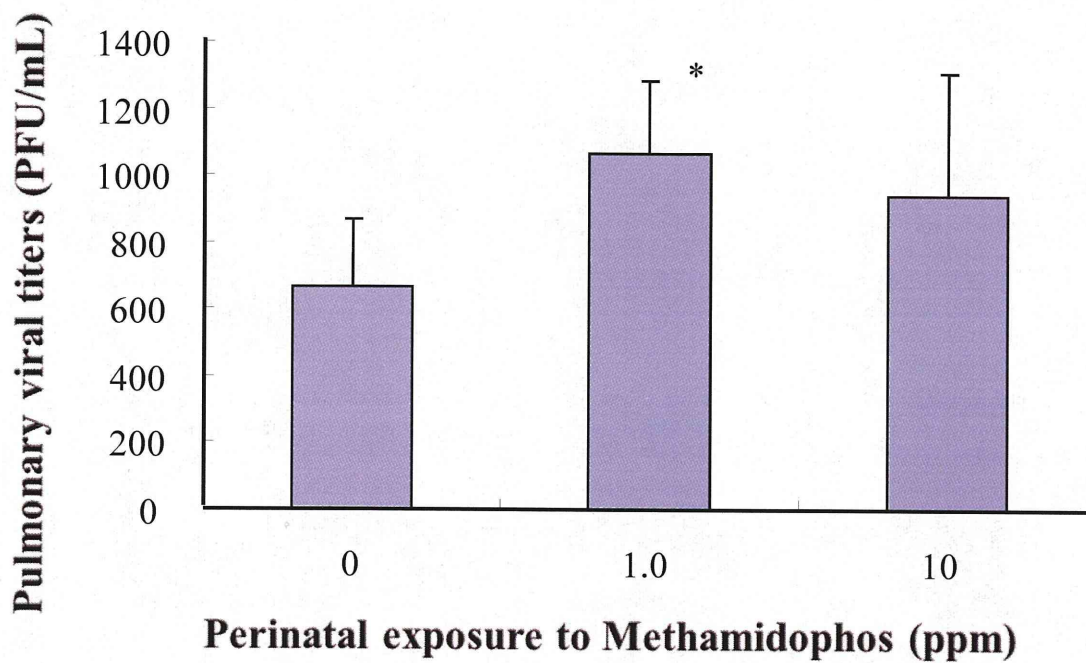


Fig. 61
Effect of perinatal exposure to Methamidophos on pulmonary viral titers in RSV-infected offspring mice



* $P < 0.01$ (vs. Control, Student's *t*-test)

Fig. 62
GeneSpring®によるデータマイニング

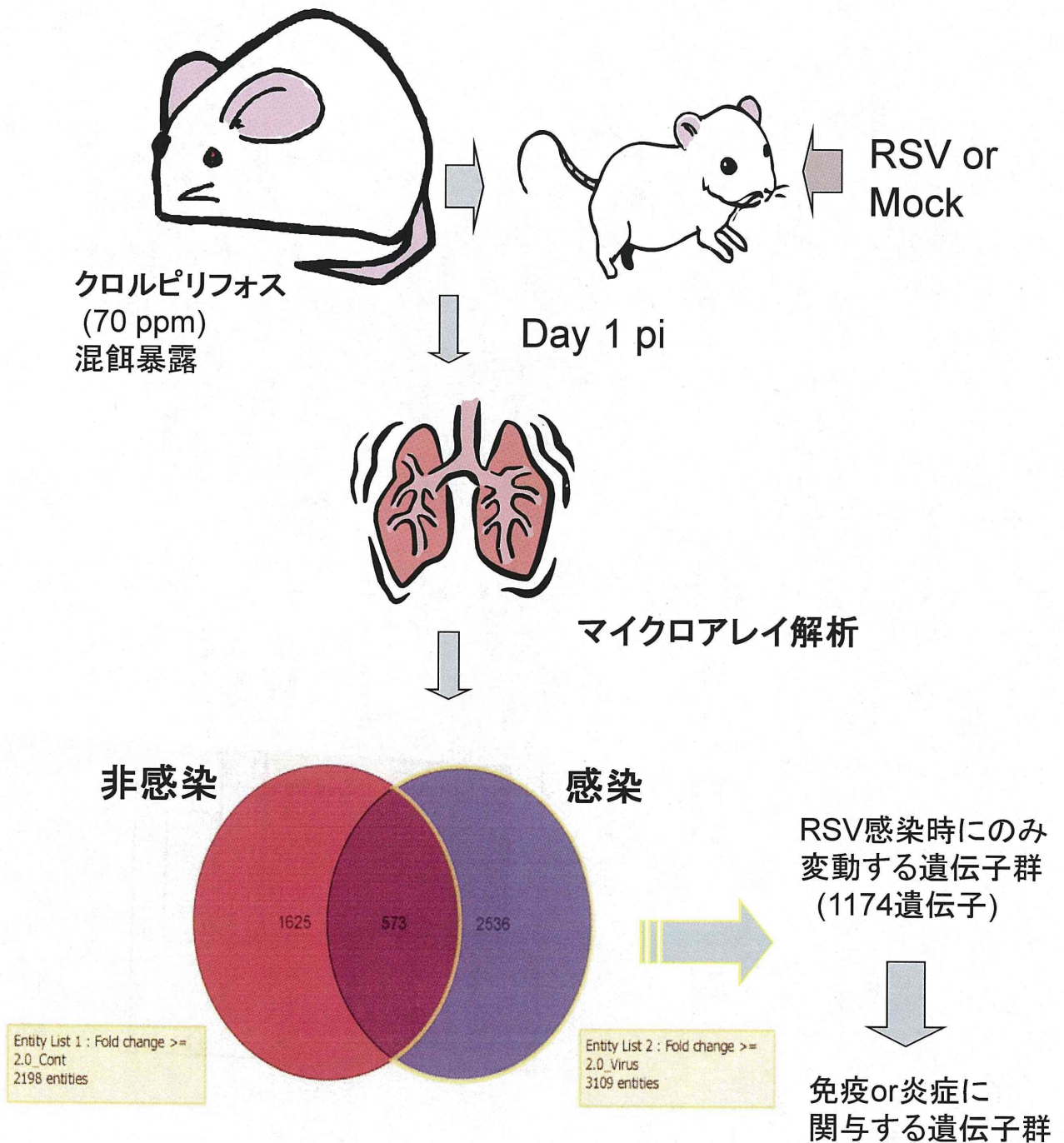


Fig. 63

Effects of treatment of methamidophos on IL-6 production from RSV-infected J774.1 cells

