" ¥ ¡ G « ° →fi ƒ ¡

ƒ < F | Œ fi a < · ' e › ß • | , §U–M^D< ª

¡ ¥HDextromethorphan " v Ł ƒ ¥ fi ¤ ¯ –w"‴¥ifl '°

¡ ° " « „ Œ ¯ ⁄ ¸ {§ , ¯ ßƒ ¡

› p ê ¡§Œ › §O«‹ › pe¡ @ ¡ @ ¡ …ª ƒ Ÿ ‹

› pe‰ ›„¡ GNSC89¡–2314¡–B¡–038¡–011¡–

ɪ ƒ ·`¡¶G88 ƒ~08 ⁄°01 ƒ 89 ƒ~07 ⁄°31 ⁄Ø

› pe¥ D ø⁄HG, › •¥

ƒ @ ƒ P ‰«pG⁄H

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¡…› u Œ ¥ ~ ¥ X fi t ' ¸ ‹ ª ⁄ –o†ł§i⁄@¥

¡…› u ⁄ j † ƒ a ˇ ¥ X fi t ' ‹ª † ⁄ –o†ł§i⁄@¥

¡ … ¥ X fi u Œ » · ł N • | ˜ ł ⁄ – ɸł§i⁄¸ o" ⁄§‰ ⁄ ƒU⁄@¥

¡… Œ› ƒX§@‹ ª¤s› pe Œ ¥‹¤ªsł §ifi ⁄ ¶

Ł ł ƒ ¡G¥ x ¥ _ ⁄j · ´ ‹·ª¤ ‡

⁄⁄¡@ ¡@¥`¡@ Œ¡@ i90 ƒ~01 ⁄°29 ⁄Ø

/ / / ”K›n

Dextromethorphan(DM) ‹ ` { Ş ⁄W40¥¸¥H⁄W“ ” « D ł ´ K˚¡⁄C«ƒy bfl¥ « e ™‹ ªDMł «Cł{ ⁄ Ć NMDA(N-methyl-D-aspartate)– ¤¯Ø”´ ⁄ l ł ₫D“fl¡C NMDA – ¤¯Ø⁄Ovoltage-gated ´ ł÷q „D¡ A • ¥ ƒ ®‹¡¡Ą˘fi _ † M‰¡⁄¥h•€¶t˘ ⁄l⁄ ”y¡ A › P †›M°¿.÷₩[¡ A ƒ † ›M⁄”¶lt ¿ @ « … ₩[•@¤¶B ‹ ¡ ˃†“”›M« › ¤ˆfl A ƒ⁄ o⁄@† ₴Œ“”¥ ˝ † z ' ¸ ffl†₱Cƒ˝ ƒ÷, DM ¤ ª ƒ ₭œŞ NMDA – ¤¯Ø⁄ Ø”, £ ₭,¥g ´ † z ¦fl˙Ť˜z⁄˘¡C„L¥h“”÷ Ş i ф{¡ADM ¥i¥ ₣bƒ ¤ „ « Ş¤⁄¥ ™« ‰Ł⁄ o' z“”Ş@¥¸¡Cƒ ƒ„¥ » „ Œ ¯ – ĐM ƒ bo¤ fi ·`“”¥fi„«, £⁄‹ OŞ_ƒ÷ƒ P.¸“”Ş ' z$¥@¸¡CŞ › ¥H¥fi„« „ Œ °“«¡AŞQ¥¸kainic acid(KA) ¡Epentylenetetrazol (PTZ)⁄ ¸γ-hydroxybutyric acid (GHB)»⁄ o ¯ w ' fo$@A“ƒ÷₭¥ĐM ¤ ⁄ F , ‹ O Ş _ ƒŞ“”fi ™G¡• C‰₦¥¡A‹ ¶ i ⁄ @ ¤ B ÷ Q«ø˜ „ L @fl℗ ” z ‹ O Ş _ • | … v ¯ T , £ ÷ ¡ « P † ›M¥ƒ„₹T¡°A$”⁄ ’› ƒ$“Q ₭{¸⁄ ˇ ´ ¿ »EƒX Q^ (Reverse transcription-polymerase chain reaction¡ERT-PCR)“”⁄ Ł ™ k»PŒZ „ ⁄j, £¥ ₾⁄e-fos¡B-jun¡B bcl-2 ⁄¸bax mRNA ™”™ †{⁄Ş.. v̄T¡A¤ ¥B⁄ F DM ‹ Ş_⁄ ł ª ƒ ÷ ⁄ ƒ]' z⁄ _“”, ffl ‹gt › M”¥^ ¥\¥¸¡Cƒ ¥ Œ¯™G ƀ†{¡C(1) DM ¥iŞ ¤ †˜14¡B30 ⁄¸60 ⁄ ⁄j“”ƒ „«¡A, gPTZ ' » ⁄ o“generalized clonic-tonic seizure¡Aƒ „ ¤ l“ ” zƒ ‹ ¤^ L ŒĐ¯™”Ş ¤ Ş@¥¸¡C(2) DM ¥i¥ H·¥ › ŞCbcl-2/bax ratio ¤ Ş¤apoptosis “ ” ₤¥¡˝C ƒƒ₣, b ` { Ş“”¥”¤Ť¥¸⁄W¡AŞ › „ w` DM ¥i‹ ⁄@ƒ ₩ ¡B' ‰→¤ ¥B ˇŞ@¥¸ ⁄p“”Ş ' zˆ ™«¡A¥i¥¸ƒb, ß⁄j• ł … ¥fi⁄Ş generalized clonic-tonic seizure¡C

Abstract

Dextromethorphan (DM) is an effectively and widely used nonnarcotic antitussive agent for 40 years. Recent investigations have indicated that DM is an N-methyl-D-aspartate (NMDA) receptor antagonist. In particularly, DM could prevent or inhibit the NMDA receptor-mediated neuropathology including hypoxia-ischemia neurotoxicity and seizure activity. However, most of the studies were conducted on adult animals or adult patients. The anticonvulsant effect of DM on the seizure activity in the developing age is not yet well determined. We, therefore, determined whether DM could effectively attenuate the chemical-induces seizure and brain damage in developing rats. The chemical materials used to induced seizure are pentylenetetrazol (PTZ) and γ-hydroxybutyric acid (GHB), which induce absence-like seizure and generalized clonic-tonic seizure. We also used reverse transcription-polymerase chain reaction (RT-PCR) to determine the effect of DM on the gene expression associated with apoptosis, including c-jun, c-fos, bcl-2 and bax mRNA in the developing brain after PTZ and GHB-induced seizure. Our results showed that (1) DM could attenuate the PTZ induced- generalized clonic-tonic seizure on developing rats with age of 14, 30 or 60 rats, but could not affect the GHB-induced seizure; (2) DM could reverse the PTZ-induced decrease in the bcl-2/bax ratio in the cortex of rats with age of 7 days but not in other age. This result suggest that DM have anticonvulsant effect in treating generalized clonic-tonic seizure of PND 30 and 60 rats. And we can use DM to cure generalized clonic-tonic seizure in older children.

癎(Epilepsy)、腦部疾病、腦外傷、腦血管疾病、腦腫瘤、腦感染、腦寄生蟲病、腦膿瘍、腦炎、腦膜炎、腦水腫、腦缺氧、腦中風、腦出血、腦梗塞、腦栓塞、腦動脈瘤、腦血管畸形、腦血管硬化、腦血管阻塞、腦血管破裂、腦血管出血、腦血管梗塞、腦血管栓塞、腦血管

K ' ° ⁄«y Cfl¤ ⁄ « y ˜ †zodeine×P • ¡ F ƒ « o ƒ ‹ ¡S Af¥ ¥ H ƒ· Nodeine ƒ¤« ` { S⁄W

† – ' ¤¥¸⁄S¥x^¡˜C¥ ' DM " " ⁄ ˇ ·†codeine ^ ƒ ¡A G¤ ⁄] ªƒ¶Mcodeine ‹ ^ ƒ ⁄S⁄ « ŷ˜†z

´ ¡ A S ¤ «y„ ´ ⁄ ˇ fi g ⁄ ¸ˇ⁄S¥¥ª´y K ' ° ⁄«y Fflƒfl ¥ ¯Ø⁄ ˇ ·†"S– ¥œ' ⁄ £P¡A G¤ ^£

¤ ƒ†ƒ¤¯}¡B⁄ h¡ B S ¤'¡I S Blœ⁄¡ B Kfl»P¶ " ¸¥¥i¸˜¡C

DM ⁄ w † Q ^„ N MDA (N-methyl-D-aspartate)– ¤ ¯Ø"″«D˜ v " S «««œfS C NMDA – ¤ ¯Ø‹ O¿ †˜

' ° ¢ i»˜ ¤ ¯Ø (glutamate receptor)"″⁄ ¡A¥ «e⁄w" ˜ v " S «««œfS¥ ‹ A pencyclidine (PCP)¡B 3-3

(2-carboxypiperazine-4-yl) propyl- 1- phosphonate (CPP)¡B MK-801¡B 2-amino-5-phosphonopentanoic scid

(AP5)¡B.. ¥(Collingridge et al,1989¡B Lodge et al, 1990¡B Folbergrova, 1997¡B Greenamyre et al, 1994)¡C

¥ ' NMDA – ¤ ¯Ø‹ O⁄ voltage-gated "″´ ⁄ ‡q¡„D¥ƒ†Q‹ ¡⁄˜fi ¡A† › M ‰ •⁄¥Ÿ¡•A¥ ⁄ o¶t

´ ⁄ ‡″¸A› Þ ¿›M†˜' °… W[¡Aƒ † › M ⁄ ¶t«´ …⁄W¿¥ª ¶⁄¶Q¤ B¡⁄˜† ›M"› « › ¤^ƒfAƒ ⁄ o

⁄@† $C"″¥˝†z' fl¸ƒ†z⁄˜ ‡(Pumain et al, 1992)¡C b NMDA – ¤ ¯Ø"″´ ⁄ ‡q„Bƒ†DM " "†ƒ X ƒ„¤A

ƒ DM ‹ OS@¥ ¸ƒb† o ƒ „m¤ "´N MDA "″´ ⁄ ‡q¡„D› ⁄ NMDA ´ ⁄ ‡q"¶ } – W†(Church et

al., 1994; Takahama et al., 1997)¡C ƒb "«„C¯ o† {¡A DM ¥i¥H¥ ¸¤ S ¤ NMDA – ¤ ¯Ø„L« ‹ ¡⁄˜' †£

¥˝"″, £ fl,¥ƒ˝†z' fl¸ƒ†z¯ ⁄˜¡C‹ ƒ p¡(Feşkany et al., 1988)¡A ƒb, £† ¡ flfiłæ¸fl ƒ , £ fl,ˆg ƒ„(Goldberg

et al, 1987¡B Prince et al., 1988¡B Tortella et al., 1989, Choi et al., 1987¡B Haberecht et al.,1997)¡C ƒ]ƒ„¡Aƒ†

^ DM ¥¸¤ ‹ ` $ fleflf¤ ¥¸"″, ¯ ⁄wƒ†« • ƒh"″† ‡ S flSS Q„ ' ¹z¸¯ ¤wŁ¡›C¥ «e "«„C¯ ¯ª

¥ ¡A DM ¥i¥H S ¤ ' ¸· ‰wkainic acid ' ⁄ _ƒ¤ƒ~ "«"″' zS@¥ ¸(Church et al ,1985¡B Feeser, 1988¡B

Kim et al, 1996¡B Loscher et al, 1993)¡C ¥ ¥˜¡A⁄ ƒ†† \ƒh"″^ $, ¯ ¤ ¥¸DM ¤ " v ‡ ƒ¥fi«« ' zƒ

