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CHEMICAL EFFECTS

How neurobehavior and brain development in alternative whole-organism models can contribute to prediction of developmental neurotoxicity

2024-03-27

Developmental neurotoxicity (DNT) is not routinely evaluated in chemical risk assessment because current test paradigms for DNT require the use of mammalian models which are ethically controversial, expensive, and resource demanding. Consequently, efforts have focused on revolutionizing DNT testing through affordable novel alternative methods for risk assessment. The goal is to develop a DNT in vitro test battery amenable to high-throughput screening (HTS). Currently, the DNT in vitro test battery consists primarily of human cell-based assays because of their immediate relevance to human health. However, such cell-based assays alone are unable to capture the complexity of a developing nervous system. Whole organismal systems that qualify as 3R (Replace, Reduce and Refine) models are urgently needed to complement cell-based DNT testing. These models can provide the necessary organismal context and be used to explore the impact of chemicals on brain function by linking molecular and/or cellular changes to behavioural readouts. The nematode *Caenorhabditis elegans*, the planarian *Dugesia japonica*, and embryos of the zebrafish *Danio rerio* are all suited to low-cost HTS and each has unique strengths for DNT testing. Here, we review the strengths and the complementarity of these organisms in a novel, integrative context and highlight how they can augment current cell-based assays for more comprehensive and robust DNT screening of chemicals. Considering the limitations of all in vitro test systems, we discuss how a smart combinatory use of these systems will contribute to a better human relevant risk assessment of chemicals that considers the complexity of the developing brain.

Authors: Eva-Maria S Collins, Ellen V S Hessel, Samantha Hughes

Full Source: *Neurotoxicology* 2024 Mar 27;50(161-813X(24)00031-7. doi: 10.1016/j.neuro.2024.03.005.

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Light oxygenated volatile organic compound concentrations in an Eastern Mediterranean urban atmosphere rivalling those in megacities

2024-03-29

Highly resolved measurements of primary and secondary oxygenated volatile organic compounds (OVOCs) by proton-transfer-reaction mass spectrometry (PTR-MS) and the AMOVOC sampler (Airborne Measurements Of VOC) were performed in Beirut, Lebanon, during the ECOCEM (Emissions and Chemistry of Organic Carbon in the East Mediterranean) experiments. The OVOC concentrations (0.15–7.0 ppb) rival those reported for international megacities like Paris, Tokyo, or São Paulo (0.3–6.5 ppb). This study highlights the seasonal variability of OVOCs, the potential role of background pollution on OVOC concentrations, traffic emissions of OVOCs, and the secondary production of OVOCs during both summer and winter. The primary and secondary OVOC fractions were estimated using two methods based on the night-time emission ratio and photochemical age. Our calculations coupled with a correlation analysis revealed the following: firstly, background concentrations contributed significantly, especially for longer-lived OVOCs, such as methanol and acetone (30%–80%). Secondly, secondary production in summer increased up to 60%, except for methanol and isoprene oxidation products, i.e., for methacrolein and methyl vinyl ketone. Thirdly, the secondary production in the Eastern Mediterranean persisted in winter, and finally, strong primary traffic emissions dominated the primary biogenic emissions. Finally, the emission ratios were used to evaluate the global anthropogenic emission inventories downscaled to Lebanon. Although limited to two individual non-lumped species (formaldehyde and acetone), the emission ratios compared well, within a factor of 2. However, the emissions of aldehydes and ketones from the CAMS, Edgar, and MACCITY inventories showed discrepancies of up to three orders of magnitude. This demonstrates a need for improved OVOC representation in emission inventories, considering the atmospheric relevance and abundance of OVOCs and their use in volatile chemical products.

Authors: Agnès Borbon, Thérèse Salameh, Stéphane Sauvage, Charbel Affif

Full Source: *Environmental pollution (Barking, Essex : 1987)* 2024 Mar 29;123797. doi: 10.1016/j.envpol.2024.123797.

Highly resolved measurements of primary and secondary oxygenated volatile organic compounds (OVOCs) by proton-transfer-reaction mass spectrometry (PTR-MS) and the AMOVOC sampler (Airborne Measurements Of VOC) were performed in Beirut, Lebanon, during the ECOCEM (Emissions and Chemistry of Organic Carbon in the East Mediterranean) experiments.