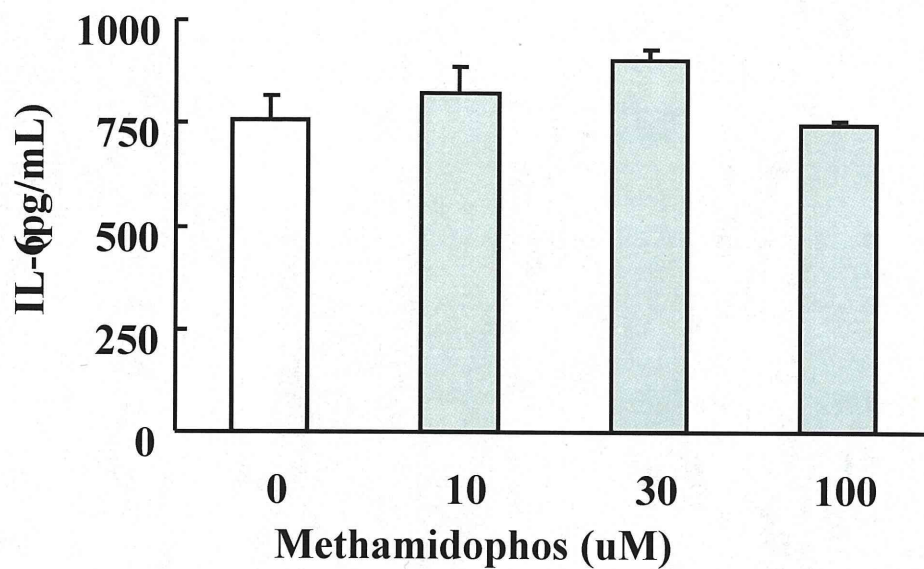


Fig. 64

Effects of treatment of methamidophos on IL-6 production from LPS-stimulated RAW264.7 cells

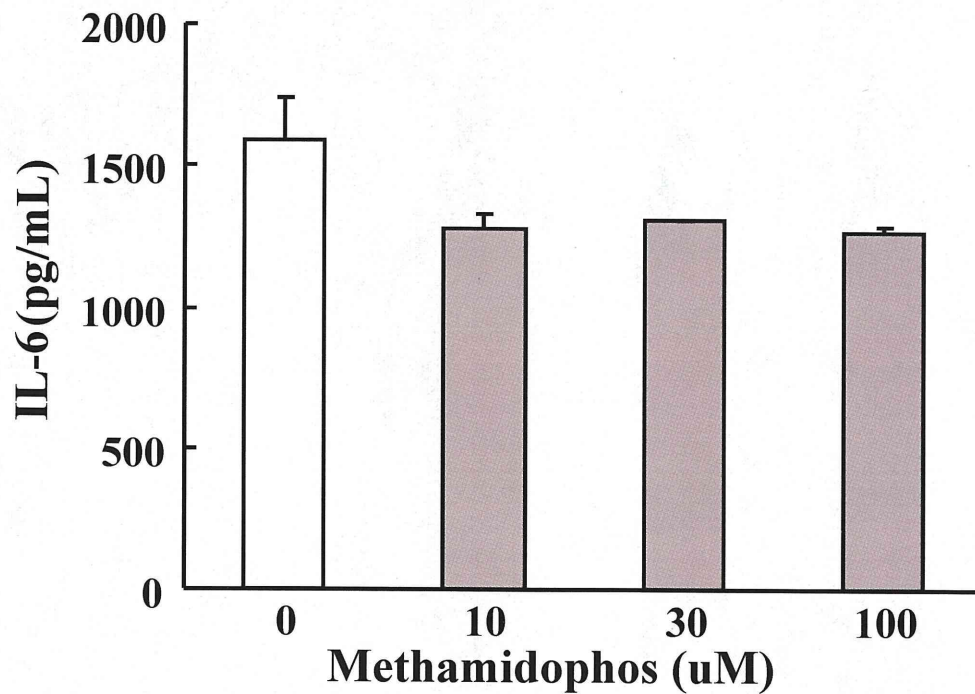
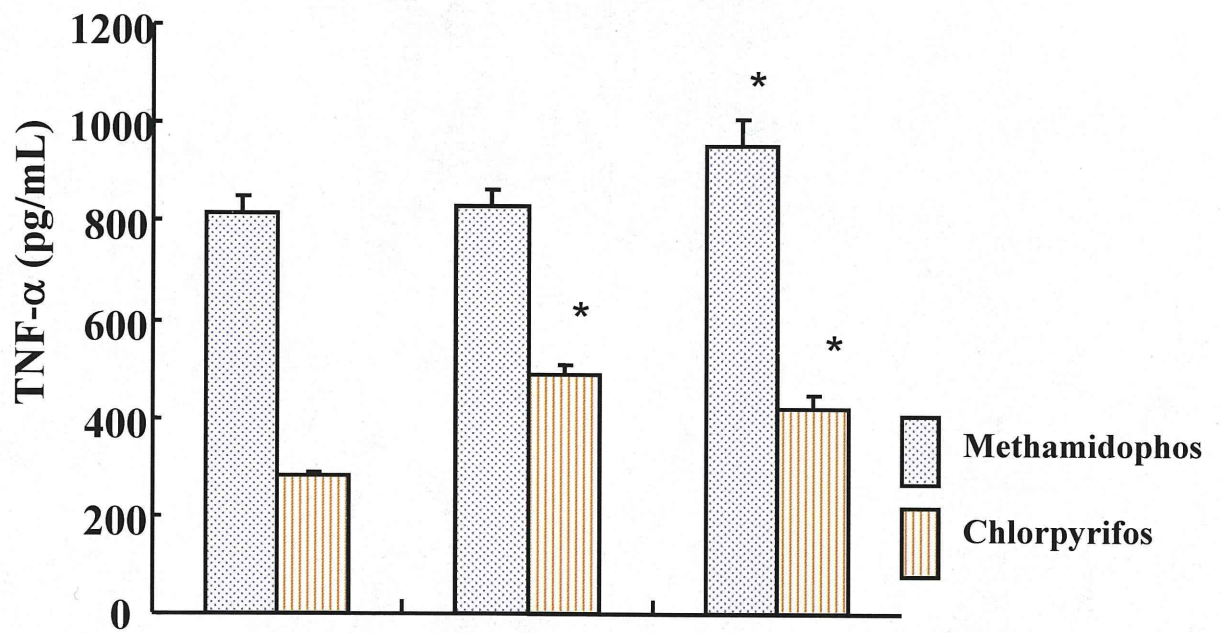