¤ †"G¤^ L⁄@›P' °¡Cƒ„« ª ¤ spx„K O• Q¶i⁄@¤B‰ Tw DM ‹ OS_¥i¥H· ‰w¥fiƒ~ "«ƒ]^˜"«' ⁄ o"″'

z¡AS ›–¥¸T" ⁄ £P"″^˜"«¤ ⁄ o¥fiƒ~⁄ £Pƒ~˜ "″ "«¤ †£¥˝' zSY kian acid (KA),

Pentylenetetrazol (PTZ) ⁄¸gamma-hydroxybutyric acid (GHB)¡C KA ¥i¥H†£¥˝complex partial seizure

with secondary generalized seziutre¡C ƒ PTZ ¥H⁄¸GHB ¥i¥H ƒb SC f¶ q U†£¥˝¥¢fl«' °¯ w' ¸myoclonic

seizures¡ A „ ⁄ "f¶qfi ¡A¥i⁄ o generalized tonic-clonic seizure (Loscher et al, 1991)¡C

PTZ ‹ O GABA – ¤ ¯Ø"″« S fl(antagonist)¡A¥ƒ¥D›n‹ OS@¥ ¸ƒb GABAA – ¤ ¯Ø(GABAA receptor)

⁄W¡C ƒ ' ‹ †«Æ M‰"″ GABA – ¤ ¯Ø• |»P–qfl ‹g‹ ˜†¥‰" ˜ 'æ¥X"″ GABA †ƒX¡A« h ´ ‡q

„ Þ |¥·¶}ƒ ›Þ ´ ⁄l"″†qƒ†z' °(conductance)… W[¡A' ‹ O† › M ‰•ƒ]⁄j¶q· ´ ‡¶¡Jƒ ¤Þ ‹g†

›M¿ †˜' °⁄U› ¡C⁄@¥„ PTZ S@¥ ¸ƒb GABA – ¤ ¯Ø⁄W¡A«h• |" ´_· ´ ⁄l"″†qƒ†z' °ƒ ¤˜fl ‹g† ›M†S–'¿†

˜¡A ›P' z } o' °„qƒ ƒ ⁄ b zƒ ‹ "″†£¥˝¡C¤ PTZ f¶q "S C' " †{¥X¤ "″ƒ ‹ … ƒ¡¤ ^£‹ ƒP

(Loscher et al, 1996, 1991¡B Ruethrich et al, 1996)¡C ƒb SC f¶q¥D› n |†£¥˝¥ ¤ › oS ¡B´ S ¡B«Æ"˜' ‹¡B

' CZ.. ¥ ° ¤ƒ¡ <A ƒ b ƒ ‡ mminimal seizure (» · • Lo)§@fb " fl ¶ q ¥ D › n ‹ Œ£¡¥ Ê¥¥"˘ L⁄O ƒ Ê ¡ B ¥ ¤ › ' ƒæ Ê§@... }¥¡¸A ƒ b ƒ ‡ mMajor seizure (› « «'¥¸ ‡¡ §@)¡Cfb⁄ § « e ™⁄ ˜m ¯ ¥ ¡A§C ¶q"˝PTZ ' † ¥˝"˝minimal seizure • | ƒ ‰ absence "˝ƒ ‹ † ¥˝¡A¥ B g¥EEG ' · ¤X"˝ , £ „ q ¶¯‹Œ˘ƒ absence seizure¡Af]ƒ„minimal seizure ' ¥ ¶ "˝‹ Oabsence seizure "˝... ƒ¡¡Ê major seizure ƒ]‹ ¥]‹ A⁄F generalized tonic-clonic seizure ⁄¸myoclonic seizure¡A' ¥Hƒ‡¥ fl ‹ O˝ generalized motor seizure "˝... ƒ¡¡Ct z ‰⁄¡W‡ ¤ ˝ ⁄ £ ƒ R‹ ™˝Aseizure ¤ o¥˝"˝ ¤ ƒ‡« ⁄j"˝⁄ ¥P¡C jP⁄W¡absence seizure ⁄ w{‹ ‹O o¥˝ƒb¥C„£ (thalamus) ⁄¸j„£¥ ‰Ê(cortex)⁄§¶¡¡Af generalized seizure ⁄§ o¥ ˝ Ê›n ‹Of ƒb⁄j„£¥ ‰Ê(Coulter et al, 1990¡FEbert et al, 1995¡FPrevett et al, 1995¡FRichards et al, 1995¡FSnead et al, 1995¡FSutor et al, 1995)¡ C ⁄ §e‡"˝§i¯ ¥ ¡APTZ "˝"' z¥ ¥H‡ Q @fl™˝§ ' ˆ˜"«⁄¸NMDA – ¤ „"˝«œ§ flMK-801¡BCPP ' § ¤ (Fisher, 1989, Mares and Haugvicova, 1997, Velisek et al, 1992¡F Loscher et al, 1988, Velisek et al, 1991, Xie et al, 1991)¡Af]ƒ„– ·œPTZ ¥ fl • |‡ ¥ƒ¤NMDA – ¤ ¯ ØL« ‹ ¡⁄˘(Chimirri et al, 1997¡FPumain et al, 1992¡FVelisek et al, 1997¡B1995)¡C¥ » Œ¯' ¥¸"˝¥t⁄@˝ ˆ˜"« GHB¥ D ¤‹ GABA "˝¥N ´†£"«succinic semialdehyde ,gdehydrogenation §@¥¸ƒ † ¥˝¡CGHB‹ OGABAB – ¤ ¯Ø"˝›Pfi˜ fl (agonist) ¡A¥ƒ¥ ¥H§ ¤ GABA "˝˜ 'æ¡A¤ˆ• |§@¥¸ƒbGABA – ¤ ¯Ø⁄W¡Af ¤ ƒX⁄O « Ð ™˝fiz¡CGHB "˝§@¥¸¥ ¥H‡QGABA – ¤ ¯Ø"˝«œ§ fl (CGP35348) ' «œ§ (Banerjee et al, 1995a¡F Bernasconi et al, 1992)¡ C §«ƒe‡⁄ ˜m« ¥X¡ Ab‹ Y ¤ fl°¥Succinic semialdehyde dehydrogenase (¥i–N succinic semialdehyde fiæ˘ƒ¤succinic acid)"˝¥ fi £⁄¡A¤ GHB "˝¿@« • |... W[¤ˆ• |† ¥˝⁄@¤ ¨ § ⁄W"˝ fl ›‹ (Cooper et al, 1996)¡C¤ ƒp¡A⁄ ·...' „B ° ƒ‹• |¿ ‰w (motor and mental retardation)¡Bƒ –i⁄O⁄£¤‹ (hypotonia)¡B„B °¥ ‰ (ataxia)... ¥¡C¥tƒ‡‹ ¤s« ¥X¡G¥ƒ§Q¥¸GHB ' ⁄ o⁄§' z¡A¥ D ¤‹ Œ ' "xo ' °«D' z §@ (Generalized-nonconvulsion)"˝⁄@˝ ¯ w« ˝A¡Fƒ b °"„« Œ ot{ GHB • |⁄ o" ‡fi ¶¡ƒ¤ R⁄¸¥¢fl«"˝™‹˝A¥H⁄¸¥ EEG ' · ¤X"˝, £ g"„¡˘ˆ ƒ ¥¢fl«' °¯ w (absence seizure) (Aizawa et al, 1997¡EBanerjee et al, 1992¡B1995b¡EMarescaux et al, 1992¡FSnead et al, 1993¡B1990¡EZhang et al,1991)¡F ƒ ƒb⁄H ˆ "˝ˆ § ‹ ¤s⁄ ot{¡A‡o˝ ¤ «‹¥¢fl« §@` ⁄£• |"‰– ‡ ¥ƒ¤¥˝' R M ¡IAƒ ƒ]¤ §@ W˜c¡A• |...v ¯ T ·‡fl ⁄O (Penry et al, 1975¡FSato et al, 1976)¡Af ]ƒ „b` § ⁄Wƒ ¤˘¥¸ ˘§@¥⁄ ⁄§ethosuximide¡B valproate… ¥ˆ ˜"«¤ ¥ ¡C–q⁄W›zƒ ¤¥¡A§ › §˘§Q¥¸‡ ˝ ˆ˜"«¡ Ab⁄ ¥P fl¶q⁄U¡A¤ ⁄ o¥fiƒ~ ° "«‡ ¥˝absence-like seizure ⁄¸generalized seizure¡A¤ ‹ DM „ ‡ ˝ ' z« ˝Aƒ‡ƒ §@¥¸¡C

ˆ ' ' z §@• |„ ,ffl«„g† ›M† ¥˝¶ fi‘ƒ ›P† › M"(McDonald et al, 1993¡FSchmid et al, 1999¡FMoshe, 1998)¡C„I¥h»{‹ ‹Ofl˚fiæfl˚ƒ ' ›Pfl«„gˆaƒ"¡Af ‹O‡ "æƒ‡⁄H o†{¡A¥ƒ‹O„g„L† ›M›p „"' °ƒ ˝ (apoptosis) (Johnson, 1995)¡F¤ ƒp kainic acid " fig' ⁄ _"˝„£† › M"¡A¥ƒ‡¯ª ‡¡⁄ ‹O¥H