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The bioremediation of the typical persistent organic pollutants (POPs) by microalgae-bacteria consortia: A systematic review

2024-03-29

With industrialisation and the rapidly growing agricultural demand, many organic compounds have been leaked into the environment, causing serious damage to the biosphere. Persistent organic pollutants (POPs) are a type of toxic chemicals that are resistant to degradation through normal chemical, biological or photolytic approaches. With their stable chemical structures, POPs can be accumulated in the environment, and transported through wind and water, causing global environmental issues. Many researches have been conducted to remediate POPs contamination using various kinds of biological methods, and significant results have been seen. Microalgae-bacteria consortium is a newly developed concept for biological technology in contamination treatment, with the synergetic effects between microalgae and bacteria, their potential for pollutants degradation can be further released. In this review, two types of POPs (polychlorinated biphenyls and polycyclic aromatic hydrocarbons) are selected as the targeted pollutants to give a systematic analysis of the biodegradation through microalgae and bacteria, including the species selection, the identification of dominant enzymes, as well as the real application performance of the consortia. In the end, some outlooks and suggestions are given to further guide the development of applying microalgae-bacteria consortia in remediating POPs contamination. In general, the coculturing of microalgae and bacteria is a novel and efficient way to fulfil the advanced treatment of POPs in soil or liquid phase, and both monooxygenase and dioxygenase belonging to oxygenase play a vital role in the biodegradation of PCBs and PAHs. This review provides a general guide in the future investigation of biological treatment of POPs. Authors: Wenbo Guo, Hongyu Ren, Yinzhu Jin, Zetang Chai, Bingfeng Liu Full Source: Chemosphere 2024 Mar 29;141852. doi: 10.1016/j.chemosphere.2024.141852.

With industrialisation and the rapidly growing agricultural demand, many organic compounds have been leaked into the environment, causing serious damage to the biosphere.

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ENVIRONMENTAL RESEARCH

Development of a computational model to inform environmental surveillance sampling plans for *Salmonella enterica* serovar Typhi in wastewater

2024-03-29

Typhoid fever-an acute febrile disease caused by infection with the bacterium *Salmonella enterica* serotype Typhi (*S. Typhi*)-continues to be a leading cause of global morbidity and mortality, particularly in developing countries with limited access to safe drinking water and adequate sanitation. Environmental surveillance, the process of detecting and enumerating disease-causing agents in wastewater, is a useful tool to monitor the circulation of typhoid fever in endemic regions. The design of environmental surveillance sampling plans and the interpretation of sampling results is complicated by a high degree of uncertainty and variability in factors that affect the final measured pathogens in wastewater samples, such as pathogen travel time through a wastewater network, pathogen dilution, decay and degradation, and laboratory processing methods. Computational models can, to an extent, assist in the design of sampling plans and aid in the evaluation of how different contributing factors affect sampling results. This study presents a computational model combining dynamic and probabilistic modeling techniques to estimate-on a spatial and temporal scale-the approximate probability of detecting *S. Typhi* within a wastewater system. This model may be utilized to inform environmental surveillance sampling plans and may provide useful insight into selecting appropriate sampling locations and times and interpreting results. A simulated applied modeling scenario is presented to demonstrate the model's functionality for aiding an environmental surveillance study in a typhoid-endemic community. Authors: Elisabeth Burnor, Cory W Morin, Jeffrey H Shirai, Nicolette A Zhou, John Scott Meschke Full Source: PLoS neglected tropical diseases 2024 Mar 29;18(3):e0011468. doi: 10.1371/journal.pntd.0011468.

Typhoid fever-an acute febrile disease caused by infection with the bacterium *Salmonella enterica* serotype Typhi (*S.*

European soybean to benefit people and the environment

2024-03-31

Europe imports large amounts of soybean that are predominantly used for livestock feed, mainly sourced from Brazil, USA and Argentina. In addition, the demand for GM-free soybean for human consumption is project to increase. Soybean has higher protein quality and digestibility than other

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legumes, along with high concentrations of isoflavones, phytosterols and minerals that enhance the nutritional value as a human food ingredient. Here, we examine the potential to increase soybean production across Europe for livestock feed and direct human consumption, and review possible effects on the environment and human health. Simulations and field data indicate rainfed soybean yields of $3.1 \pm 1.2 \text{ t ha}^{-1}$ from southern UK through to southern Europe (compared to a 3.5 t ha^{-1} average from North America). Drought-prone southern regions and cooler northern regions require breeding to incorporate stress-tolerance traits. Literature synthesized in this work evidenced soybean properties important to human nutrition, health, and traits related to food processing compared to alternative protein sources. While acknowledging the uncertainties inherent in any modelling exercise, our findings suggest that further integrating soybean into European agriculture could reduce GHG emissions by 37-291 Mt CO₂e year⁻¹ and fertiliser N use by 0.6-1.2 Mt year⁻¹, concurrently improving human health and nutrition.