Fig. 65

Effects of treatment of methamidophos or chlorpyrifos on TNF- α production from Fluv.A-infected P388D1 cells



**Methamido-
phos (uM)**

0

30

100

**Chlorpyri-
fos (uM)**

0

10

30

*** $P < 0.01$ (vs 0 uM)**

Fig. 66

Effects of perinatal exposure to MnCl₂ on IFN- γ level in BALF from RSV-infected offspring on day 5 post-infection

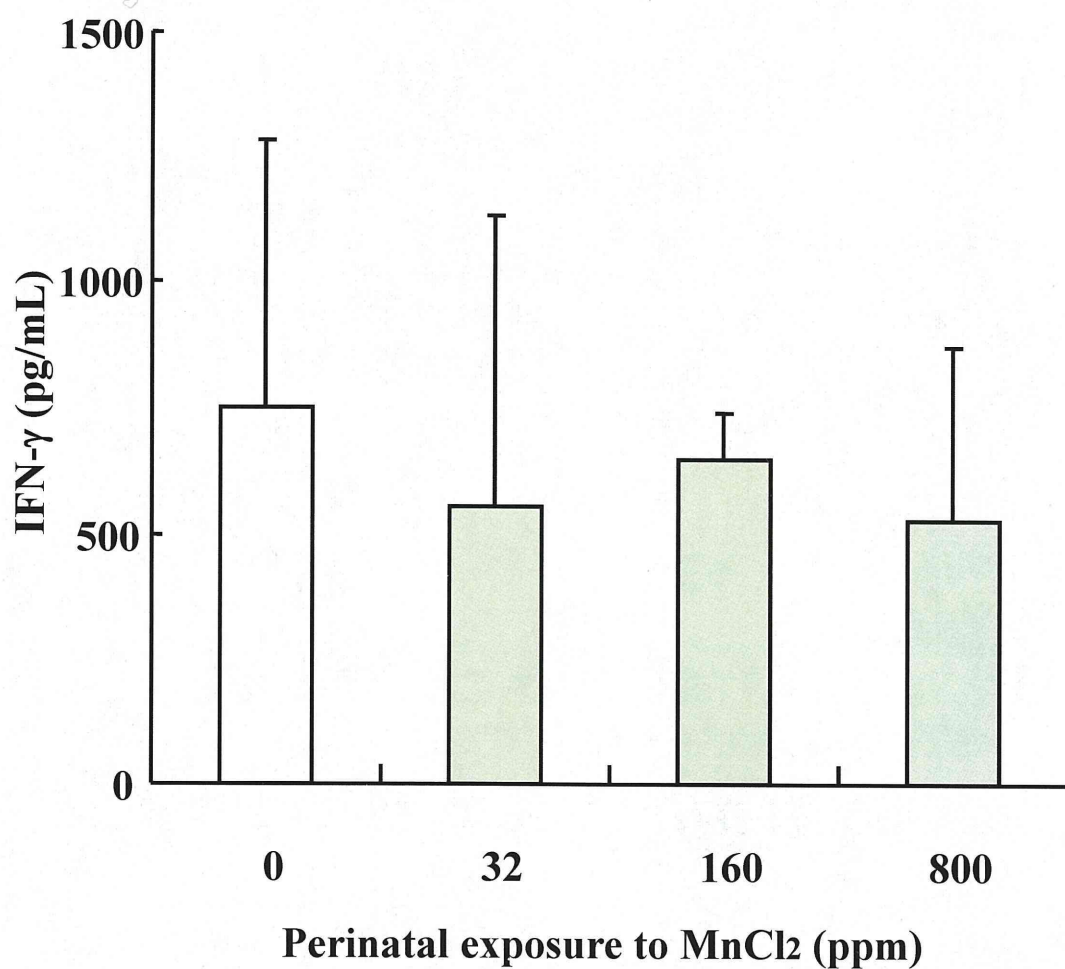


Table 56a Effects of Methamidophos on cytokine concentration in BALF from RSV-infected offspring

Cytokine (ng/mL)	Day 1 post-infection		
	Control	Methamidophos 10	20
TNF-α	0.83 (0.24)	0.68 (0.28)	0.53 (0.18)
IL-6	0.50 (0.10)	0.33* (0.02)	0.25** (0.07)
IL-1 β	<0.04	<0.04	<0.04
IL-12	<0.08	<0.08	<0.08
IFN- γ	ND	ND	ND
IL-4	<0.04	<0.04	<0.04
IL-10	0.11 (0.01)	0.12 (0.02)	0.18 (0.06)

Numbers in parentheses indicate SD of mean values.

ND: not determined

*P<0.05, **P<0.01

Table 56b Effects of Methamidophos on cytokine concentration in BALF from RSV-infected offspring

Cytokine (ng/mL)	Day 5 post-infection		
	Control	Methamidophos 10	20
TNF-α	ND	ND	ND
IL-6	ND	ND	ND
IL-1 β	ND	ND	ND
IL-12	ND	ND	ND
IFN-γ	1.50 (0.47)	1.33 (0.78)	0.81* (0.38)
IL-4	<0.04	<0.04	<0.04
IL-10	0.26 (0.13)	0.25 (0.13)	0.14 (0.02)

Numbers in parentheses indicate SD of mean values.