apoptosis " " ⁄ Ł ƒ¶i(Pollard et al, 1994)¡ C ‹ » apoptosis ? ƒ b fl Æ ¯ Ł "«† A´ †⁄M′ƒ ″ ⁄ £¡ ¥ i † ⁄ ⁄ ‹ ¡¤ G″ † M^(necrosis)»P apoptosis (Duvall & Wyllie, 1986¡ EEllis *et al.*, 1991)¡ C ^ a ƒ‹ ⁄@ " † Q ° " ƒ″¡ A⁄Łƒ|¡ „ † › M † ÿ¤¡ apoptosis h ©¥ƒ‰ , †{¶EA ‹ † ƒ›M o fi ¡L {⁄ ¥ H ⁄ ¸ „ ¤°¿Ef⁄U¥$ • ·" ƒ ″ ⁄(McConkey *et al.*, 1990)¡ CApoptosis ƒ b ¥ ˝ " « · " ″‹» ›n'°‹ £ ƒ hl¡"B ƒ † fi "″¡† A›M ƒ p ƒ b F¡›Afifl·Æ · ¥ ˝ " »″¡fl«A, ¥g«Æ†«g⁄,† ›M»Pfl «c‰ƒ† ›M¡A ƒb ¤|"″„ L {⁄† ›M• | ƒ Mapoptosis¡ Afl « , g ¤†S¸"¿″¡fl«KO†z„Lƒ „ ⁄ @Ł¡ƒF ¥¥¡~Aapoptosis ⁄] ¥ i ‰ –→SK‹ ¸"″cfii¡ Bƒ ›'ƒ¿¤.. "″„ L{¥ H ⁄ ¸ , ‰F· ¶⁄¡ Ø⁄″″¥ ¿¯(Ferrer et al,1992,1994; Koike et al, 1994; Oppenheim et al, 1991)¡ CApoptosis ‹ C¥ ƒ]⁻¤ "″⁄ ˇ†¡ C¥ « e ₩″″‰ ––ƒ ƒlƒ† †\fh¡ A ¤ƒ℗ S @ ƒ‹¶¡k℗proto-oncogene)' ¸ƒ ″ \«P¶if ƒl (oncogene) "″ Bcl-2 fi a (Bcl-2 family) ' ¸‹ Oimmediate early gene ⁄ ⁄Sc-fos¡ Bc-jun¡ A ¤ ¥ D › n " ¥\ transcription factor¡ Cb Bcl-2 fi a ⁄⁄¡A¥ i ¥ H « P ¶ ‡ "›Mƒƒs‹ ¡ ß ¥‹¡Abcl-2¡ Bbcl-xl¡ Bbcl-w… ¥¡ F « P ¶ ‡ ƒ›M′ ″″ƒ ¤ß«h¥] A⁄FG bax¡ Bbad¡ Bbak ⁄ ¸bik¡ C⁄ W › z ƒ'″″† ƒ{¥ †Qff¥ ¡A• | S¥Ç ″ (-COOH terminal) " ' † , ¢Ø‰W¡ B† ›Mi ‰⁄⁄W⁄ ¸ ″ ‰″ (Newmeyer, 1994¡ EReed et al, 1994)¡ A• Bcl-2 family † ¤·† ¥ ›n ƒ ¤ ¥ƒfi ¡A• |¥ S ¸ƒ¤⁄ C,¯Ø (homodimer ' ¸heterodimer)¡ Af A † o ¤ ⁄G¯Ø″″⁄ æ ¤ ƒh¤„ ¤ Mw‹ O ›m» ⁄ ' ¸" ⁄ † ›M¤ « ƒ V p„″″ƒ° ″ ′¡ C` ¤ ¤ »¡¡A• Bcl-2 (¥iS ¤ ƒ ″)″″† ¥ ⁄ ¶q" †{fi ¡ABcl-2/Bcl-2 ⁄ C,¯Ø″″⁄ æ • |… W[¡A‹ „ "″• |«P¤˘† ›Mƒ ″″″⁄ C,¯Ø (¤ ƒp¡ABad/Bad) ⁄ æ · ⁄ ¡C¥ ' †o ¤·† ¥ ⁄ æ "″¯ ⁄˘¡A• |¤˘–oapoptosis "″ ¤ †QS ¤ ƒ ¡C¥ ¥~¡Afos ⁄]‹ ƒ ″ ′« ¶if]⁄l (oncogene) "″ ⁄ @ ¡A¥ƒ¥ ¥H¤ †\fh¤ ° E,"″⁄‹ ¡⁄˘ƒ †yƒ¤ ƒ]⁄ ¶q" †{¡A¥] ‹ A ¥M′ƒ]⁄l¡ Bƒ †M¡ B¶ t ⁄l¿ @ "″ ¯ ⁄˘… ¥¡ Fƒ ¤ ⁄ ¶q" †{"″ ƒ]«of]‹ ƒ S "″S ¤ S@¥¸¤˘–ofos ¥H ₩″″⁄ £¡¥ ⁄{fb† ›M⁄¡C, gfos ƒ]´ ˜¶¥ ⁄ "″† ¥ ¡ A ″c⁄W¥]St†\fh"″ leucine zipper (Landschulz et al, 1988)¡ Af „ ˘ ¥i'MJun "″ leucine zipper S ¸ƒ¤⁄ C,¯Ø (heterodimer ' ¸homodimer) (Rauscher et al, 1988)¡ A¥ H R¶ transcription "″† tv(Chiu et al, 1988)¡ C· ¿ ƒ † ‡S¥X¤A›£¥X¥˝` ƒb› ¤¯″″ƒ „«¡ Af†⁄æ, ß j"″ fos " †{ (Wintrip et al, 1997)¡ F £O (stress) ⁄]• |†yf¤ fos "′″ †{ (Senba et al, 1994¡ EUmemoto, 1994)¡ C¥ ¥~¡AKA ' »⁄ o "″' z¡ Afbf¤ƒ ~°"«"″ hippocampus ⁄⁄• |⁄ _*bax* (apoptosis gene) " ″ " † ¶q..(Wiu[et al, 1999)¡ C ¤ † y ƒ] ¥ i fl ‹ O ƒ] ‹ fl « , g † ›M¤ apoptosis†gene⁄j¶ x℗ †"d¡"Af B†ƒ ″M¡ Cfb„L¥h ƒ † ¤fi℗PTZ ⁄ ¸GHB ¤ ¤¯¡A o†{ c-fos¡ Bc-jun • |… W[(Andre et al, 1998¡ EZhang et al, 1991)¡ Af ‹ O ¤Sƒ †H o†{†o¤ › ƒ]"″‹ ¡ ›'M apoptosis ƒ†^ ¡ C ¶ i ⁄ @ ¤ B – ·Q„¤a˜¤P"′ z‹ OS_• |… v ¯ T£†¡ apoptosis gene " ƒ"… v̄T¡ CS ›¥℗PTZ ⁄ ¸GHB ' ƒ£¥"″S ¥¸¡Afl SO‹ C¥ ¸ " ¶q† ¥£˝« õ ¡B˜ ¥«"″ ' zƒ ‹ ¡A¤ ‹ ‹ OS_• |… v̄T⁄j, £¥ £⁄c-fos¡ Bc-jun¡ Bbcl-2 ⁄ ¸bax ƒ]" ″ "†¡{C¥H⁄ ¸DM ‹ OS_¥i¥H

… v ¯ T ƒ] ' z ⁄ _ " " , fl«¡¸©† ›Mƒ"⁄'"¥\¥¸

‹ ª ¤ s § fi ˘ P„Œ¯/Ł"k

⁄@¡ B „ Œ ¯Š fi˘

(⁄@)¡ B Œ¯ ° " « ⁄¿¤ •‰

ƒ Ł»„ Œ ' ¤˜¥¿Š Sprague-Dawley „ « ‹ O ` ° ¶ Œ‹"«•|⁄ ⁄Š 200 ¤ 250 ⁄ ‰ Š J ñ¥„¥¥¶ Å ¤ ¥ ˝ † £ « Æ iƒ¡ AA• j˙ †.¥˜„«¶fi„ Œ ⁄˜ ℘„¡ A ⁄ ‡ ¡ ¥ « h fl⁄ŠŠ¥ ¿Š© t"

(⁄G)¡ B Œ¯⁄ Łk

1. PTZ ⁄ ф „«⁄Š' zƒ ‹ … ⁄ƒ¿˜ ƒ

ƒ Ł»„ Œ „ ¥ ⁄U" fl©PTZ «Æ"ƒ „«⁄Šƒ ‹ … ƒ¡⁄ fl„¡Å¥ D¤‹ O¤ Wolfgang L.(1996, 1991) ⁄¸ Hilmi U. (1996)⁄ ‡„⁄Š· y›z¡ŒPTZ " fl©ƒ ¥X¥ ˝ ⁄…⁄ ƒŁP(†˜7¡Bl4¡B30¡B60 ⁄)⁄Šƒ „«¥ «Æ• |Še †{⁄Uƒ C fl©"¸A¤ ¤ ˜ Y › « « ¤¥¡f–N ‹ … ⁄ƒ¸ 5 fl¯¡G

†˜„sfl• L ¯⁄(ño pentylenetetrazol-induced phenomena)

†˜1 fl¯• † Š – ' ƒ ‹ ("= automatisms)

¤ ƒp¡ G k˜p B ‹`¡¥Š ¡ B ¥⁄¡ A ƒ b ƒ „ ¥ fl ‹ O¥Ł˜[„ Š

†˜2 fl¯• « D ¤ « (atSypical minimal seizures)

¤ ƒp¡ G …Š¡ B « Æ "'¡ B‹Œ˜¿Z A ƒ b ƒ „ ¥ fl ¯ O¥¡Ł˜[„ ´…Š

« Æ " ˘ ' ‹‹ •·

†˜3 fl¯• » · • Lo(Šminimal seizures)

¤ ƒp¡ G « e "ƒ(Ł† ¡fl¥)

†˜4 fl¯• › « « o(Šmajor seizures)

¤ ƒp¡ ©˜(¶ ¶])¡ B · "a(˜‹14d)¡Bƒ Ł (⁄ £ fl fl,)¥¡B

¡Bfl ¥ ŁO(Š ƒ „ « Š _¤¸‹ƒA'kæŠU–ƒG¶ d¶

°)

†˜5 fl¯• ¥ † ¡ o(Šomplete major seizures)

¤ ƒp¡G¥ ¤ › ' (¥ ¶˘' ‹)ƒ æ H } ŠQ(⁄ £ fl fl,)¥

¥ ' ‹ I ¥ · " fl ¶ d¶|⁄ z¸ƒ×(¤jflP"" w ƒ ˚«… ƒ ¡ – N ¥„¥Ł¤ †˜† ˜ ›¶flÆ„

major seizure or motor seizure)

7

90mg/kg

14

90mg/kg 40mg/kg

30

90mg/kg 60mg/kg

60

90mg/kg 60mg/kg

2 GHB

Wolfgang L.(1996)

GHB

(immobility) (staring) (facial myoclonus) (vibrissal twitching)

GHB

EEG

(absence seizure)(Marescaux et al, 1992; Snead et al, 1993; 1990; Zhang et al,1991)

100mg/kg(

3. 7 14 30 60 (normal saline)(

DM 10mg/kg; 30mg/kg; 50mg/kg(30

KA PTZ GHB

760

1

(ratio) (latency) (frequency)

GHB

DM

(

PTZ GHB 2

(cortex hippocampus…)

eppendorff -70

7 14 30 60

‹ ' œ ` A ¤ ¥ ¸ PTZ(90mg/kg)／ o ƒ „ « £¥´¦A ¢ƒO S _ • | „ ／j bcl-2¡Bax¡B c-fos¡Bc-jun ¥ ƒ† ¥´... v¯T¡ F ¥／DM " " „／' O S•S| ¤ ¦· apoptosis "" † ¥´¡Cƒ]ƒ S › ¤ ¥ ¸／ Se " fl¶qPTZ／ _' z／S ° " « ' ~"'„„„／£¡A¤ „ Œ ¯ †] › ¤£3H¥¡／SYtime course †¡B2／fi sample †／¸24／fi sample †¡C¤ ‹ I ¥／¡HBƒ¡"«¤^／£‹ ƒP¡Cƒbtime course †／¡A¥ i／ƒ6 " †S¡AS¥• − − ¤† (¥ ... ¥ · ¥ ƒ¡Control¡F)¡F • • ‹ O／ S‹ normal saline (NS¡FN) 1／fi ¡B2／fi ／¸24／fi « Æ ~ ° ／¤œ¡F• • ‹ O／ S‹ PTZ (PTZ¡FP) 1／fi ¡B2／fi ／¸24／fi « Æ ~ ° ／¤œ¥£¥~¡ A ‹ ¥·^ ~ " « S／£ÆÐ2／fi ／¸24／fi sample † ¦¥i ƒ¤ ‹ ¥·• NS¡F• PTZ¡F• DM10 mg/kg¡F• DM 30 mg/kg¡F• DM 50 mg/kg¡ A ¤ ^ ／S O2／†fi ／¸†~24／fi ~ ° ‹ ¤œ¡F C ／S « Æ ' ¤ œ／¡£¥mRNA¡ ÆS"¥ RT-PCR ¤／"R¡A¥ H F, ‹ ¥·PTZ ' ／○S z ƒ‹¡A‹ O S _ • .v,¯fl¤"fl ¤g† M／S ƒ] ¡†C

1. RNA "" ¤œ
   a. −N' » tissue samples¡] ¤ fl ¶ q ' ˆ~"«／£Æ¶F C "‹ 50~100mg¡ ˆm' eppendorff／¡C
   b. ¥ {J1ml TRIzol¡C
   c. ¥H ª ¿ i · ¸ ª¿ifi¤ ‹tissue ‹ ／¡C
   d. ' æ ƒ k¤·(15~30¢J) R¸m5／ ~`¡C
   e. ƒA¥ {J0.2ml chloroform¡C
   f. ¥¸／ »•m15 ‹ ¡C
   g. ' æ ƒ k¤·•／ R¸m2-3／ ~`¡C
   h. ¥H12000rpm ´／ 15／ ~`¡A4¢J¡C
   i. −N／ W † M¶GÆ• s"" eppendorff／／¡C
   j. ¥ {J500λ¡]1λ=1μl¡ ^isopropyl alcohol¡C
   k. ' æ ƒ b « · ¯•／10 R¸m`¡C
   l. ¥H12000rpm ´／ 10／ ~`¡A4¢J¡C
   m. † ¥ h W†¦M†]GÆ−¡¡^C
   n. ¥H75¢Malcohol 1ml wash
      ¡]TRIzol¡GAlc = 1¡Gl¡ ^
   o. ¥H¡ 7500rpm ´／ 10／ ~`¡A4¢J¡C
   p. † ¥ h W†¦M†]GÆ−¡¡^A¥ ¸ Vacaum fl u " ¯fi¡CŒ

q. −N20µl ⁄S TE ¥ [⁄ Jfi⁄ sample ⁄⁄¡Apipeting¡C

r. ¤ œ @¤¡]1µl¡ ^œO.D. ›¨¡C

2. ·œO.D.