Authors: Jose L Rotundo, Rachel Marshall, Ryan McCormick, Sandra K Truong, David Styles, Jose A Gerde, Emmanuel Gonzalez-Escobar, Elizabete Carmo-Silva, Victoria Janes-Bassett, Jennifer Logue, Paolo Annicchiarico, Chris de Visser, Alice Dind, Ian C Dodd, Louise Dye, Stephen P Long, Marta S Lopes, Joke Pannecoucq, Moritz Reckling, Jonathan Rushton, Nathaniel Schmid, Ian Shield, Marco Signor, Carlos D Messina, Mariana C Rufino

Full Source: Scientific reports 2024 Mar 31;14(1):7612. doi: 10.1038/s41598-024-57522-z.

PHARMACEUTICAL/TOXICOLOGY

Association of exposures to environmental chemicals estimated through primary teeth biomatrix and health outcomes in children and adolescents - A systematic review

2024-03-28

Children's heightened susceptibility to environmental exposure arises from their underdeveloped detoxification mechanisms and augmented per-unit body-weight absorption capacity for chemical compounds. Primary teeth are an emerging biomatrix, which aid in storing crucial data on early exposure to harmful substances and developmental illnesses. This systematic review aimed to evaluate the association between environmental chemical exposure and health outcomes in children and adolescents using primary teeth as a matrix. The study protocol was

Children's heightened susceptibility to environmental exposure arises from their underdeveloped detoxification mechanisms and augmented per-unit body-weight absorption capacity for chemical compounds.

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registered with PROSPERO (CRD42023428013). The review spanned studies published between 1974 and 2023, identified through an extensive literature search on databases like MEDLINE, EMBASE, LILACS, CINAHL, the Cochrane Oral Health Group Specialized Register, Scopus, and Web of Science. Distiller SR software was used to assess study quality and extract the outcome data. The NTP-OHAT scale assessed evidence quality, and case-control, cross-sectional, and cohort studies in English were included. Comprehensively reviewing 5287 articles resulted in 29 studies being included in the final analysis, comprising 15 cross-sectional, seven case-control, and seven cohort studies. All 29 studies qualified for qualitative analysis. Eleven studies analyzed lead (Pb) effects on health outcomes, four analyzed manganese (Mn), and 14 investigated other element groups. Primary teeth biomatrix assessed various health outcomes: neurobehavior, childhood behaviour, ADHD, birth outcomes, fetal alcohol syndrome disease, inflammatory bowel disease, and dental caries. This study contributes to existing evidence, reinforcing a link between environmental metal exposure and health consequences. The evidence extends to prenatal and postnatal periods, substantiated by primary teeth biomatrix analysis. Lead level fluctuations can influence neuropsychological functioning, potentially causing cognitive impairments. Altered manganese levels correlate with behavioral issues, adverse effects on visuospatial development, and birth weight changes. Primary teeth biomatrices aid fetal alcohol spectrum disorders diagnosis, and correlations between organo-chemical exposure and autism were observed.

Authors: Krithika Gupta, M S Muthu, Ankita Saikia, Swetha Sriram, Latha Nirmal, Umesh Wadgave, Vineet Dhar

Full Source: The Science of the total environment 2024 Mar 28:172032. doi: 10.1016/j.scitotenv.2024.172032.

A Case of Multidrug-Resistant Tuberculosis in an Active Duty Military Health Care Worker

2024-03-29

Cases of active tuberculosis (TB) in the U.S. Military have fallen over the last century in large part due to improved screening and treatment options. The subset of multidrug-resistant TB (MDR-TB) is almost nonexistent within the U.S. Military. We present a case of MDR-TB in an active duty U.S. Military health care worker and discuss several considerations for treatment that may present challenges for U.S. Military medical practitioners. A 30-year-old active duty Soldier was referred to Army public health services after a bronchoscopy sample was positive for Mycobacterium tuberculosis

Cases of active tuberculosis (TB) in the U.S.