ND: not determined

*P<0.05

Table 58**Effects of perinatal exposure to methamidophos (30 ppm) on the gene expression in the lung tissues of RSV-infected offspring mice by microarray analysis (Day 1pi)**

Gene symbol	Fold change (down-regulated)	Gene Name
Reg3g	7.04	regenerating islet-derived 3 gamma
Xcl1	4.64	chemokine (C motif) ligand 1
Il6	4.21	interleukin 6
Il18rap	3.72	interleukin 18 receptor accessory protein
Cd1d2	3.64	CD1d2 antigen
Csf3	3.49	<u>colony stimulating factor 3 (granulocyte)</u>
Mylk3	3.08	myosin light chain kinase 3
Ifng	2.97	interferon gamma
Ido1	2.88	indoleamine 2,3-dioxygenase 1
Tbk1	2.69	TANK-binding kinase 1
Ccr5	2.61	<u>chemokine (C-C motif) receptor 5</u>
Mefv	2.53	Mediterranean fever
F3	2.40	coagulation factor III
1200009O22 Rik	2.23	RIKEN cDNA 1200009O22 gene
Thbs1	2.22	thrombospondin 1
Tlr3	2.22	<u>toll-like receptor 3</u>
Il1a	2.21	<u>interleukin 1 alpha</u>
Fcgr3	2.07	Fc receptor, IgG, low affinity III
Irgm1	2.01	immunity-related GTPase family M member 1

Table 59a
Effects of Chlorpyrifos on cytokine concentration in BALF
from RSV-infected offspring mice

Cytokine (pg/mL)	Day 1 post-infection	
	Control	Chlorpyrifos14
TNF-α	265 (134.5)	116* (25.5)
IL-6	431.5 (173)	402 (104.5)
IL-1 β	<39	<39
IL-12	<78	<78
IFN-γ	ND	ND
IL-4	ND	ND
IL-10	ND	ND

Numbers in parentheses indicate SD of mean values.

ND: not determined

*P<0.05

Table 59b
Effects of Chlorpyrifos on cytokine concentration in BALF from RSV-infected offspring mice

Cytokine (pg/mL)	Day 5 post-infection		
	Control	Chlorpyrifos14	70
TNF-α	ND	ND	ND
IL-6	ND	ND	ND
IL-1 β	ND	ND	ND
IL-12	ND	ND	ND
IFN-γ	699 (265.5)	794 (381.5)	1547 (1060.7)
IL-4	<20	<20	<20
IL-10	109 (22.2)	77 (27.4)	81 (35.2)

Numbers in parentheses indicate SD of mean values.

ND: not determined

*P<0.05

Table 61**Effects of perinatal exposure to chlorpyrifos (70 ppm) on the gene expression in the lung tissues of RSV-infected offspring mice by microarray analysis (Day 1pi)**

Gene symbol	Fold change	Gene Name
Il1r2	3.4	IL-1 receptor type II
Il17f	2.9	IL-17f
Slurp1	2.1	Secreted Ly6/Plaur domain 1
Il17rb	2.0	IL-17 receptor B
Gm13271	0.5	-
Bmp8b	0.4	Bone morphogenetic protein 8b
Ccr4	0.1	Chemokine (C-C motif) receptor 4

