), 1212–1218.

© COPYRIGHT UPM

Yadav, R. S., Sankhwar, M. L., Shukla, R. K., Chandra, R., Pant, A. B., Islam, F., & Khanna, V. K. (2009). Attenuation of arsenic neurotoxicity by curcumin in rats. *Toxicology and Applied Pharmacology, 240*(3), 367–376.

Yang, D., Lauridsen, H., Buels, K., Chi, L. H., La Du, J., Bruun, D. A., … Lein, P. J. (2011). Chlorpyrifos-oxon disrupts zebrafish axonal growth and motor behavior. *Toxicological Sciences, 121*(1), 146–159.

Yang, L., Ho, N. Y., Alshut, R., Legradi, J., Weiss, C., Reischl, M., … Strähle, U. (2009). Zebrafish embryos as models for embryotoxic and teratological effects of chemicals. *Reproductive Toxicology, 28*(2), 245-53.

Yasutake, A., Marumoto, M., & Yoshida, M. (2010). Neurotoxic action of inorganic mercury injected in the intraventricular space of mouse cerebrum. *The Journal of Toxicological Sciences, 35*(5), 767–71.

Yorifuji, T., Kato, T., Ohta, H., Bellinger, D. C., Matsuoka, K., & Grandjean, P. (2016). Neurological and neuropsychological functions in adults with a history of developmental arsenic poisoning from contaminated milk powder. *Neurotoxicology and Teratology, 53*, 75–80.

Yorifuji, T., Kato, T., Kado, Y., Tokinobu, A., Yamakawa, M., Tsuda, T., & Sanada, S. (2015). Intrauterine exposure to methylmercury and neurocognitive functions: Minamata disease. *Archives of Environmental & Occupational Health, 70*(5), 297–302.

Yorifuji, T., Tsuda, T., Inoue, S., Takao, S., & Harada, M. (2011). Long-term exposure to methylmercury and psychiatric symptoms in residents of Minamata, Japan. *Environment International, 37*(5), 907–913.

Yoshida, M., Watanabe, C., Honda, A., & Satoh, M. (2013). Emergence of delayed behavioral effects in offspring mice exposed to low levels of mercury vapor during the lactation period. *The Journal of Toxicological Sciences, 38*(1), 1–6.

Young, J. W., Minassian, A., Paulus, M. P., Geyer, M. A., & Perry, W. (2007). A reverse-translational approach to bipolar disorder: Rodent and human studies in the Behavioral Pattern Monitor. *Neuroscience & Biobehavioral Reviews, 31*(6), 882–896.

Zagury, G. J., Dobran, S., Estrela, S., & Deschenes, L. (2008). Inorganic arsenic speciation in soil and groundwater near in-service chromated copper arsenate-treated wood poles. *Environmental Toxicology and Chemistry, 27*(4), 799–807.

Zhang, Q. F., Li, Y. W., Liu, Z. H., & Chen, Q. L. (2016). Exposure to mercuric chloride induces developmental damage, oxidative stress and immunotoxicity in zebrafish embryos-larvae. *Aquatic Toxicology, 181*, 76–85.

Zhen, H., Wen, M., Yang, Y., Can, Z., Hui, G., Li, X., & Deli, L. (2014). Toxic effects of $HgCl_2$ on activities of SOD, AchE and relative expression of SOD, AChE, CYP1A1 of zebrafish. *Ecotoxicology, 23*(10), 1842–1845.

Zhu, Y., Xi, S., Li, M., Ding, T., Liu, N., Cao, F., … Jiang, S. (2017). Fluoride and arsenic exposure affects spatial memory and activates the ERK/CREB signaling pathway in offspring rats. *NeuroToxicology, 59*, 56–64.

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