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complex. Sputum smears were negative for acid-fast bacilli, suggesting lower risk for community spread. One month after initiation of the standard 4-drug regimen for active TB, genetic susceptibility testing found the patient's *M. tuberculosis* isolate to be resistant to rifampin, isoniazid, and pyrazinamide. Contact investigation efforts among co-workers and family members fortunately found no new interferon-gamma release assay conversions. Coordination of public health assets to ensure a successful treatment regimen occurred across varied local, state, and federal agencies. Atypical medications required coordination with the FDA for procurement. An extensive surveillance plan for medication adverse effects was required. Finally, questions of public health authority versus patient autonomy arose requiring multidisciplinary input and ethical discussions.

Authors: Amanda E Saunders, Kevin M Shanahan, John W Downs
Full Source: *Military medicine* 2024 Mar 29;usae104. doi: 10.1093/milmed/usae104.

OCCUPATIONAL

Impact of occupational characteristics on return to work for employed patients after elective cervical spine surgery

2024-03-29

Objective: In a cohort of employed patients undergoing elective cervical spine surgery with an uncomplicated postoperative course, the authors sought to determine the demographic, functional, and occupational characteristics associated with return to work (RTW) following surgery.

Methods: A retrospective cohort study of prospectively collected data was undertaken of patients undergoing elective cervical spine surgery for degenerative disease in the Quality Outcomes Database. Study inclusion criteria were:

1. employed prior to surgery and planned to RTW,
2. no unplanned readmissions,
3. achieved 30% improvement on the Neck Disability Index (NDI), and
4. were satisfied with the surgical outcome at 3 or 12 months postoperatively. A multivariable Cox regression model was built using demographic, functional, operative, and occupational characteristic to predict time to RTW.

Results: Of 5110 included patients, 4788 (93.7%) returned to work within 12 months, with a median time of 35 (IQR 19-60) days. Patients who did RTW were significantly younger (51.3 ± 9.4 vs 55.8 ± 9.6 years, $p < 0.001$), more often underwent an anterior approach (85.8% vs 80.7% , $p = 0.009$),

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were significantly more privately insured (82.1% vs 64.0% , $p < 0.001$), and were less likely to have workers' disability insurance (6.7% vs 14.6% , $p < 0.001$) compared with patients who did not RTW. On multivariable Cox regression, demographic factors associated with a longer RTW were older age (hazard ratio [HR] 0.99, 95% CI 0.99-1.00, $p < 0.001$) and Black race (HR 0.71, 95% CI 0.62-0.81, $p < 0.001$). Male sex was associated with a shorter RTW time (HR 1.19, 95% CI 1.11-1.26, $p < 0.001$). Regarding baseline functional status, worse preoperative NDI (HR 0.99, 95% CI 0.99-0.99, $p < 0.001$) was associated with a longer RTW, whereas the absence of myelopathy was associated with a shorter RTW (HR 1.17, 95% CI 1.09-1.25, $p < 0.001$). Having a sedentary (HR 1.81, 95% CI 1.65-1.99, $p < 0.001$), light-intensity (HR 1.60, 95% CI 1.45-1.76, $p < 0.001$), and medium-intensity (HR 1.11, 95% CI 1.01-1.22, $p = 0.037$) occupation was associated with a shorter RTW time compared with a heavy-intensity occupation at any time point. Heavy-intensity occupations were independently the strongest predictor of longer RTW. Similar predictors of shorter RTW were found in a subanalysis of occupation intensity and among operative approaches used.

Conclusions: Among patients undergoing elective degenerative cervical spine surgery who had favorable surgical outcomes and planned to RTW before surgery, 94% had a successful RTW. Age was the strongest predictor of lower odds of RTW. Regarding time to RTW, having a sedentary, light-intensity, or medium-intensity occupation was associated with a shorter RTW time compared with a heavy-intensity occupation. These findings highlight the importance of considering the demographic and occupational characteristics when predicting postoperative RTW in patients with satisfactory surgical outcomes.

Authors: Hani Chanbour, Jacquelyn S Pennings, Claudia Davidson, Andrew J Croft, Jeffrey W Chen, Wilson E Vaughan, Inamullah Khan, Kristin R Archer, Raymond J Gardocki, Amir M Abtahi, Byron F Stephens, Scott L Zuckerman
Full Source: *Journal of neurosurgery. Spine* 2024 Mar 29;1-13. doi: 10.3171/2024.1.SPINE231060.