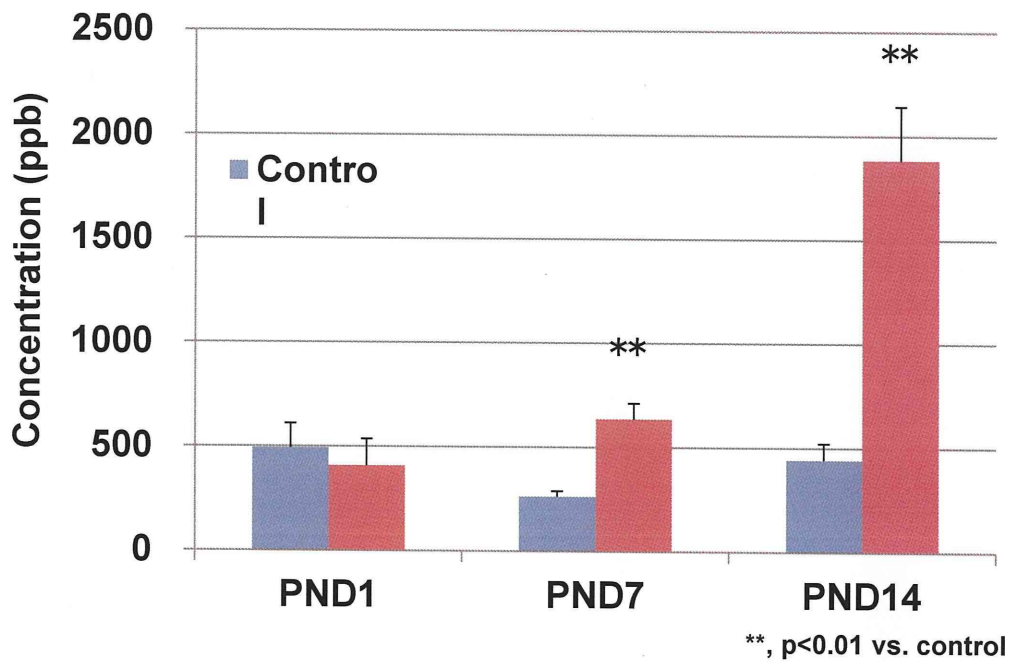


Fig. 67
Mn concentration in milk

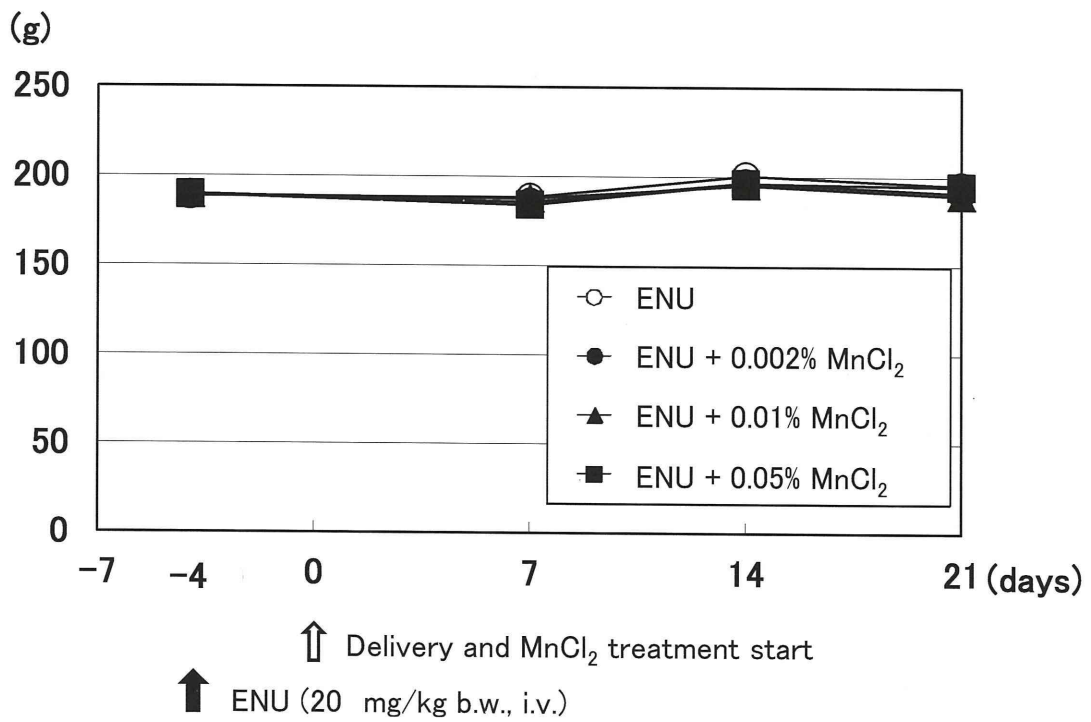


Fig. 68
Body weight curves of dams treated with manganese

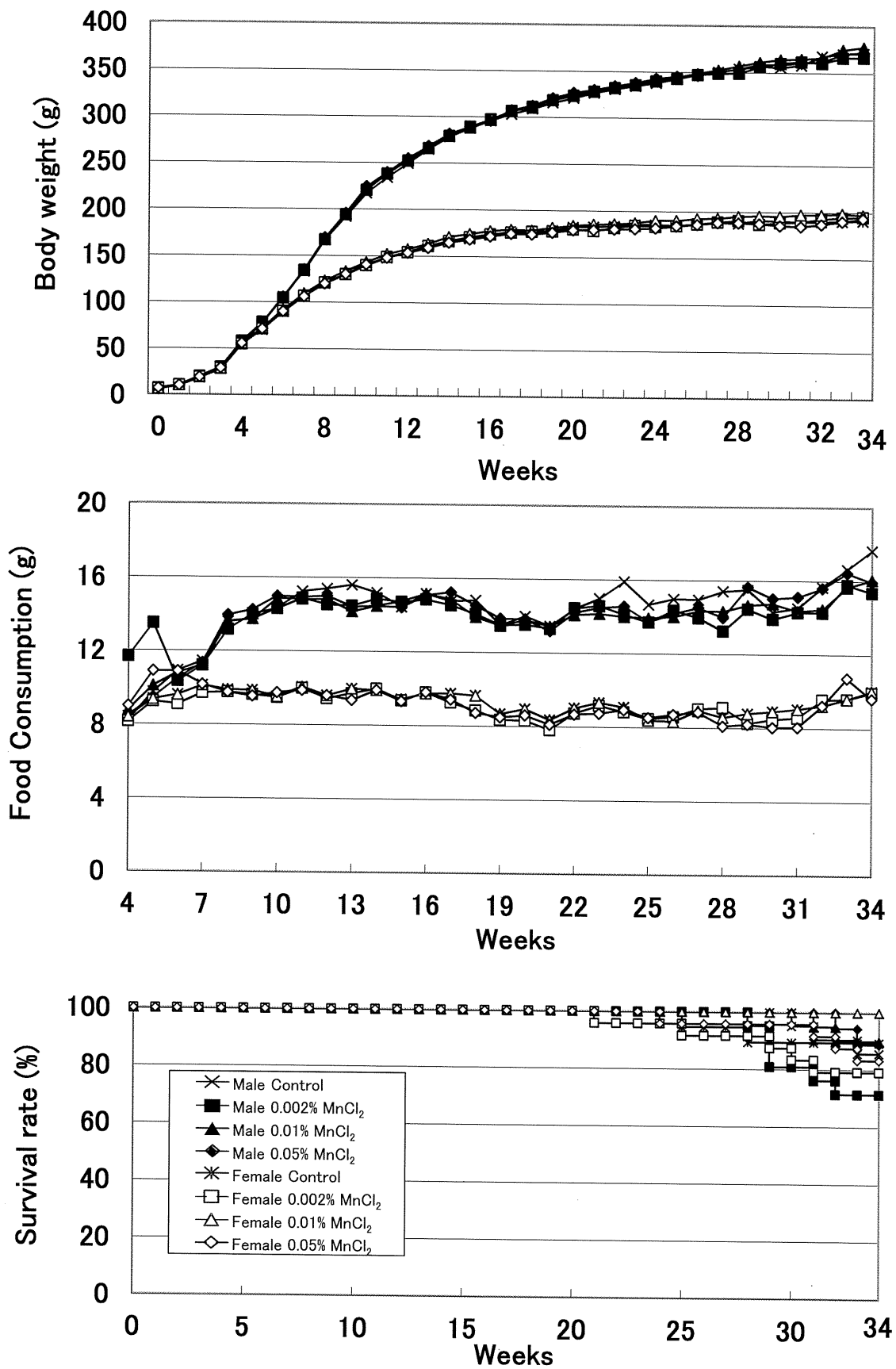


Fig. 69
Body weight, food consumption and survival rate of offspring treated with manganese

