Development-progressive neurotoxicity regulated neuroinflammation with prenatal chemical exposure on the rat. • 炎症が制御する発達依存的な神経毒性発現

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Administrating schedules

第126回日本解剖学会総会・全国学術集会/ 第98回日本生理学会大会シンポジウムより抜粋

Background

Autism (AD), Attention deficit hyperactivity disorder (ADHD), Learning disorder (LD), Pervasive Developmental Disorder (PDD) Mental disorders are increased in modern societies.

How do these risk factors induce neuronal disorders?

Autism-inducing risk factors from cohort study

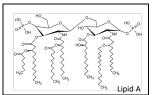
- Smoking
- Organophosphate
- Organochlorine
- Antibiotics Age of fathers
- Assisted reproduction
- Caesarean birth
- - 4 times up as smoking in first pregnancy 2.25 times up to mother expose1.71 times up to children expose

 - s up to children expose
 - Some risk
- material risk

T.FUJIWARA, I. TAKAMATSU J.Natl.Inst.Public Health,59(4):2010 Interrelated

Experimental inducer of

Lipopolysaccharide (LPS)



autism or schizophrenia

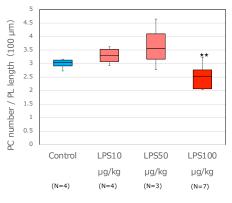
Well-known **endotoxins** found in the outer membrane of Gram-negative bacteria. It binds the CD14/TLR4/MD2 receptor complex in many cell types, but especially in monocytes, dendritic cells, macrophages and B cells, which promotes the secretion of pro-inflammatory cytokines.

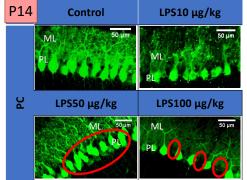
Valproate (VPA)



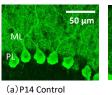
Medications primarily used to treat epilepsy and

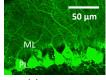
Lipopolysaccharide (LPS)

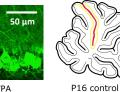




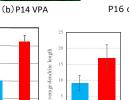
Valproate (VPA)

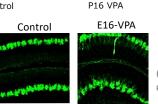












Conclusions

	LPS	VPA	GLY	CPF
Inflammatory cytokines	high	low	transient	N.D.
Microglia	±	_	+	+
PC number	Delayed decrease	±	decrease	increase
Dendrite length of PC	elongate	elongate	shorten	shorten
Excess folding	+	+ +	±	+
GFAP/GLAST expression	N.D.	+	-	N.D.

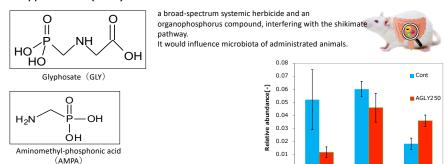
· Chemical-induced inflammation would induce neuronal dead-or-alive, however, it is not definitive. delayed.

- Microglia is one of the important key factors for neuronal development.
- [glutamate]_{out} control would decide neuronal death or excess survival.

Glyphosate (GLY)
Chlorpyrifos (CPF) and donepezil (DPZ)

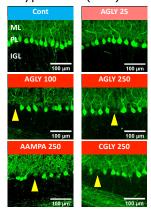
Case studies: Valproate (VPA)
Lipopolysaccharide (LPS)

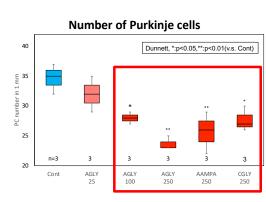
Glyphosate (GLY)



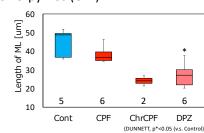
Glyphosate (GLY)

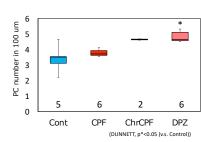
Glyphosate is readily degraded by soil microbes to aminomethylphosphonic acid (AMPA).

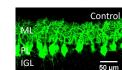


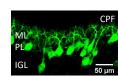


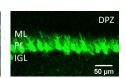
Chlorpyrifos (CPF)











PC formation stained with CalbindinD-28k antibodies