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# Pallidal administrations of gabazine and 5-AVA affect pressure-induced behavioral disorders in rats

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**Abstract**

The aim of this work was to study the role of pallidal GABAa and GABAb neurotransmission in the behavioral disorders induced by pressure. The effects of GABAb antagonist 5-aminovalleric acid (5-AVA) or GABAa antagonist gabazine administrations in the globus pallidus (GP) on locomotor and motor hyperactivity (LMA) and myoclonia expressions in the model of the rat submitted to 8 MPa of helium–oxygen breathing mixture were analyzed. The administration of GABAa antagonist gabazine enhances the occurrence of the epileptic seizures, slightly increases LMA but decreases myoclonia. In contrast, the administration of GABAb antagonist 5-AVA decreases both LMA and myoclonia during the compression and the beginning of the holding time at 8 MPa. These data indicate that some behavioral disorders induced by pressure are in relation with GABAergic neurotransmission and establish clearly that GABAa and GABAb receptor mediations have distinct functions in the GP of the rat. 

*Keywords:* LMA; Myoclonia; Basal ganglia; GABAa; GABAb; Amino acids; HPNS; Helium; Neurotransmitters

## 1. Introduction

The High-Pressure Neurological Syndrome (HPNS) is a term applied to a set of symptoms, which appears when mammals, including man, are exposed to high pressure of helium–oxygen ($He-O_2$) breathing mixture. The principal symptoms consist of electrophysiological disturbances and behavioral disorders. In the rat, behavioral disorders include tremor, locomotor and motor hyperactivities (LMA), myoclonia and, when pressure exceeds 9 MPa, epileptic seizures. These behavioral disorders are related in part to central neurotransmission changes (for review, see Rostain, 1993).

Pharmacological studies have established that glutamatergic (Meldrum et al., 1983; Wardley-Smith and Meldrum, 1984; Wardley Smith and Wann, 1989), GABAergic (Bichard and Little, 1982; Rostain et al., 1986) and dopaminergic (Abraini and Rostain, 1991) neurotransmission changes at central level are involved in some behavioral disorders induced by pressure. Numerous studies in vivo have clearly established that the occurrence of several motor disorders involves neurotransmission changes in the basal ganglia circuitry, especially in the striatum (Abraini et al., 1991; Requin and Risso, 1992; Darbin et al., 1997a,b, 1999, 2000, 2001), the globus pallidus (GP; Darbin et al., 2000), the entopedoncular nucleus (Millan et al., 1989), the substantia nigra (Millan et al., 1989) and the thalamus (Millan et al., 1990).

Recently, we reported that LMA development, but not myoclonia expression, requires both striatal dopaminergic and NMDA receptor activities in the rat (Darbin et al. 1999). In fact, both dopaminergic (D1 or D2) and NMDA antagonists have protective effects against LMA when drug administrations take place in this input structure of basal ganglia. This finding, in agreement with previous works performed at normal pressure (Hu and White, 1997), suggests that pressure could enhance the permissive effects of dopamine on excitatory amino acid neurotransmission (Darbin et al., 1999). This set of evidences, showing that pressure affects the interactions between dopaminergic and glutamatergic neurotransmissions at striatal level, suggests also that striatal output pathway activities should be affected.

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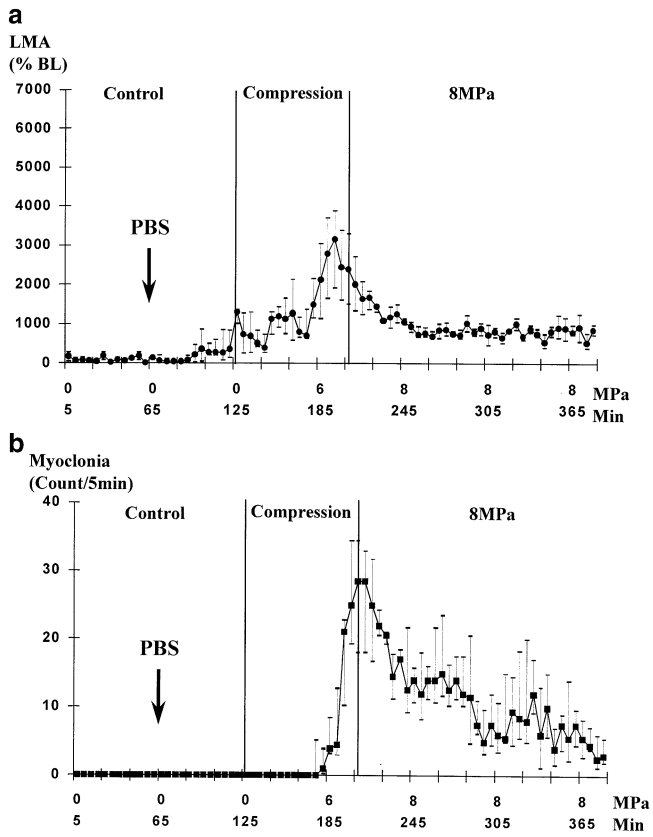