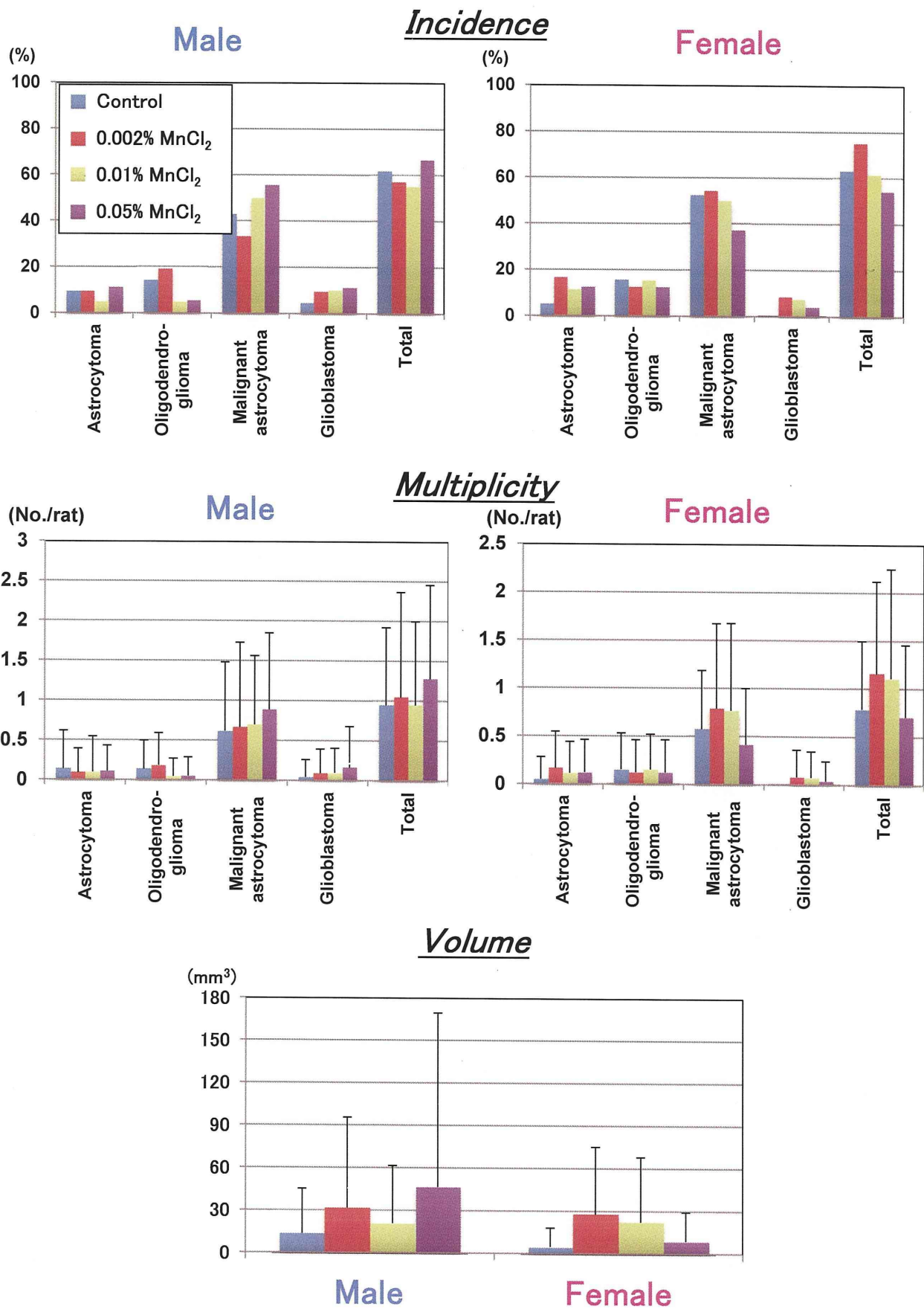
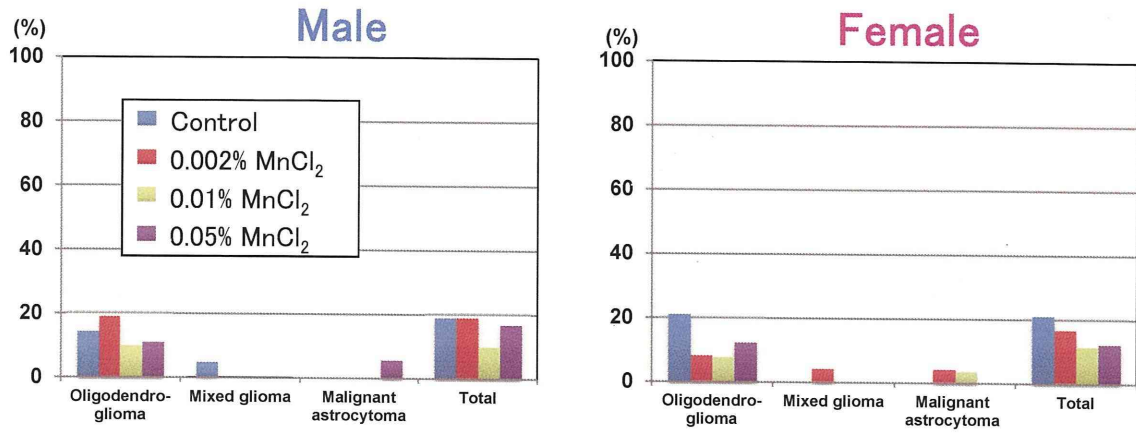


Fig. 70
Incidence, multiplicity and volume of neural tumors in offspring treated with manganese (Brain)

Tumors in spinal cord



Schwannoma in peripheral nervous system

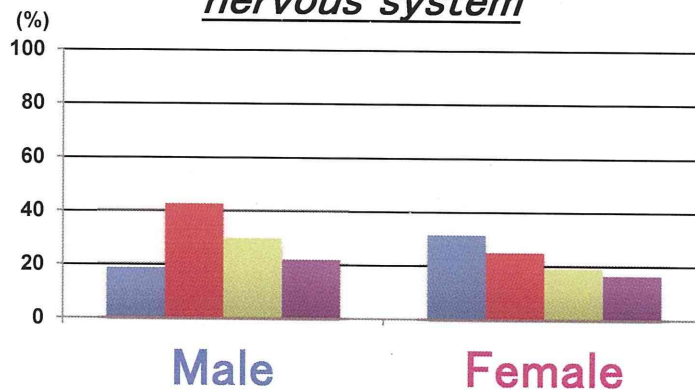


Fig. 71
Incidence of neural tumors in offspring treated with manganese (Spinal cord and peripheral nervous system)