A tool to assess risk of bias in non-randomized follow-up studies of exposure effects (ROBINS-E)

2024-03-24

Background: Observational epidemiologic studies provide critical data for the evaluation of the potential effects of environmental, occupational and behavioural exposures on human health. Systematic reviews of these studies play a key role in informing policy and practice. Systematic reviews

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should incorporate assessments of the risk of bias in results of the included studies.

Objective: To develop a new tool, Risk Of Bias In Non-randomized Studies - of Exposures (ROBINS-E) to assess risk of bias in estimates from cohort studies of the causal effect of an exposure on an outcome.

Methods and results: ROBINS-E was developed by a large group of researchers from diverse research and public health disciplines through a series of working groups, in-person meetings and pilot testing phases. The tool aims to assess the risk of bias in a specific result (exposure effect estimate) from an individual observational study that examines the effect of an exposure on an outcome. A series of preliminary considerations informs the core ROBINS-E assessment, including details of the result being assessed and the causal effect being estimated. The assessment addresses bias within seven domains, through a series of 'signalling questions'. Domain-level judgements about risk of bias are derived from the answers to these questions, then combined to produce an overall risk of bias judgement for the result, together with judgements about the direction of bias.

Conclusion: ROBINS-E provides a standardized framework for examining potential biases in results from cohort studies. Future work will produce variants of the tool for other epidemiologic study designs (e.g. case-control studies). We believe that ROBINS-E represents an important development in the integration of exposure assessment, evidence synthesis and causal inference.

Authors: Julian P T Higgins, Rebecca L Morgan, Andrew A Rooney, Kyla W Taylor, Kristina A Thayer, Raquel A Silva, Courtney Lemeris, Elie A Akl, Thomas F Bateson, Nancy D Berkman, Barbara S Glenn, Asbjørn Hróbjartsson, Judy S LaKind, Alexandra McAleenan, Joerg J Meerpohl, Rebecca M Nachman, Julie E Obbagy, Annette O'Connor, Elizabeth G Radke, Jelena Savović, Holger J Schünemann, Beverley Shea, Kate Tilling, Jos Verbeek, Meera Viswanathan, Jonathan A C Sterne
Full Source: Environment international 2024 Mar 24;186:108602. doi: 10.1016/j.envint.2024.108602.

Job function as determinant of clinker exposure at workplaces during cement production

2024-03-29

Objectives: In the cement production industry, exposure to airborne particulate matter is associated with a decline in lung function and increased airway symptoms. Exposure to clinker—the major constituent of cement and supposedly the cause of the observed adverse health effects—

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was determined recently in 15 cement production plants located in 8 different countries (Estonia, Greece, Italy, Norway, Sweden, Switzerland, Spain, Turkey). It was shown that the median clinker abundance in the thoracic fraction varied between approximately 20% and 70% for individual plants. The present study complements the previous work by investigating the significance of job function as a determinant of clinker exposure.

Methods: The elemental composition (water and acid-soluble fractions separately) of 1,227 personal thoracic workplace samples was analyzed by positive matrix factorization (PMF) to determine the contribution of different sources to the composition of airborne particulate matter and to quantify the clinker content.

Results: Median thoracic mass air concentrations varied for individual job functions between 0.094 and 12 mg/m³ (estimated separately for different plants). The PMF 5-factor solution yielded median relative clinker abundances in the personal thoracic samples between 7.6% and 81% for individual job functions. Thoracic clinker air concentrations are highest for cleaning, production, and maintenance work, and lowest for administration and other work. Foremen and laboratory personnel show intermediate exposure levels. The plant was found to have a much higher contribution to the total variance of the thoracic clinker air concentrations than the job function. Thoracic clinker air concentrations (medians between 0.01 and 5.5 mg/m³) are strongly correlated with the thoracic mass air concentrations and to a lesser extent with the relative clinker abundance in an aerosol sample.

Conclusions: Job function is an important predictor of exposure to clinker in the cement production industry. As clinker is suspected to be the causal agent for the observed adverse health effects among cement production workers, the clinker air concentration may be a better exposure metric than thoracic air mass concentration despite the strong correlation between the two. Reduction strategies should focus on the most exposed job categories cleaning, production, and maintenance work.

Authors: Stephan Weinbruch, Mark Scerri, Wijnand Eduard, Yngvar Thomassen, Karl-Christian Nordby, Hilde Notø
Full Source: Annals of work exposures and health 2024 Mar 29;wxae022. doi: 10.1093/annweh/wxae022.

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