a. ¤œ1µl RNA ¥ ŧJ69µl TE ⁄⁄

(1µl RNA+ 69µl Q ⁄ ⇒70µl¡ i }˜70 › ¿j¡^

b. ¥HTE • S @ … •·ΦGD›œ¨¡C

2. RNA ⁄ ˇ ´¿S@¥¸

a. ƒb200 ml "" eppendorff ⁄ ⁄ ¥⁄J

RNA	2µg
oligo dT^{12-18} primer¡]500µg/ml¡^	1µl
Milli-Q water ,	¤ƒ12µl

b. 'æ⁄JGeneAmp PCR system 9600 (Perkin Elmer)¡A70¢J¡C

c. ƒA¥ ŧJ5X First Strand buffer 4µl

0.1 M DTT 2µl

10 mM dNTP 1µl

d. † V ƒ ¡¡C

e. ƒA¥ ŧJ1µl Super Script II¡C

f. † V ƒ ¡¤⁄ ^ S C ŧ ´¥H £ ¥ ƒA" ⁄W•»†G¡C

g. 'æ⁄JPerkin Elmer GeneAmp PCR system(9600)⁄⁄

42¢J¡B50 ⁄ ˜` → ƒ H70¢J¡B15 ⁄ ˜ ` ¥ h ƒC‹¡'°

3. » E ƒ X Q $´Œ⁄ˇ ŧ

a. ƒb200 ml "" eppendorff ⁄ ⁄ ¥⁄J

Reagent	**Stock conc.**	**Final conc.**
$MgCl_2$	50mM	2µg
PCR buffer	10X	1X
dNTP	25mM	0.25mM
primer (sence)	20µM	0.4µM
primer (anti-sence)	20µM	0.4µM
Taq polymerase	5U/µl	0.025U/µl
DNA		2µl

Milli-Q warter

Total 25µl

b. ¥HGeneAmp PCR System 2400¡]Perkin Elmer¡^ ¶ƒPCR¡C

4. ^ £ fl ‰ƒ„q"a

a. ¤œ2g agarose ' æ ' ⁄ T ¤ ‰ŒT~⁄⁄

b. ¥ {J0.5X TBE 150ml(ƒ„gel conc.‹ 2%)¡C

c. • Ti¥[... ¤ ˇ ¤ S „ ¥ ‰ƒ,¡Cƒ¤†z'œ"‹

d. ¥Hstir bar ¯ ' ¤ ¤ S N «ƒ50~60¢J¡C

e. ¥ {JEtBr¡]10 mg/ml¡^15 µl¡C

f. › ¸ ⁄ J » s † ˇ £fltrayi‰ƒ¦"'A ¦⁄womb¡A« ¤ fi'T¡C

g. S fi'T⁄S^ £ fl fi‰ƒJ„ q a...⁄¡Aƒ [⁄Jbuffer¡C

h. −NDNA marker⁄¸PCR product ⁄ S'loading dye S ¡ ⁄ †VƒX

¡AƒAload ƒ ‰ƒ⁄Swell⁄⁄¡C

i. ¥ H ‹ _ „ F ... ˇ ƒ•—N ¤t"†G @ ¡CU¤

...ˇ † ¿p/Ł“k

ƒ b ° " « „ Œ onS0¥y ANOVA with Newman-Keuls test ¤ ⁄ æßPTZ 'MDM ƒ ₩ (PTZ vs. DM10¡BPTZ vs. DM30¡BPTZ vs. DM50) o ¥ ' "'Z. æ·(latency)‹ OS ƒ†† ¸› p N,¤F ¥¥¡Aˇ ¥¸one-way ANOVA with Chi-square test ¥h⁄ æßPTZ 'MDM ƒ ₩ ƒ† o ¥ ' "'Z ƒ...ˇ⁄æ¤ (ratio) ‹OS ƒ†† ¸›p⁄W"'• Nq¡C

„ Œ¯ † G»P/“R

⁄@¡B‹ ¥·PTZ⁄S„ Œ ¯ °†"«

(1) ¥X¥˝« Æ˜7⁄ ƒ„'Z"ƒ ‹ ... ƒ¡ˇ[„

ƒbPTZ " fl¶(90mg/kg)⁄U¡A⁄ ƒj¡⁄ "'ƒ „«• †£¥˝¥ ¤›' ‹(¥ †ˇ' ‹)ƒ æ H }ŏSʃ@(⁄£ fl ƒ‚l¥)"'– $¸¡Cƒbƒ " •|¥ ¥˝S ¡B´ S "'† ¶H¡F– ⁄ ₩ « S·N|ƒ†«Æ"ˇ' ‹"'†£¥˝⁄S«Æ•|¶} ' l ¥·"'¥X†{¥ ¤›' ‹(¥ †ˇ' ‹)ƒ æ H }ŏSʃ@(⁄ £ fl fl„)¥¸¥ †ˇƒ Œ¡Aƒ „ † ¶H˜ Y «fi•|⁄@ " ‰ « ø ˜ ¤ ´_¡CŸ¥‹¥„⁄U‹ ¥·DM 10mg/kg¡B30mg/kg¡B' ¸50mg/kg¡A ¥¤ 30⁄ ˜`«ÆƒA"' figPTZ ¤ »⁄ ' zfl ¥‹⁄S†£¥˝¡C @ ˇ „ 1⁄pfi ¡A o†{' z"'– $¸¤ ˆSƒ† − S ¡A‰·•|¥ ·

" " ¥ X † { ¥¤(¥'†˘'‹ ‹)ƒ æ H } ¯(¿ ÐSŒfl,)¥¿¥ †˘ƒ Œ¡ A ƒ"†{¶ H ˜ Y › « fi ƒ•|«ø˜ ¤
´ _ Ÿ°ŗG„

(2) ¥X¥ ˝ Æ†14 ⁄ ƒ„Ÿ"ƒ ‹ … ƒ¡˘[„

ƒbPTZ Š C fl¶(40mg/kg)⁄U¡A⁄ j †⁄"˜"ƒ „«• |¥ †£¥˝´ Š ¡A⁄Š«ÆƒbƒA¥ Ÿ{«Æ"˘' ‹ ¥†{¶H¡C
› Y ‹ O ¥ Ÿ¥DM¥10mg/kg¡B30mg/kg¡B' ¸50mg/kg¡A ¥¤ 30 ⁄ ˜`«ÆƒA" figPTZ ¤ » ' z
fl ‹⁄ $£¥˝¡C @ ˘ ƒ 1 ⁄pfi ¡A¥ „ Œ ¯ †ðG{ z"˜– ¡ Š ¸ ¤ ^ ¤ S ƒ ¡A¥oŠ ¥ ‰ † ¸ p †"G–o
" ¡«Æ"˘' ‹ "˜" ƒ … ˘ ƒ'Ÿ"…ª¥ [(Table 12) (ratio ¥ 1/6 … ¥[ƒ 6/6)¡A¥ifl „ 14 ⁄ "˜"ƒ „«ƒ ¤¥¡A
DM "˜" „'•|ƒ†‹ ±°"˜"¶ ƒV¡R ¥·PTZ " ¶lq(90mg/kg)«Æ¡A⁄ j †⁄"˜"ƒ „«• •|†£¥˝¥ ¤ › (¥‹|
"˘' ‹)ƒ æ H } ¯(¿ ÐSŒfl,)¥"– Š¸¡Cfb› Ł ¶'‹l ¥·fi ¡ A|¥ o¥˝Š ¡B´ Š " ƒ{¶H¡F– ⁄U
¤ « Š·N|ƒ†«Æ"˘' ‹ "ƒ£¥˝¡A⁄Š«Æ¶ } ' ¥ " ˜" ¥ X † { ¥¤(¥'†˘'‹ ‹)ƒ æ H } ¯(¿ ÐSŒ
fl ¥)⁄¿¥ †˘ƒ Œ¡ A ƒ"†{¶ H ˜ Y «fi⁄ ‰ø« ø ˜ ¤ ´ ¡¥C›°¥„¥ ¥ ⁄UÐDM¥10mg/kg¡B
30mg/kg¡B' ¸50mg/kg¡A ¥¤ 30 ⁄ ˜`«ÆƒA" figPTZ ¤ » ' z fl˜"‹ $£¥˝¡C @ ˘ ƒ 1 ⁄pfi ¡A
o†{DM ¥i' ‰w¥ ¤ › ƒ æ H } ¯˜"fi›¶‰(Table 25)

(3) ¥X¥ ˝ Æ†30 ⁄ ƒ„Ÿ"ƒ ‹ … ƒ¡˘[„

ƒb× ¥·PTZ Š C fl¶(60mg/kg)«Æ¡A⁄ j †⁄ƒ «ƒb ¥·^˜ fl⁄£⁄[¡AŠY• |†£¥˝´ Š ¡B«Æ"˘' ‹
¥†{¶H¡C› Y ‹ O ¥ Ÿ¥« ‹Œ¥flDM 10mg/kg¡B30mg/kg¡B' ¸50mg/kg¡A ¥¤ 30 ⁄ ˜`«ÆƒA" fig
PTZ ¤ » ' z fl˜"‹ $£¥˝¡C @ ˘ ƒ 1 ⁄pfi ¡A¥ „ Œ ¯ †ðG{DM ¥i' ‰w´ Š Š‰"˜fi ¶¡
(Table 7)¡F‹ ¥· " ¶lqPTZ (90mg/kg)«Æ¡A⁄ j †⁄"˜"ƒ „«• |†£¥˝¥ ¤ › (¥‹†˘'‹ ‹)ƒ æ H } ¯¸
Š‰(⁄ £ fl fl,)¥"– Š¸¡Cfb× ¥·^˜"«⁄£⁄[¡ A|¥ ƒ†´ Š " ƒ{¶H¡F– ⁄U¤ « Š·N|ƒ†Š "˜"†£¥˝¡A
⁄Š«Æ• |ƒ†´ _ ´ ˜ "˜ " ¥ ¤›'(¥ †˘'‹ ‹)ƒ æ H } ¯(¿ ÐSŒfl,)¥¿¥ †˘ƒ Œ¡ A ƒ"†{¶ H Y ›«
fi •|⁄ ‰ø« ø ˜ ¤ ´ ¡¥C›°¥„¥ ¥ ⁄UÐDM¥10mg/kg¡B30mg/kg¡B' ¸50mg/kg¡A ¥¤ 30 ⁄ ˜`
«ÆƒA" figPTZ ¤ » ' z fl˜"‹ $£¥˝¡C @ ˘ ƒ 1 ⁄pfi ¡A o†{DM ¥i· ⁄ o¥˝ƒb Ł¡B¥ †˘ƒŒ
† ⁄¿¥ ¤ › (¥‹†˘'‹ ‹)ƒ æ H } ¯(¿ ÐSŒfl,)¥Š ƒ.˘(Table 18¡B22¡B26)¡Cƒ „ Š ¡B´ Š ⁄¸
«Æ"˘' ‹ "˜" †{– ¡ Š ¸ ¤ ^ ¤ S ƒ ¡C¥ÐŒ¡ß⁄ ‰ƒ „« Š‰' z"˜"ƒ ‹ fl ⁄ ‰ø« ø ˜ ¤ ¶i¡† ⁄ ¡C⁄æ
,ß× ¥·PTZ ⁄¸DM † ƒ „«˜" Š‰fl¯…˘(score)¡A o†{DM ¥i› ŠC " ¶lqƒ „«' z"˜"†£¥˝¡C