Fig. 1. LMA (a) and myoclonia (b) developments in control rats during pressure exposure. Represented on each graphic: (1) Left: basal value recorded at atmospheric conditions during 1 h before and after PBS or drug administration. (2) Middle: compression up to 8 MPa; duration 80 min. (3) Right: isobaric condition at 8 MPa; duration 3 h. *X*-axis: pressure expressed in MPa and time expressed in min. (a) LMA development in rats pretreated by PBS ($n=6$). *Y*-axis: LMA level expressed as a percentage from a 1-h control period taken as 100% value; median value and 25–75th percentiles. (b) Myoclonia development in rats pretreated by PBS ($n=6$). *Y*-axis: Myoclonia expressed in count/5 min; median value and 25–75th percentiles.

The major populations of efferent striatal neurons project principally to the substantia nigra and the GP, using GABA as a neurotransmitter (for review, see Gerfen, 1999). The fact that pressure enhances the striatal NMDA neurotransmission suggests that pallidal GABAergic neurotransmission may be enhanced by pressure. To date, the contribution of pallidal GABAergic neurotransmission remains unknown. The aim of this work was to study the role of pallidal GABAa and GABAb neurotransmission in the behavioral disorders induced by pressure.

This study reports the effects of pallidal administration of gabazine (a selective GABAa antagonist; Seutin et al., 1997) or 5-aminovalleric acid (5-AVA; a GABAa/GABAb antagonist; Luzzi et al., 1985) on LMA and myoclonia expressions in the model of the rat submitted to a relative pressure of 8 MPa (80 atm) of helium–oxygen breathing mixture.

## 2. Material and methods

### 2.1. Drugs

Gabazine and 5-AVA were obtained from RBI (Illkirch-France). All solutions were prepared daily in PBS.

### 2.2. Animals and surgery

All procedures and experiments involving animals in this study were approved by the local animal research authority and conducted according to the European convention of the protection of vertebrates used for scientific purposes. Subjects consisted of male Sprague–Dawley rats (IFFA-

