Effects of Early Bisphenol A Exposure on Cortical Excitatory and Inhibitory Balance and Behaviour in Mice

Effets de l'exposition précoce au bisphénol A sur l'équilibre et le comportement excitateurs et inhibiteurs corticales chez la souris

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Abstract | Résumé

Exposure to endocrine-disrupting chemicals such as 4-[2-(4-hydroxyphenyl)propan-2-yl]phenol (BPA) during development has been linked to altered neurodevelopment and increased risk for autism spectrum disorder (ASD) (1-5). During pregnancy, BPA exposure occurs through ingestion of contaminated food or beverages from polycarbonate plastics and epoxy resin-lined containers, allowing it to enter maternal circulation and cross the placenta (6-7). A proposed neurobiological mechanism underlying ASD involves disruption of cortical excitatory/inhibitory (E/I) synaptic balance, critical for neural network function and behavioural regulation (3, 8-12). However, it remains unclear whether combined prenatal and early postnatal BPA exposure alters cortical E/I organization in a dose-dependent and sex-specific manner. This study will investigate how early-life BPA exposure influences cortical synaptic markers and ASD-relevant behaviours in C57BL/6J mice. Eighteen pregnant dams (n = 6 per group) will be randomly assigned to control (water), low-dose BPA, or high-dose BPA groups. Through oral gavage, BPA will be administered from gestational day 0 through postnatal day 21 (PND21), targeting a critical window of synaptogenesis. This study will include only full-term offspring. BPA doses will model environmentally relevant human exposure (13-15). The experiment will divide offspring into molecular and behavioural cohorts. Molecular analyses will quantify excitatory (VGLUT1, PSD-95) and inhibitory (GAD67) synaptic markers using immunohistochemistry and western blotting to calculate cortical E/I ratios at PND21. Adolescent offspring will undergo behavioural testing between PND35 and PND60, including the three-chamber social interaction and open-field tests to assess sociability and anxiety-related behaviours. The study expects to determine that early-life BPA exposure produces dose-dependent and sex-specific alterations in cortical E/I balance accompanied by ASD-relevant behavioural changes (1, 3, 16-21). By integrating molecular and behavioural outcomes, this study will clarify whether early-life BPA exposure disrupts cortical E/I balance, a neurobiological feature implicated in ASD. This link would strengthen mechanistic evidence that environmental chemicals influence neurodevelopment and guide public health strategies to reduce exposure during critical developmental periods

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L'exposition à des substances perturbatrices endocriniennes telles que le 4-[2-(4-hydroxyphényl)propane-2-yl]phénol (BPA) au cours du développement a été associée à un neurodéveloppement altéré et à un risque accru de trouble du spectre de l'autisme (TSA) (1-5). Pendant la grossesse, l'exposition au BPA se produit par l'ingestion d'aliments ou de boissons contaminés provenant de plastiques polycarbonates et de contenants doublés de résine époxy, ce qui lui permet d'entrer dans la circulation maternelle et de traverser le placenta (6-7). Un mécanisme neurobiologique proposé sous-jacent au TSA implique la perturbation de l'équilibre synaptique cortical-excitateur/inhibiteur (E/I), essentiel au fonctionnement des réseaux neuronaux et à la régulation comportementale (3, 8-12). Cependant, il reste incertain si l'exposition combinée prénatale et précoce au BPA postnatal modifie l'organisation corticale de l'E/I de manière dépendant de la dose et spécifique au sexe. Cette étude étudiera comment l'exposition au BPA au début de la vie influence les marqueurs synaptiques corticales et les comportements liés au TSA chez les souris C57BL/6J. Dix-huit mères gestantes (n = 6 par groupe) seront assignées au hasard aux groupes témoins (eau), à faible dose de BPA ou à forte dose de BPA. Par voie orale, le BPA sera administré du jour 0 gestationnel au jour postnatal 21 (PND21), ciblant une fenêtre critique de synaptogenèse. Cette étude n'inclura que les enfants à terme. Les doses de BPA modélisent l'exposition humaine environnementale (13-15). L'expérience divisera la descendance en cohortes moléculaires et comportementales. Les analyses moléculaires quantifieront les marqueurs synaptiques excitateurs (VGLUT1, PSD-95) et inhibiteurs (GAD67) en utilisant l'immunohistochimie et le transfert de protéines pour calculer les rapports corticaux E/I à PND21. Les enfants adolescents subiront des tests comportementaux entre PND35 et PND60, incluant les tests d'interaction sociale à trois chambres et des tests en champ ouvert pour évaluer la sociabilité et les comportements liés à l'anxiété. L'étude s'attend à déterminer que l'exposition au BPA au début de la vie entraîne des altérations dépendantes de la dose et spécifiques au sexe dans l'équilibre cortical/E/I, accompagnées de changements comportementaux liés au TSA (1, 3, 16-21). En intégrant les résultats moléculaires et comportementaux, cette étude clarifiera si l'exposition au BPA au début de la vie perturbe l'équilibre cortical/E/I, une caractéristique neurobiologique impliquée dans le TSA. Ce lien renforcerait les preuves mécanistes que les substances chimiques environnementales influencent le neurodéveloppement et guiderait les stratégies de santé publique pour réduire l'exposition durant les périodes critiques du développement.

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