(4) ¥X¥ ˝ Æ†60 ⁄ ƒ„Ÿ"ƒ ‹ … ƒ¡˘[„

ƒbPTZ§ C fl¶(60mg/kg)«Æ¡Cƒb† " < I ¥ ˆ˜¡"«A/£/j† ¡ / ƒ „ §Y¡• |A†£¥§ Æ¶§'l
¥ X † { ¥ ¤ ›¡ ª§– / U ¤ « § · N ƒ«Æ"˜ › Y «"Ø†¥{¶HDM 10mg/kg¡B30mg/kg¡B'。
50mg/kg¡A ¥ 30 / ˜`«Æƒ A "fiGPTZ ¤ » / ' z fG"< § £¥¡"C O ¿ ˘[/ fi ¡A¥ „ Œ ¯ †Ø"G
†{DM ¥ i '‰ẃ… § §@"fi ¶¡(Table 7)¡F< ¥· " ¶qPTZ(90mg/kg)«Æ˜ / @ / fi ¡ A / j † / ""
ƒ „ « • | † £ ¥¥(¥¤|›'˘ '<)ƒ æ H }ƆS@(/ffl fl¥)"–§¸¡Cƒb† " < I ¥ ˆ˜¡"A/£¥[
ƒ§ /¸´ … § "†¡{A¶H §Æ• | † ˜˜¥ƒ¤a† { ¥ ¤ ›(¥|"<˘ ')ƒ æ H }ƆS@(/ffl fl¥)/¸¥|
"˘ƒ Æ (Table 18¡22¡26)¡Aƒ „ † ¶H˜ ¥«fi • |/@" ‰ø˜ ¤ ´ _ Y°¡<C„ › Y ¥ ¥/DM¥θmg/kg¡B
30mg/kg¡B'。50mg/kg¡A ¥ 30 / ˜`«Æƒ A "fiGPTZ ¤ » / ¯ wfl ϑ</ § £¥¡"C O ¿ ˘[/ fi ¡A
ϕ{DM ¥i· / ¥"ƒb ŁO¡B¥|"˘ƒ Æ /¸¥ ¤ › (¥<|" ˘ ')ƒ æ H }ƆS@(/ffl fl¥)/§ ƒ
…˘¡Cƒ „ § ¡B´ §/¸« Æ " ˘ ' ›"{– §¸¤ ûSƒ† – § ¡@¥ Bß/ ƒ ‹' z""ƒ < fl /@" ‰ø˜
¤ fi ¶¡† / ¡C

(5) – – ¤†ƒ ‹"ƒ" < … ƒ¡˘ /

ƒb× ¥·PTZ /¸DM † "ƒPfi ¡A" fiG¥˝† z › „ Q/@§ < Ffj¬B˜ }ifbf P.¸¥˝" ł „" ƒ
„«¡C O ¿ ˘[/ fi ¡C¥ ˘ / "G ϕ{¡ @ƒ < ' M ¥–ƒ„«¤^ L/£ƒP¡C

/G¡B× ¥·GHB /§„ Œ °"«†

(1) ¥ X ¥«Æ˜7 / ƒ ‹"ƒ" < … ƒ¡˘ /

ƒb¥»„ Œ /¡ A ł¥GHB (100mg/kg)«Æ˜ / @ / fi ¡ A ƒ„«• | ¥†{R/ /£ °""– §¸¡C›"¥
ƒ „ «|/£"§ ˜o¡F– / U ¤ « §·N¶|†£¥°" " ƒ¶HC„ g«ø˜ /@ qfi ¶¡/ §Æ¡ A ƒ „«•y|
< < ¡ °/@U¡ A §«Æ§« § ƒa¶ i ∂ R/£ °"""<"A¡Cƒ „ † { ¶ffi• |¥ · " " ¥†{@" ‰ø˜ ¤ ´ _
Y °<¡„C › Y ¥ ¥/DM¥θmg/kg¡B30mg/kg¡B'。50mg/kg¡A ¥ 30 / ˜`«Æƒ A "fiGGHB ¤
» / ' z fG"< § £¥¡"C O ¿ ˘[/ fi ¡ A ϕ{'z""– §¸¤ ûSƒ† – § ¡Æ·• | ¥ o¥R/
/£ °" " ƒ¶HF«ø˜ /@ qfi ¶¡/ §Æ¡ A ƒ„«y< < ¡ °/@U¡ A «§ƒa/S• | £¥˝R/ /£ °¡Cƒ „ † ¶H
ƒ†fi • |¥ · " " ¥†{@" ‰ø˜ ¤ ´ _ Y°‹C„

(2) ¥ X ¥«Æ˜14 / ƒ ‹"ƒ" < … ƒ¡˘ /

ƒb¥»„ Œ /¡ A ł¥GHB (100mg/kg)«Æ˜ / @ / fi ¡ A ƒ„«• | ¥†{R/ /£ °""– §¸¡Cƒb†

" ¡ A • | ¥ o ¥ ˝£¡ -A"˝SS ˜«oÆ • | † ¥˝¡ ÆA˝ƒ˝-£ fi° • | ƒ æ H ›–ǂ Ç' « œ" "˝˝Ç{¶Ç H
fi ¶ ˝Sǀ«ÆƒÆ „ « y ‹‹(ƒ ⁄bœ«Ç¶q˝U¶¡˝·• |¥ ˂ ,o¤ ¥L" " ' ƒz‹ ¡A¤ ƒpǀGS ˜q B ¥˝)¡A
« S ƒa•˝S| † £ ¥ ˝ R˝¡Cƒ£„°† { ¶ H ƒfi¥ •| "˝"¥X† ˂@"%« õ ¤ ´ _ Y˜¡ºÇ›„¥¥ ¥ ˝U‹ ¥·
DM 10mg/kg¡B30mg/kg¡B' ¸50mg/kg¡A ¥¤ 30˝ ˜`«Æƒ A "fiGHB ¤ » ' zfl ⁄g‹˝ S ƒ£¥¡˝C
O ¿ ˇ[˩˝pfi ¡ A o † { – z"S ¤^ƒ¤S – S ¡Æ·• | ¥ o ¥ ˝ R ˝˝ƒF«°Ø"˝†{¶Ç H q
fi ¶ ˝Sǀ«ÆƒÆ „ « • | ¥ (ƒ¡⁄bœ«Ç¶q˝>¶¡˝·• |¥ ˂ ,o¤ ¥L" " ' ƒz‹ ¡A¤ ƒpǀGS ˜o¡ B¥
˝)¡A« S ƒa•˝S| † £ ¥ ˝ R˝¡Cƒ£„°† { ¶ H ƒfi¥ •| "˝"¥X† ˂@"%« õ ¤ ´ _ Y˜¡ºÇ„

(3) ¥X¥ «Æ†˜30˝ ƒ ‹"ƒ‹ … ƒ¡˘ ˩

ƒb¥ » „ Æ ¡Æ« ¥·GHB (200mg/kg)«Æ˘ ˩ ˝@› ˝pfi ¡ A ƒ„«« • |¥X† { R ˝ ˝£– S"˝Cƒb†
" ¡ A • | ¥ o ¥ ˝£¡F-¥ ‹S˝ Ç@o‹ q fi ¶ ¡ ˝ S « Æ †£¥A˝ƒR†˝fi˝£ °H › – ǂ' z""
¶H(ƒ ⁄bœ q·`¶¡˝·• |¥ ˂ ,o¤ ¥L" "¯ wƒ‹ ¡A¤ ƒpǀGS ˜o¡ B¥˝)¡Cƒ „ † { ¶ H ƒfi¥ •| "
¥X† ˂@"%« õ ¤ ´ _ Y˜¡ºÇ›„¥¥ ¥ ˝U‹ ¥·DM 10mg/kg¡B30mg/kg¡B' ¸50mg/kg¡A ¥¤ 30˝
˜`«Æƒ A "fiGHB ¤ » ' zfl ⁄g‹˝ S ƒ£¥¡˝C O ¿ ˇ[˩˝pfi ¡ A o†DM "" „ ˝ ' ¥ ¥Hƒ „«
› – ǂ ¦ ' z o ¥"" Wv(Table 12)¡C¤ l' z"˝ ¡ S ¤^ƒ¤S – S ¡Æ‰

(4) ¥X¥ «Æ†˜60˝ ƒ ‹"ƒ‹ … ƒ¡˘ ˩

ƒb¥ » „ Æ ¡Æ« ¥·GHB (200mg/kg)«Æ˘ ˩ ˝@› ˝pfi ¡ A ƒ„«« • |¥X† { R ˝ ˝£– S"˝Cƒb
ǂ " ¡ A • | ¥ o ¥ ˝£¡F-¥ ‹S˝ Ç@o‹ q fi ¶ ¡ ˝ S « Æ †£¥A˝ƒR†˝fi˝£ °H › – ǂ¡'
" " ǂ¶Hƒ ⁄bœ q·`¶¡˝·• |¥ ˂ ,o¤ ¥L" " ' ƒz‹ ¡A¤ ƒpǀGS ˜o¡ B¥˝)¡Cƒ „ † { ¶ H ƒfi¥ •|
· "˝"¥X† ˂@"%« õ ¤ ´ _ Y˜¡ºÇ›„¥¥ ¥ ˝U‹ ¥·DM 10mg/kg¡B30mg/kg¡B' ¸50mg/kg¡A ¥¤
30˝ ˜`«Æƒ A "fiGHB ¤ » ' zfl ⁄g‹˝ S ƒ£¥¡˝C O ¿ ˇ[˩˝pfi ¡ A o†DM "" ˝'• |¥ ǂt
R ˝ S"@" " ƒ£¥¡˝C l' z"˝ ¡ S ¤^ƒ¤S – S ¡Æ‰

(5) – – ¤†ƒ ‹"ƒ‹ … ƒ¡˘ ˩

ƒb‹ ¥·GHB ˝¸DM † "˝"ƒPfi ¡A" fiG¥˝"† z › „ Q˝˝ÇS ‹ Ƒƒ¡-Ɛ„ }ifbƒ P.¸¥˝" ǂ „"˝"
ƒ „«¡C O ¿ ˇ[˩˝pfi ¡C¥ ˇ ˩ "G ф{¡ G ¤ƒ‹ ' M ¥-ƒ" „«¤^ L˝£ƒP¡C

／T ／ æ , ƒbUbax ¡Ebcl-2 ¡Ec-fos ¡Ec-jun ¡ENSE mRNA ƒb7 ¡El4 ¡E30 ／ ¸60 ／ ƒ „ « ／ S ／ j , ¥ ‰Ł"" "
S ¸¡G

ƒb¥ » „ Œ ¡／A ‹ ／ F ' œ ` A ˇ ₱TZ™ fl¶q ƒb „«† ¥˝™"' zƒ‹ ¡A‹ O S _ ┼...ˇv ¯jT, ¥ ‰Ł
／／bax ¡B bcl-2 ¡B c-fos ¡B c-jun ¡ENSE mRNA " " "†¡{A‹ SQ¥ ¸RT-PCR "" ／ Ł " k ₦／ƒ ™R／
...ˇƒ „ « ／ S j, ₤¥€ ‰¥¥K˝« Æ °‹／„...ˇ™"／ ₤₱(PND)¥i／ ƒ¤7 ¡El4 ¡E30 ¡E60 ／ ¡ Œ „ Œ † ÞÞp™"
／ ₤₱¥i／ ƒ¤3 † ¡GSYtime course † ¡E2 ／ ₤i sample † ／ ¸24 ／ ₤i sample † (¤ ₫¥·Ł ƒ ¡ ‰ — •
†˜22 ›¶／ S Œ¯／ ₤k(／›)¡Af@13 ƒ¡C¥ '¤₫C „ Œ ‹ «´3ƒ,¡A¥B¤ 3ƒ," " Œ¯ ₱G‹ ¤ ª ₣／@
› ₱°¡Af] ₣·₦／ »"1 † ₱G¤ ／ "R¡G

(1) NSE mRNA " " "†¡{G

ƒbƒ U／ ...ˇ／U¡A‹ ¥·NS¡EPTZ／¸DM¡A o†{ NSE mRNA " " " †{¤¶q₱Sƒ₮'œ¯ª"˝¯ ／ˇ („ ¥...
" ／W)¡C