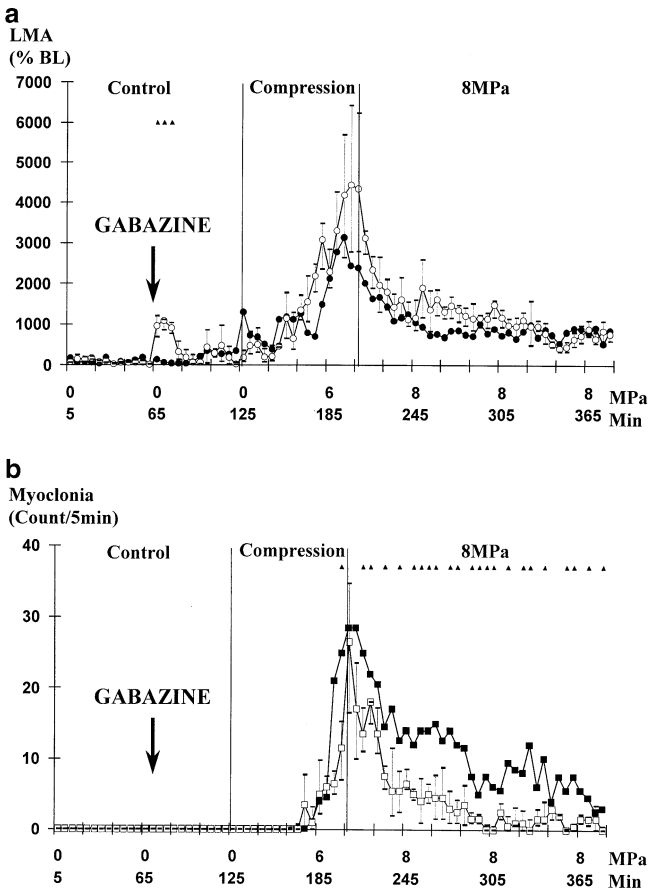


Fig. 2. Effects of gabazine (0.5 nmol/side) injection into the GP on the LMA and myoclonia developments. Represented on each graphic: (1) Left: basal value recorded at atmospheric conditions during 1 h before and after PBS or drug administration. (2) Middle: compression up to 8 MPa; duration 80 min. (3) Right: isobaric condition at 8 MPa; duration 3 h. *X*-axis: pressure expressed in MPa and time expressed in min. (* $P<.05$, control rats vs. treated rats). (a) LMA development in rats pretreated by gabazine ($n=4$) into the GP. *Y*-axis: LMA level expressed as a percentage from a 1-h control period taken as 100% value; median value and 25–75th percentiles [for the sake of comparison, Fig. 1a is redrawn on (a)]. (b) Myoclonia development in rats pretreated by gabazine ($n=4$) in the GP. *Y*-axis: Myoclonia expressed in count/5 min; median value and 25–75th percentiles [for the sake of comparison, Fig. 1b is redrawn on (b)].

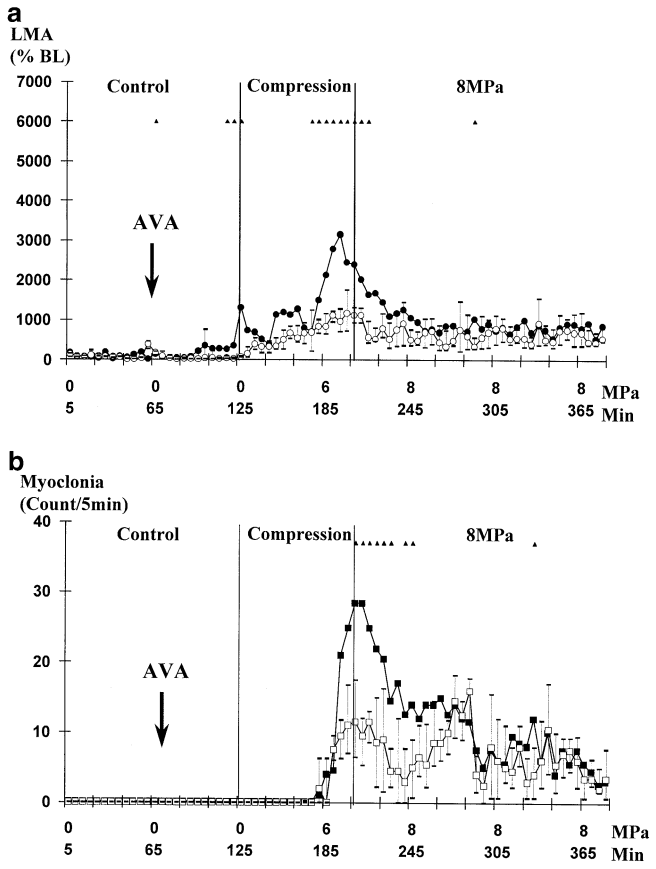


Fig. 3. Effects of AVA (10 nmol/side) injection into the GP on the LMA and myoclonia developments. Represented on each graphic: (1) Left: basal value recorded at atmospheric conditions during 1 h before and after PBS or drug administration. (2) Middle: compression up to 8 MPa; duration 80 min. (3) Right: isobaric condition at 8 MPa; duration 3 h. *X*-axis: pressure expressed in MPa and time expressed in min. (* $P<.05$, control rats vs. treated rats). (a) LMA development in rats pretreated by AVA ($n=4$) into the GP. *Y*-axis: LMA level expressed as a percentage from a 1-h control period taken as 100% value; median value and 25–75th percentiles [for the sake of comparison, Fig. 1a is redrawn on (a)]. (b) Myoclonia development in rats pretreated by AVA ($n=4$) in the GP. *Y*-axis: Myoclonia expressed in count/5 min; median value and 25–75th percentiles [for the sake of comparison, Fig. 1b is redrawn on (b)].

