Common chemicals in electronics and baby products harm brain development

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A

GLUTAMATE

Cellular and Organ Effects

Monolayer in vitro cell culture
- Reduced response to glutamate (Hausherr et al. 2014)

3D in vitro cell culture
- Alternation in expression of glutamate NMDA receptor (Hogberg et al. 2021)
- NAA and L aspartic decreased (Hogberg et al. 2021)
- Reduced levels of glutamate (Hogberg et al. 2021)

Rodent in vivo
- Disruption of glutamate (Yang et al. 2018)
- Disruption of NAA, creatine and lactic acid (Yang et al. 2018)
- Increased levels of glutamate (Liu et al. 2020)
- Neuronal death (Yang et al. 2018; Liu et al. 2020)

Organism Effects

Rodent in vivo
- Impaired learning and memory (Yang et al. 2018)

Human Effects

- Adverse impacts on cognitive development, including early language ability, and fine motor skills (Doherty et al. 2019b)
- Adverse behavioral development including withdrawal, attention problems, depression, hyperactivity, and aggression (Doherty et al. 2019c)
- Decrease in IQ and working memory (Castorina et al. 2017a)
- Social behavioral problems including less responsible behavior, and more externalizing behaviors (Lipscomb et al. 2017)

B

GABA (GAMMA-AMINOBUTYRIC ACID)

Cellular and Organ Effects

Monolayer in vitro cell culture
- Inhibition of GABA R (Gant et al. 1987)

3D in vitro cell culture
- Decrease in genes involved in GABA production and signaling (Hogberg et al. 2021)
- Decrease in GABA (Hogberg et al. 2021)

Zebrafish
- Altered levels of GABA (Wang et al. 2015; Shi et al. 2018)

Rodent in vivo
- GABA antagonist (Umezu et al. 1998)
- Disruption of GABA (Yang et al. 2018)

Organism Effects

Zebrafish
- Hyperactivity (Oliveri et al. 2015)

Rodent in vivo
- Impaired learning and memory (Yang et al. 2018)
- Increased ambulatory behavior (Yang et al. 2018)

Human Effects

- Adverse impacts on cognitive development, including early language ability, and fine motor skills (Doherty et al. 2019b)
- Adverse behavioral development including withdrawal, attention problems, depression, hyperactivity, and aggression (Doherty et al. 2019c)
- Decrease in IQ and working memory (Castorina et al. 2017a)
- Social behavioral problems including less responsible behavior, and more externalizing behaviors (Lipscomb et al. 2017)

C

OTHER NEUROTRANSMITTERS

Cellular and Organ Effects

Monolayer in vitro cell culture
- Increase in differentiation of dopaminergic neurons (Dishaw et al. 2011)

3D in vitro cell culture
- Decrease in dopamine (Hogberg et al. 2021)

Zebrafish
- Dopamine levels decreased (Wang et al. 2015)
- Dopamine and dopamine signaling related genes decreased (Li et al. 2020)
- Decreased serotonin and histamine levels (Wang et al. 2015)

Rodent in vivo
- Dopamine signaling altered (Umezu et al. 1998)
- Disruption in serotonin pathways (Rock et al. 2018, 2020)
- Serotonin levels increased (Rock et al. 2020)

Organism Effects

Zebrafish
- Vulnerability to anxiety-like behavior potentially due to decrease in dopamine (Li et al. 2020)

Rodent in vivo
- Increased ambulatory behavior (Umezu et al. 1998)

Human Effects

- Adverse impacts on cognitive development, including early language ability, and fine motor skills (Doherty et al. 2019b)
- Adverse behavioral development including withdrawal, attention problems, depression, hyperactivity, and aggression (Doherty et al. 2019c)
- Decrease in IQ and working memory (Castorina et al. 2017a)
- Social behavioral problems including less responsible behavior, and more externalizing behaviors (Lipscomb et al. 2017)

Figure 1. Developmental neurotoxicity: neurotransmitters—(A) glutamate, (B) GABA, and (C) other neurotransmitters. Effects seen in humans may be associated with many different systems and thus are repeated for each outcome category. Note: 3D, three dimensional; GABA, gamma-aminobutyric acid; IQ, intelligence quotient; NAA, n-acetyl aspartate; NMDA, NN -methyl-d aspartate; R, receptor. Credit: DOI: 10.1289/EHP9285

Chemicals increasingly used as flame retardants and plasticizers pose a larger risk to children's brain development than previously thought, according to a commentary published today in *Environmental Health Perspectives*. The research team reviewed dozens of human, animal, and cell-based studies and concluded that exposure to even low levels of the chemicals—called organophosphate esters—may harm IQ, attention, and memory in children in ways not yet looked at by regulators.

The neurotoxicity of organophosphate esters used as nerve agents and pesticides is widely recognized, but the neurotoxicity of those used as flame retardants and plasticizers has been assumed to be low. As a result, they are widely used as replacements for some phased-out or banned halogenated flame retardants in electronics, car seats and other baby products, furniture, and building materials. However, the authors' analysis revealed that these chemicals are also neurotoxic, but through different mechanisms of action.

"The use of organophosphate esters in everything from TVs to car seats has proliferated under the false assumption that they're safe," said Heather Patisaul, lead author and neuroendocrinologist at North Carolina State University. "Unfortunately, these chemicals appear to be just as harmful as the chemicals they're intended to replace but act by a different mechanism."

Organophosphate esters continuously migrate out of products into air and dust. Contaminated dust gets on our hands and is then inadvertently ingested when we eat. That's why these chemicals have been detected in virtually everyone tested. Children are particularly exposed from hand-to-mouth behavior. Babies and young children consequently have much higher concentrations of these chemicals in their bodies during the most vulnerable windows of brain development.

"Organophosphate esters threaten the brain development of a whole generation," said co-author and retired NIEHS Director Linda Birnbaum. "If we don't stem their use now, the consequences will be grave and irreversible."

The authors call for a stop to unnecessary uses of all organophosphate esters. This includes their use as flame retardants to meet ineffective flammability standards in consumer products, vehicles, and building materials.

For uses where organophosphate esters are deemed essential, the authors recommend governments and industry conduct alternatives assessments and make investments in innovative solutions without harmful chemicals.

"Organophosphate esters in many products serve no essential function while posing a serious risk, especially to our children," said Carol Kwiatkowski, co-author and Science and Policy Senior Associate at the Green Science Policy Institute. "It's urgent that product manufacturers critically reevaluate the uses of organophosphate ester flame retardants and plasticizers—many may be doing more harm than good."

More information: Beyond Cholinesterase Inhibition: Developmental

Neurotoxicity of Organophosphate Ester Flame Retardants and Plasticizers, *Environmental Health Perspectives* (2021). DOI: 10.1289/EHP9285

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