(2) Bax mRNA " " "†¡{G

ƒbƒ U／ ...ˇ／U¡A‹ ¥·NS¡EPTZ／¸DM¡A o†{ bax mRNA " " " †{¤¶q₱Sƒ₮'œ¯ª"˝¯ ／ˇ („ ¥...
" ／W)¡C

(3) Bcl-2 mRNA " " "†¡{G

ƒb†˜7 ／ "˝¥fi„«¤ ›W¡A o†{‹ ¥·NS •|... ₩[bcl-2 mRNA " " "† ((Fig. 1)¡Ebcl-2 mRNA ƒb†˜
2／₤i •|ƒ₮'œ¯ª"˝／W／ ¡ A₱«Æ•|₱et{／U› " ˝¡"p¡C¥ ¥˜¡A‹ ¥·PTZ／]•|»／ obcl-2 mRNA "˝
" †{¡Af »PNS／æß _¤ ¡A‹h¤Sƒ₮'œ¯ª"˝¯ ／ˇ¡C¥ „ Œ ₱G o†{¡Afb†˜2／₤i ／¸†˜24／₤i ‹I
¥·DM+PTZ ' »／ obcl-2 mRNA " " " †{¶|¤æ† ¿Wk ¥·PTZ ¤ " ˝" (Fig. 2)¡Cƒ ¥GDM "˝ „
／'•| reverse ₮ ¿Wk ¥·PTZ ' ₮yƒ¤bcl-2 "˝／U› ¡C¥ ／W›z ₱G¯ª¥ ¡A ₤ ‹O‹ ¥·NS¡EPTZ／¸
DM‹ ¤ˇbcl-2 mRNA ƒ₮／W／ "˝` ¶ ¡A／ ¤ ‹ONS 2／₤i ₮o／@† ／₱bcl-2 mRNA ' ／W／ " " ¶₮'œ
¯ª" ˝j' — ¤ † ／¸PTZ 2／₤i † ¡Fƒ DM "˝ ₰'ƒ ¥G¥i¥ ₱¤ PTZ „ bcl-2 mRNA "˝· ‰w¡C
£ƒ„／₱¥~¡A₱ › ƒb14¡E30／¸60／ " ₣ ¤„₰W L"k » œ¤bcl-2 mRNA " " "†¡{C

(3) c-fos mRNA " " "†¡{G

ƒb7／ "˝¥fi„«¤ ›W¡A o†{‹ ¥·PTZ 1／₤i ' »／ oc-fos mRNA " " " †{¶|¤œ¯ª" ˝"' NS 1
／₤i † (Fig. 3)¡Cƒ„" ¥ PTZ ,ß' »／ oc-fos mRNA "˝† ¥˝¡Cƒ DM¤^／£•|· ／ PTZ ' »／ o
／₱c-fos " {¶q(Fig. 4)¡C¥ ¥˜¡Afb†˜14／¡B†˜30／／¸†˜60／ " ₣ ¤„₰W¡A o†{‹ ¥·NS •|
／ oc-fos mRNA ƒb†˜1／₤i ƒ₮¯ª "˝／W／ (Fig. 5¡E8)¡C¥ ¥˜¡A‹ ¥·PTZ／]•|»／ oc-fos mRNA

ƒ Þ˜1 ⁄ p fi ƒ ‡ ¯ ª ¡"A⁄Ø«Æ Þ˜2~24 ⁄ fi • | Š ⊄{¬œ"⁄ U ¡ C Ÿ…‚"¡ADM "" „ ›⁄•]|
» ¤˜c-fos mRNA ƒ Þ˜2 ⁄ ‚†˜24 ⁄ fi Š ⊄{⁄@⁄ W ⁄"„ §‚ (Fig. 6¡B7¡B9)¡C" ƒX⁄W› z †"ŒA o
†{ L ‰ ©‹ NŠ·¡BPTZ ' ‚DM ‹ • |»⁄ oc-fos mRNA "′" †{¶ q W¥¡Æ¥BDM »⁄ oc-fos mRNA
"′" †{¶q• |œ¯ ª" " PTZ 2 ⁄ fi † ¡C‡˜2 ⁄ fi ⁄ ‚†˜24 ⁄ fi ‹ ¥·DM+PTZ ' »⁄ oc-fos mRNA
"′" †{¶q• |⁄ æ ‡¿W ¥·PTZ ¤ "" "¡Cƒ] ƒ–‰ ¡ADM „ PTZ ⁄ ‚NS ' »⁄ o⁄Šc-fos mRNA "
†{¶q¤ˆ L'œ¯ ª"Š ¤fi"G¡A` • |«P¤˜c-fos mRNA "′" †{¶ q W¥¡[C

(4) c-jun mRNA "′" †{¡G

ƒ Þ˜7 ⁄ "′¥ fi ‹¤⁄W¡A o†{¥·PTZ¡BNS ⁄ ‚DM ¤ˆ⁄£• |... v̄Tc-jun mRNA "′" †{¶q („ ˇ ¥"
⁄W)¡C†˜14 ⁄ "′ƒ „«¡A o†{‹ ¥·PTZ ⁄ ‚NS ¤ˆ⁄£• |... v̄Tc-jun mRNA "′" †{¶q („ ˇ ¥"⁄W)¡Aƒ
‹ ¥·DM 2 ⁄ fi † ' »⁄ oc-jun mRNA "′" †{¶q• |œ¯ª " PTZ 2 ⁄ fi † (Fig. 10)¡C¥ ¥~¡Aƒ Þ˜
30 ⁄ "′ƒ „ ‹¤⁄W¡A o†{‹ ¥·NS ¤ˆ⁄£• |⁄ oc-jun mRNA "′" †{¶ q W¥¡[(Fig. 11)¡Aƒ ‹ ¥·PTZ 2
⁄ fi † ' »⁄ oc-jun mRNA "′" †{¶q• |œ¯ªŠC' NS 2 ⁄ fi † ⁄ ‚–→¤ † (Fig. 11)¡Cƒ„¥~¡A‹ ¥·
DM 2 ⁄ fi † ⁄ ‚24 ⁄ fi † ' »⁄ oc-jun ƒ]"′" †{¶q• |œ¯ª " PTZ 2 ⁄ fi † ⁄ ‚24 ⁄ fi † (Fig.
12)¡Cƒ Þ˜60 ⁄ "′ƒ „ ‹¤⁄W¡A o†{‹ ¥·NS ⁄ ‚PTZ ‹ • |⁄ oc-jun mRNA "′" †{ (Fig. 13)¡Aƒ
‹ ¥·PTZ † ⁄Šc-jun "′" †{¶q• |ƒb24 ⁄ p fi ⁄Š‹Æ{¯ ª "„ U ¡A‹ ¥·NS † «oŠ ⊄{« õ ⁄ W ⁄"′
–¡"p¡Cƒbƒ‚fi ¡A‹ ¥·DM • |»⁄ oc-jun "′† ¥˝¡A¥B¤ " †{¶q• |œ¯ ª" " PTZ 2 ⁄ fi † ⁄ ‚24
⁄ fi † (Fig. 14)¡C" ƒX⁄W› z †"ŒA‹ ¥·NS ' †˜7 ⁄ ¡B†˜14 ⁄ ⁄ ‚†˜30 ⁄ "′ƒ „«¡A¤ˆ⁄£• |... v̄T
c-jun ƒ]"′" †{¡Fƒ ‟' PTZ fi ¡A• |Š ¤ †˜30 ⁄ ƒ „«c-jun mRNA "′" †{¡C¥ ¥~¡Aƒbƒ U ⁄
...ˇ⁄U ‟' DM 10¡B30¡B50 mg/kg ¥i'œ¯ª«P¶ic-jun mRNA "′" †{¶ q W¥¡[Cƒ„ ¶G• ‰ DM¡ fl‚S
ŠO‹O " fl¶q¡ ^¥ifl ¤ªƒ‡‹ ⁄ˇc-jun mRNA " †{¶ q W¥"[′fi˜"G¡C

Table 1. The effect of dextromethorphan on PTZ-induced lost in righting ability on the developing rats.

PND	PTZ (high dose)	DM10	DM30	DM50
7	2/6	0/6	0/6	1/6
14	3/7	0/7	0/7	0/7
30	11/12	4/12a	2/12[a]	2/12[a]
60	11/11	11/11	5/11[a]	3/11[a]

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of PTZ
DM10 : means pre-injection of DX10 mg/kg
DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to PTZ group (Chi-square test. $p<0.05$)

Table 2. The effect of dextromethorphan on PTZ-induced generalized clonic seizures on developing rats.

PND	PTZ (high dose)	DM10	DM30	DM50
7	3/6	4/6	4/6	3/6
14	6/7	6/7	7/7	6/7
30	8/12	2/12a	12/12a	2/12a
60	9/11	8/11	6/11a	3/11a

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of PTZ
DM10 : means pre-injection of DX10 mg/kg
DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to PTZ group (Chi-square test. $p<0.05$)

Table 3. The effect of dextromethorphan on PTZ-induced generalized tonic- clonic seizures on the developing rats.

PND	PTZ (high dose)	DM10	DM30	DM50
7	5/6	4/6	5/6	5/6
14	7/7	6/7	6/7	7/7
30	10/12	7/12	2/12[a]	4/12[a]
60	11/11	8/11	8/11	5/11[a]

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of PTZ
DM10 : means pre-injection of DX10 mg/kg
DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to PTZ group (Chi-square test. $p<0.05$).

Table 4. The effect of dextromethorphan on PTZ-induced unilateral clonus on developing rats

PND	PTZ (high dose)	DM10	DM30	DM50
7	6/6	6/6	6/6	4/6
14	2/7	0/7	0/7	0/7
30	6/12	5/12	2/12	4/12
60	10/11	7/11	7/11	1/11[a]

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of PTZ
DM10 : means pre-injection of DX10 mg/kg
DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to PTZ group (Chi-square test. $p<0.05$).

Table 5. The effect of dextromethorphan on PTZ-induced tremor on the developing rats.

PND	PTZ (high dose)	DM10	DM30	DM50
7	6/6	4/6	6/6	5/6
14	7/7	7/7	7/7	7/7
30	5/12	11/12a	6/12	1/12
60	11/11	7/11	7/11	8/11

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of PTZ
DM10 : means pre-injection of DX10 mg/kg
DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to PTZ group (Chi-square test. $p<0.05$).

Table 6. The effect of dextromethorphan on PTZ-induced unilateral clonus on developing rat

PND	PTZ (low dose)	DM10	DM30	DM50
14	1/6	6/6a	6/6a	6/6a
30	0/10	0/10	0/10	1/10
60	2/7	0/7	0/7	2/7

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of PTZ
DM10 : means pre-injection of DX10 mg/kg
DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to PTZ group (Chi-square test. $p<0.05$).

Table 7. The effect of dextromethorphan on the latency of wet dog shake-induced by GHB in the developing rat

PND	GHB (sec)	GHB+DM10 (sec)	GHB+DM30 (sec)	GHB+DM50 (sec)
7	-	-	-	-
14	1911 ± 524 (n=5)	1113 ± 883 (n=2)	1433 ± 568 (n=3)	2213 ± 138 (n=2)
30	2012 ± 784 (n=5)	3223 ± 457 (n=2)	1517 ± 500 (n=5)	257± 9 (n=2)
60	497 ± 36 (n=2)	1835 ± 703 (n=2)	202	144

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of PTZ
DM10 : means pre-injection of DX10 mg/kg
DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to PTZ group (Chi-square test. $p<0.05$).

Table 8. The effect of dextromethorphan on the ratio of wet dog shake-induced by GHB in the developing rat

PND	GHB	GHB+DM10	GHB+DM30	GHB+DM50
7	0/6	0/6	0/6	0/6
14	5/6	2/6	3/6	2/6
30	5/6	2/6	5/6	2/6
60	2/6	2/6	1/6	1/6

Data were ratio of rats with PTZ-induced seizure behaviors
PTZ : means single injection of GHB
DM10 : means pre-injection of DX10 mg/kg

DM30 : means pre-injection of DX 30 mg/kg
DM50 : means pre-injection of DX 50 mg/kg
[a] means significantly different to GHB group (Chi-square test. $p<0.05$).