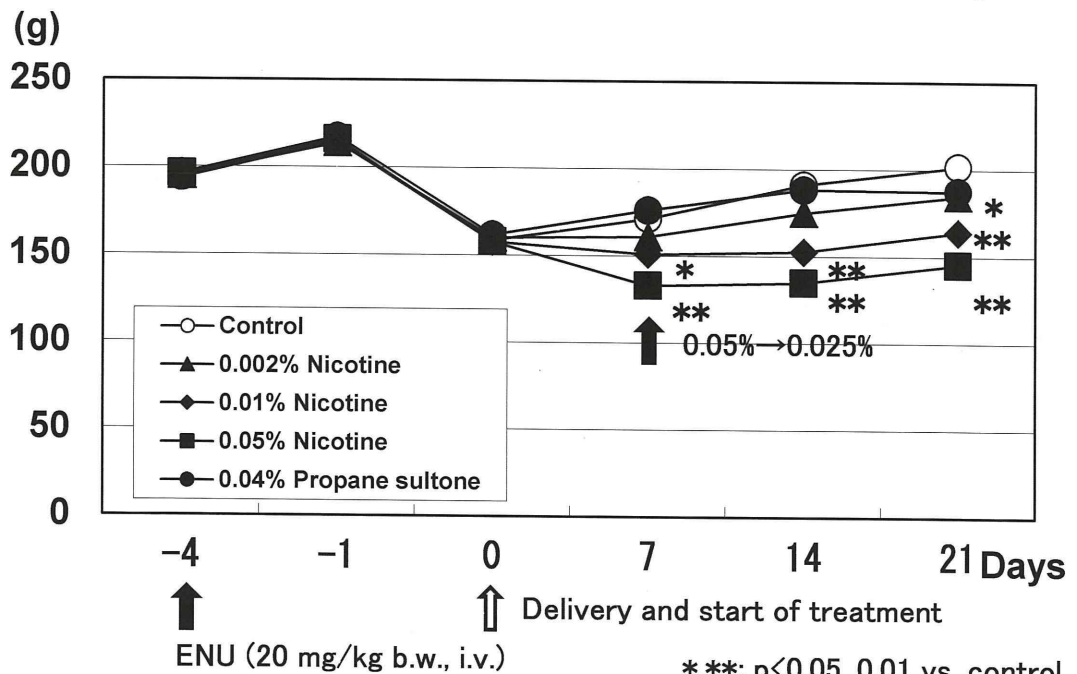


Fig. 72
Body weight curves of dams treated with nicotine or propane sultone

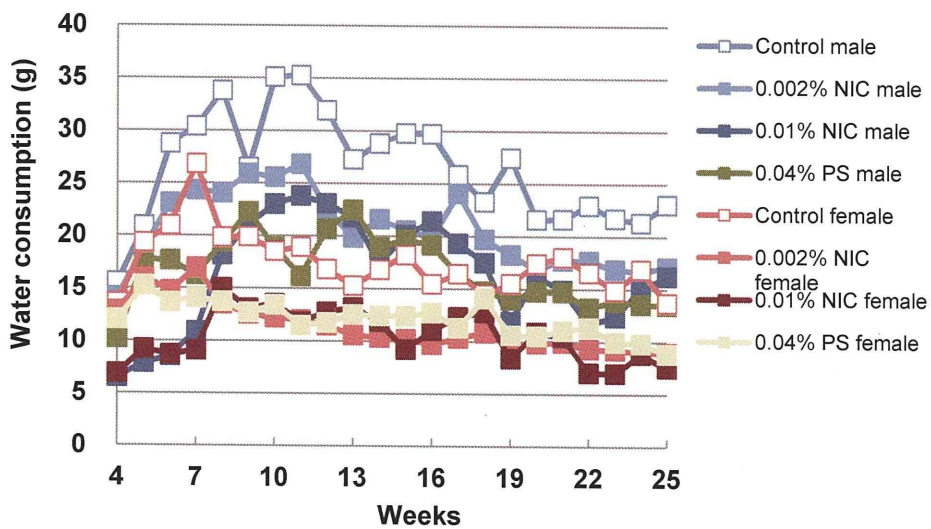
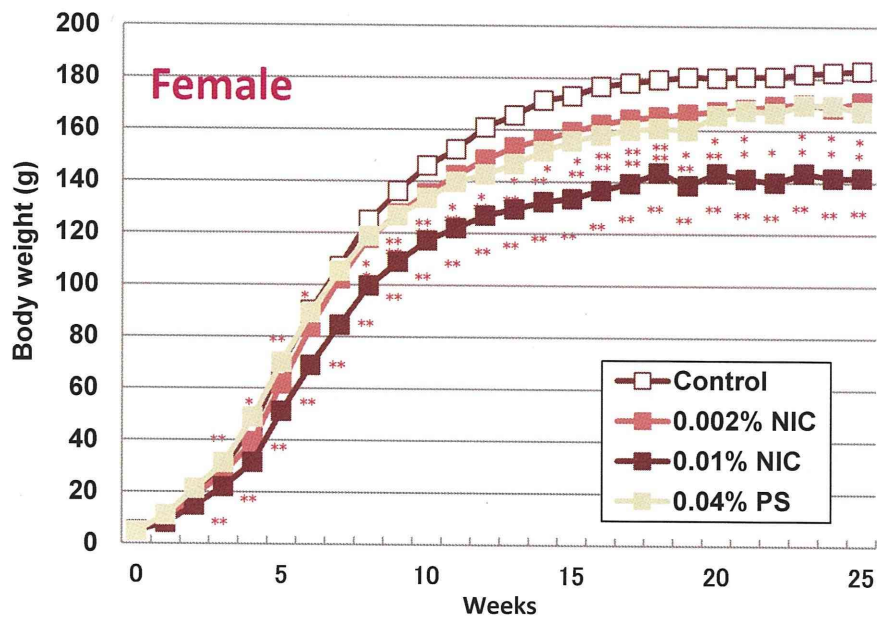
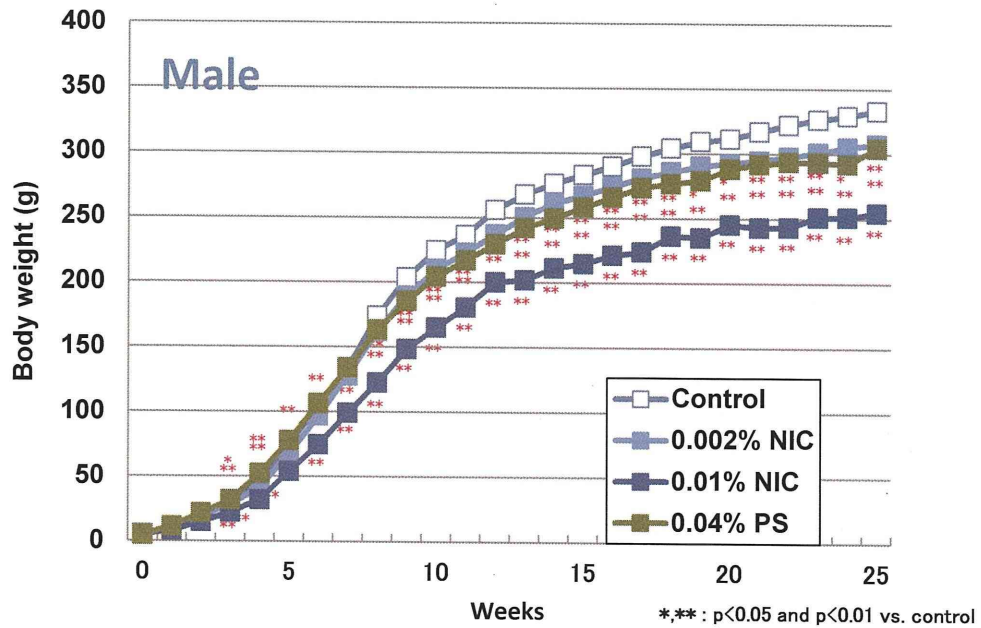
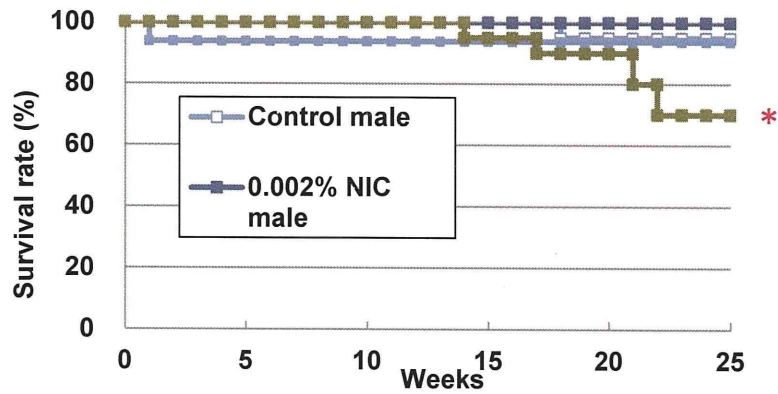
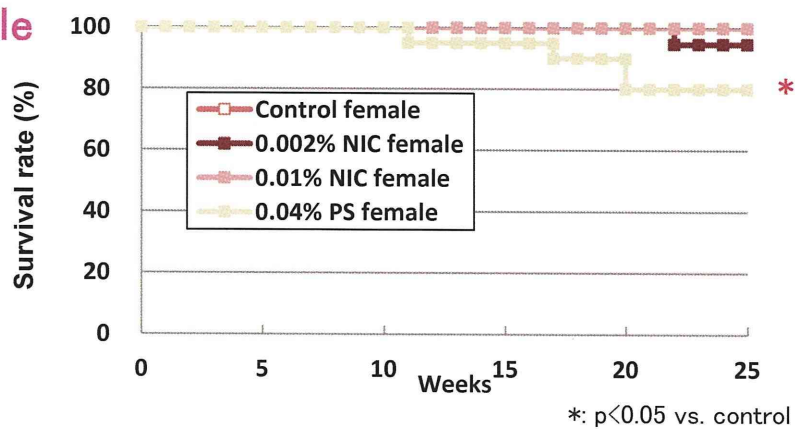