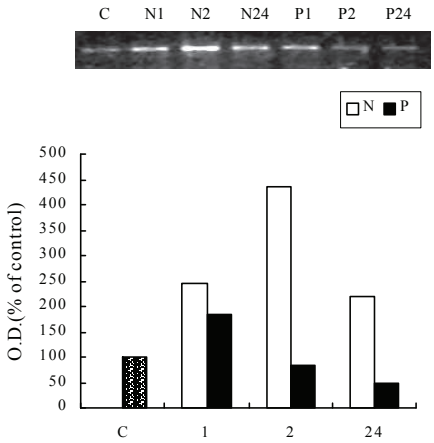
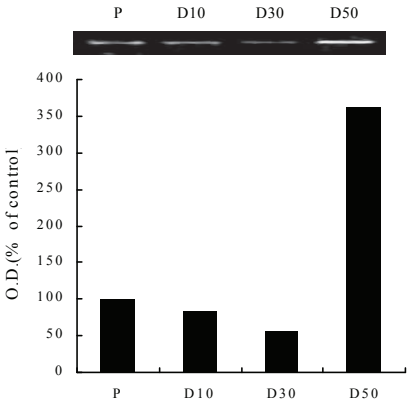


Figure1. The effect of PTZ on bcl-2 mRNA level in the cortex of PND 7 rat.
The cortical samples were taken at 1, 2 or 24 hour after injection of PTZ. Each data is normalized to the value of control (C). C: the control rats without injection. N: the rats injected with normal saline alone. P: the rats injected with PTZ .

(A)



(B)

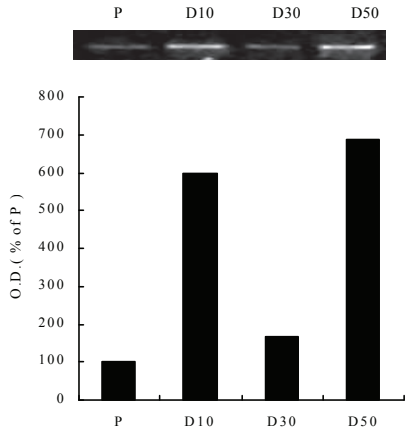


Figure2. The effect of DM on bcl-2 mRNA level in the cortex of PTZ-injected PND 7 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection of PTZ. Each value is normalized to the value of P. P: the rats injected with PTZ. D10: the rats injected with PTZ and 10 mg/kg of DM. D30: the rats injected with PTZ and 30 mg/kg of DM. D50: the rats injected with PTZ and 50 mg/kg of DM.

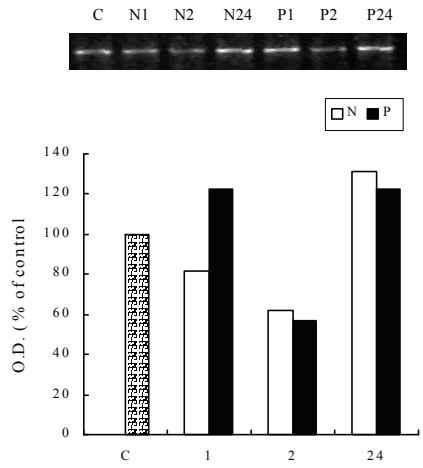
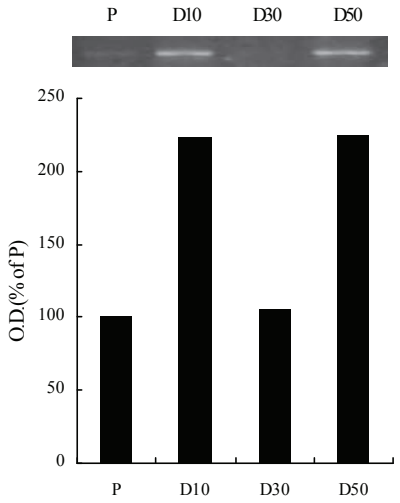


Figure 3. The effect of PTZ on c-fos mRNA level in the cortex of PND 7 rat.

The cortical samples were taken at 1, 2 or 24 hour post injection of PTZ. Each data is normalized to the value of control (C). C: the rats without injection. N: the rats injected with normal saline alone. P: the rats injected with PTZ.

(A)



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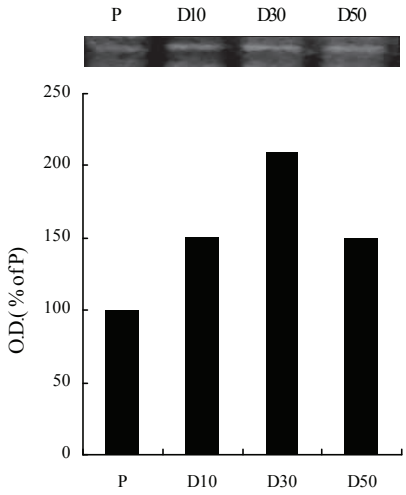


Figure 4. The effect of DM on c-fos mRNA level in the cortex of PTZ-injected PND 7 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection with PTZ. Each value is normalized to the value of P. P: the rats injected PTZ alone. D10: the rats injected with PTZ and 10 mg/kg of DM. D30: the rats injected with PTZ and 30 mg/kg of DM. D50: the rats injected with PTZ and 50 mg/kg of DM.

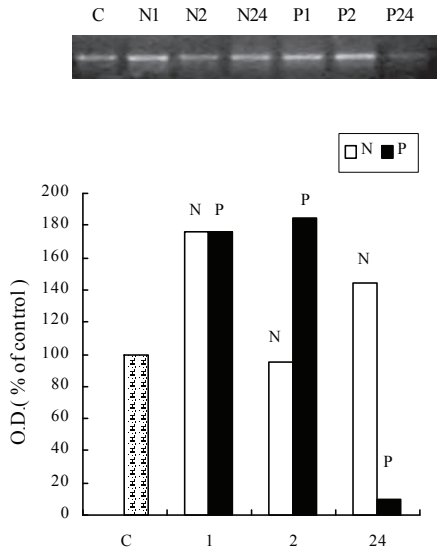


Figure 5. The effect of PTZ on c-fos mRNA level in the cortex of PND 14 rat.

The cortical samples were taken at 1, 2 or 24 hour post injection of PTZ. Each data is normalized to the value of control (C). C: the rats without injection. N: the rats injected with normal saline alone. P: the rats injected with PTZ.

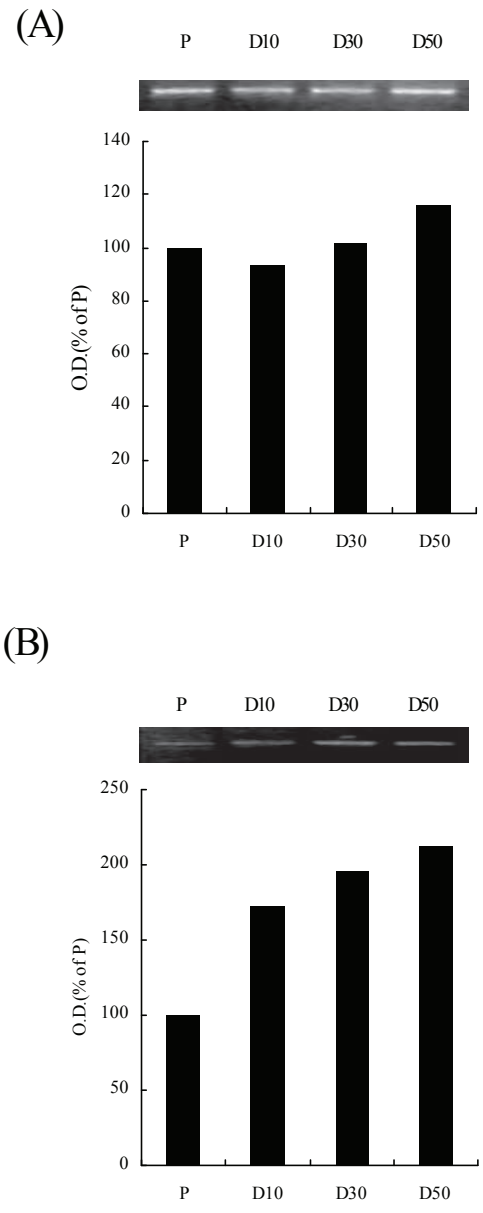
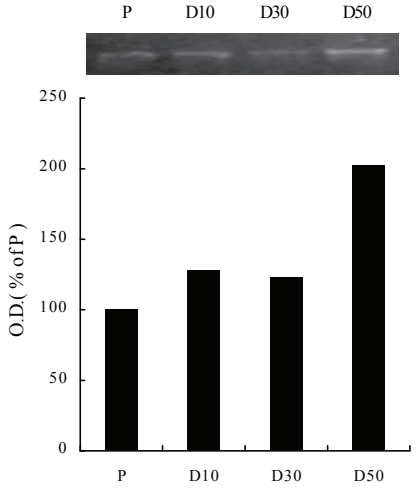


Figure 6. The effect of DM on c-fos mRNA level in cortex of PTZ-injected PND 14 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection of PTZ. Each value is normalized to the value of P. P: the rats injected with PTZ. D10: the rats injected with PTZ and 10 mg/kg of DM. D30: the rats injected with PTZ and 30 mg/kg of DM. D50: the rats injected with PTZ and 50 mg/kg of DM.

(A)



(B)

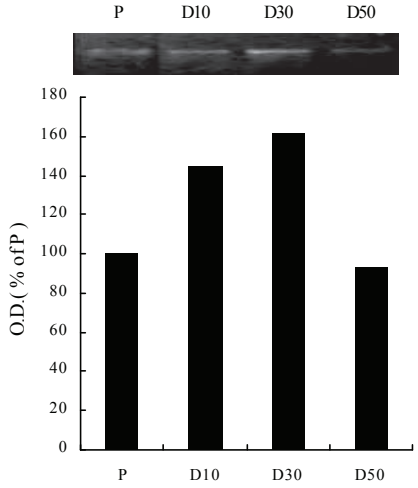


Figure 7. The effect of DM on c-fos mRNA level in the cortex of PTZ-injected PND 30 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection of PTZ. Each value is normalized to the value of P. P: the rats injected with PTZ. D10: the rats injected with PTZ and 10 mg/kg of DM. D30: the rats injected with PTZ and 30 mg/kg of DM. D50: the rats injected with PTZ and 50 mg/kg of DM.

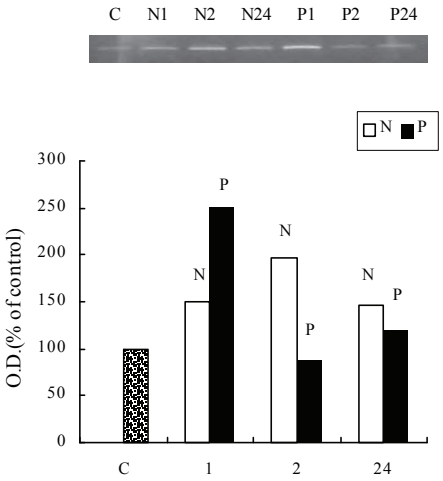


Figure 8. The effect of PTZ on c-fos mRNA level in the cortex of PND 60 rat.

The cortical samples were taken at 1, 2 or 24 hour post injection of PTZ. Each data is normalized to the value of control (C). C: the rats without injection. N: the rats injected with normal saline alone. P: the rats injected with PTZ .

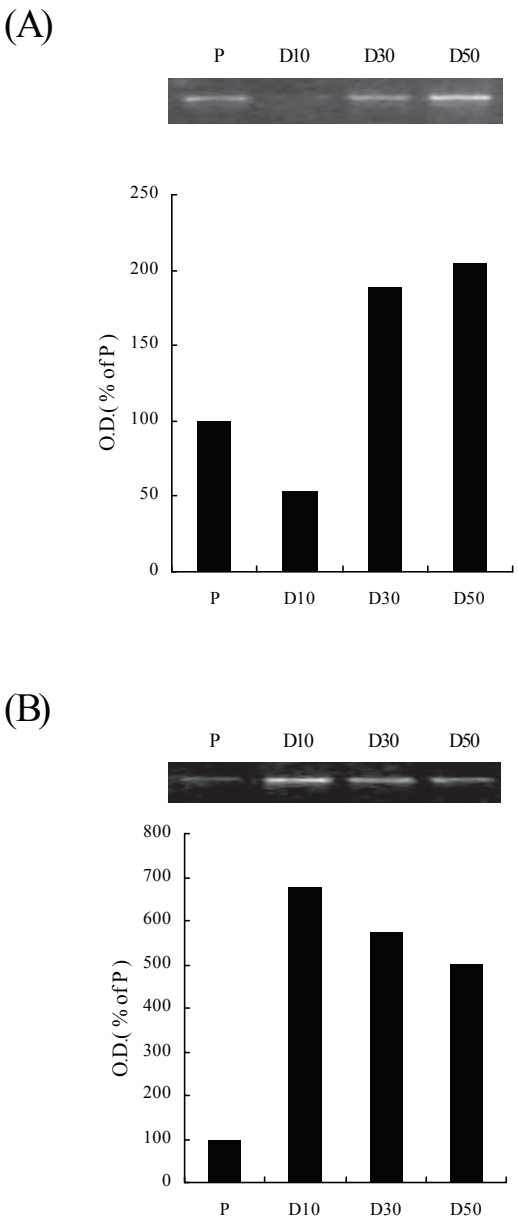


Figure 9. The effect of DM on c-fos mRNA level in the cortex of PTZ-injected PND 60 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection of PTZ. Each value is normalized to the value of P. P: the rats injected PTZ D10: the rats injected with PTZ and 10 mg/kg of DM. D30: the rats injected with PTZ and 30 mg/kg of DM. D50: the rats injected with PTZ and 50 mg/kg of DM.

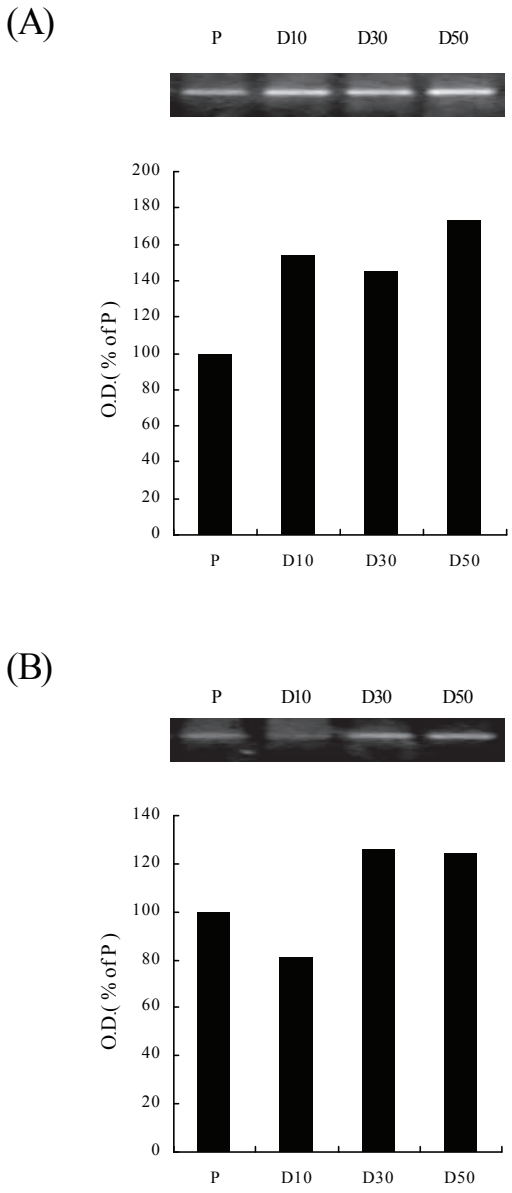


Figure 10. The effect of DM on c-jun mRNA level in the cortex of PTZ-injected PND 14 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection of PTZ. Each value is normalized to the value of P. P: the rats injected PTZ D10: the rats injected with PTZ and 10 mg/kg of DM. D30: the rats injected with 30 mg/kg of DM. D50: the rats injected with PTZ and 50 mg/kg of DM.

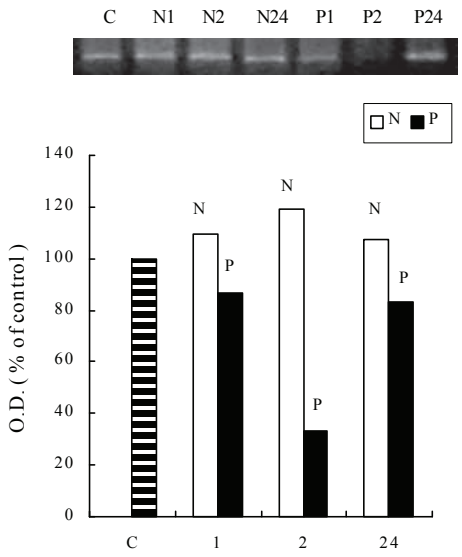
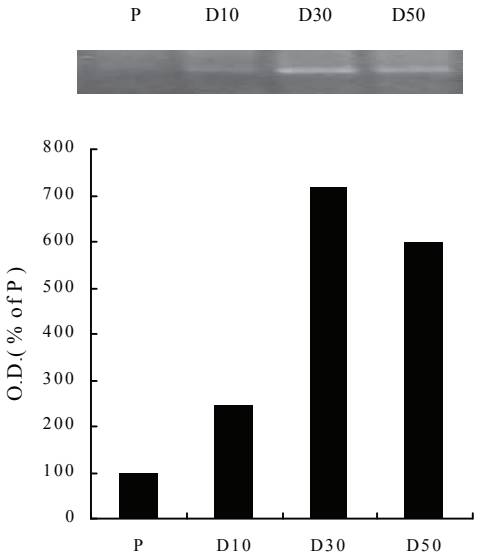


Figure 11. The effect of PTZ on c-jun mRNA level in cortex of PND 30 rat.

The cortical samples were taken at 1, 2 or 24 hour post injection of PTZ. Each data is normalized to the value of control (C). C: the rats without injection. N: the rats injected normal saline alone. P: the rats injected pentylenetetrazol.

(A)



(B)

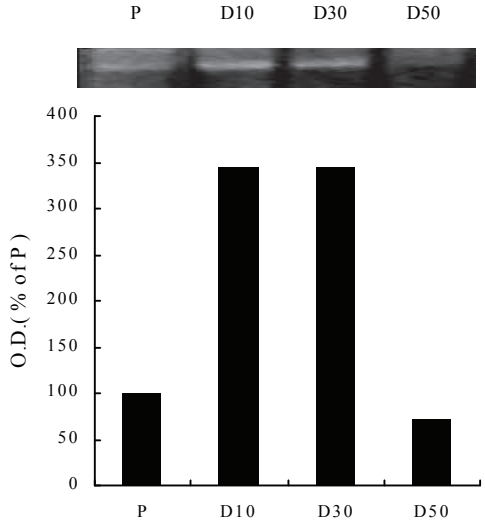


Figure 12. The effect of DM on c-jun mRNA level in cortex of PTZ-injected PND 30 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection of PTZ. Each value is normalized to the value of P. P: the rats injected pentylenetetrazol. D10: the rats injected with10 mg/kg of DM. D30: the rats injected with 30 mg/kg of DM. D50: the rats injected with 50 mg/kg of DM.

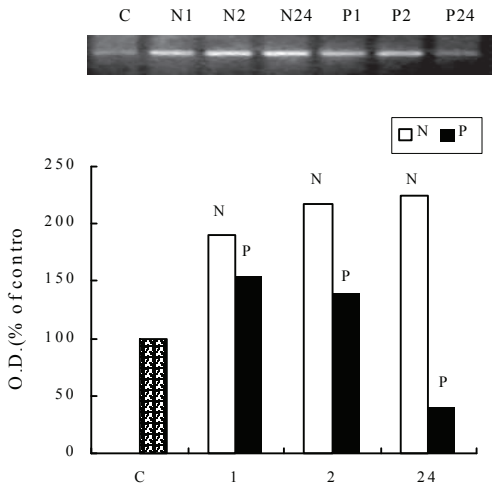


Figure 13. The effect of PTZ on c-jun mRNA level in the cortex of PND 60 rat.

The cortical samples were taken at 1, 2 or 24 hour post injection of PTZ. Each data is normalized to the value of control (C). C: the rats without injection. N: the rats injected normal saline alone. P: the rats injected PTZ.

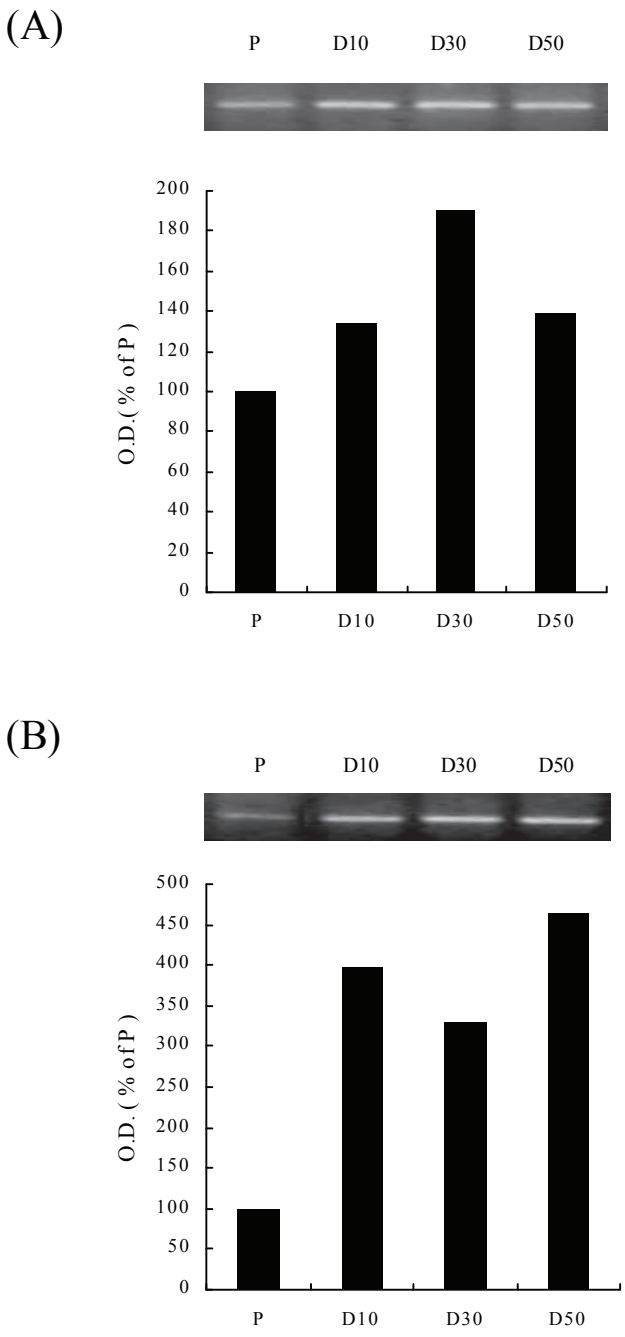


Figure 14. The effect of DM on c-jun mRNA level in the cortex of PTZ-injected PND 60 rat.

(A) 2 hr after injection of PTZ. (B) 24hr after injection of PTZ. Each value is normalized to the value of P. P: the rats injected PTZ D10: the rats injected with PTZ and 10 mg/kg of DM. D30: the rats injected with PTZ and 30 mg/kg of DM. D50: the rats injected with PTZ and 50 mg/kg of DM.

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