Fig. 73
Body weight curves and water consumption of offspring treated with nicotine or propane sultone

Male



Female



*: p<0.05 vs. control

Fig. 74
Survival rate of offspring treated with nicotine or propane sultone

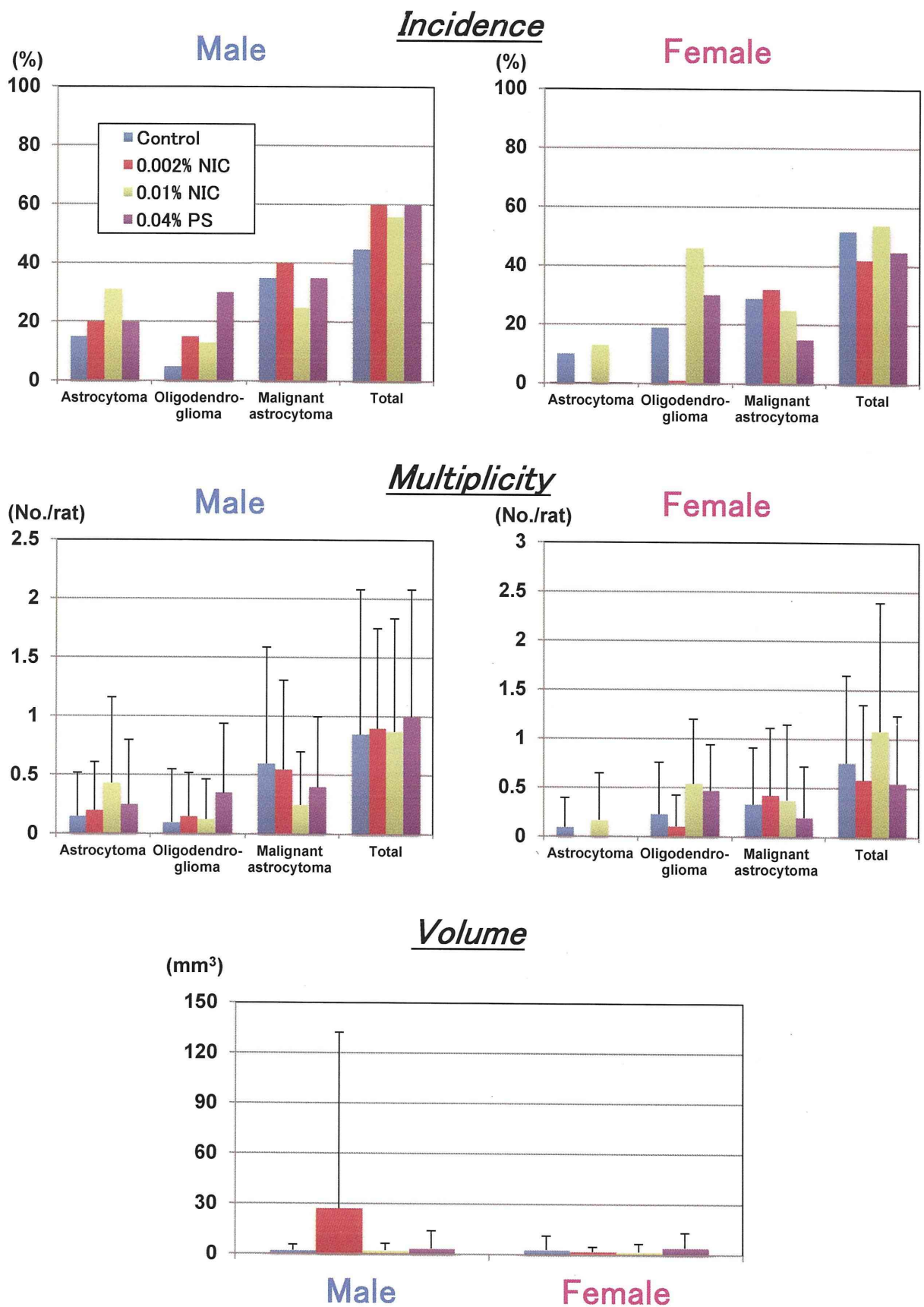


Fig. 75
Incidence, multiplicity and volume of neural tumors in offspring treated with nicotine or propane sultone (Brain)