CREDO-France) weighing 280–320 g. The rats were housed at 21±0.5 °C in individual home cages under a 12–12 h light/dark cycle (lights on from 07:00 to 19:00 h) with free access to food and water. At least 2 weeks prior to the experiments, rats were anaesthetized with sodium pentobarbital (60 mg/kg ip). Then, intracerebral guides were stereotaxically implanted in the left and the right GP (A: 6.67, L: 2.40, H: −0.5; according to the atlas of König and Klippel, 1967) and fixed with dental cement (Ivoclar Resin Cement, Liechtenstein) on the skull surface.

### 2.3. Behavioral analysis

Briefly, the behavioral device is based on an analysis of signals obtained from a piezoelectrical sensor located under the floor of the cage. The signal generated by the sensor, when the rat developed LMA, was analyzed by the Fast Fourier Transform (FFT) as described by Darbin et al. (1997a). Spectral data were collected during a 5-min period, and the mean of each unit frequency was recorded and expressed in percent of the atmospheric basal value. The values of 1–35-Hz band frequency as a function of time were represented by a 3D shaded surface graph. Band frequency associated to tremor or LMA were graphically determined on the map and integrated (Darbin et al., 1997a). Myoclonia are expressed in counts/5 min.

### 2.4. Pressure exposure

Free-moving animals were placed in a cylindrical cage equipped with a piezoelectrical sensor. This cage was placed in a 30-l pressure chamber. Three hours later, the basal values were monitored during 60 min. The dummy of the guides was removed, and the injection cannula was inserted into the GP. One microliter of solution (PBS, gabazine 0.5 nmol or 5-AVA 10 nmol) was injected into the right and the left structures at a rate of 0.5 μl/min. The behavioral activities of the animals were recorded during 60 min after drug injection. Then, the compression was started. The partial pressure of oxygen was increased to 0.04 MPa, which is the partial pressure commonly used in pressure experiments, and the rats were compressed up to 8 MPa (1 MPa=10 atm or 10 bars) with helium at a rate of 0.1 MPa/min during 80 min. Simultaneously, the temperature was slowly increased from 25 °C at atmospheric conditions to 33 °C at 8 MPa to maintain thermal comfort in a helium–oxygen environment. Animals were maintained at 8 MPa for 4 h. Following the experiment, they were decompressed at a rate of 0.006 MPa/min from 8 to 1.2 MPa and at a rate of 0.004 MPa from 1.2 MPa to atmospheric pressure.

### 2.5. Statistics

Data are expressed using median value and the 25–75th percentiles. Statistical comparisons between groups were performed using a Kruskal–Wallis analysis of variance by ranks, and the Mann–Whitney *U*-test was used for pairwise comparison (Siegel and Castellan, 1989).

## 3. Results

### 3.1. Drug effects at normal pressure

The administration of 0.5 nmol/slide of gabazine induced a transient increase of the LMA ($U=6.88$, $df=1$, $P<.01$; Fig. 1a). At higher doses (>50 nmol/slide), epileptic seizures occur a few minutes after administration (data not shown). In contrast, the administration of 10 nmol/slides of 5-AVA reduced the spontaneous activities ($U=15.00$, $df=1$, $P<.01$).

### 3.2. Drugs effects during pressure exposure

All control subjects have expressed LMA (Fig. 1a) and myoclonia (Fig. 1b) during pressure exposure. None of this control group has developed convulsive seizure.

The intrapallidal gabazine administration (0.5 nmol/slide) was without effects on LMA development during compression ($U=0.081$, $df=1$, $P>.1$) but tend to increase this behavioral disorder during the holding time at 8 MPa ($U=18.82$, $df=1$, $P<.01$) despite a lack of significant pairwise comparison during this last phase (Fig. 2a). This treatment slightly reduced the myoclonia expression ($U=43.76$, $df=1$, $P<.01$) (Fig. 2b). Nevertheless, three of the four animals developed short-latency epileptic seizures at the end of the compression (pressure >7 MPa) and during the first hour of the holding time at 8 MPa.

In contrast, the intrapallidal 5-AVA administration (10 nmol/slide) reduced both the LMA ($U=14.82$, $df=1$, $P<.01$; Fig. 3a) and the myoclonia ($U=87.42$, $df=1$, $P<.01$; Fig. 3b) during compression. No epileptic seizure was observed in the 5-AVA-pretreated groups.

## 4. Discussion

Our data established that, at pressure, the administration of GABAa antagonist gabazine enhanced the occurrence of epileptic seizures, slightly increased LMA but decreased myoclonia. In contrast, the administration of GABAb antagonist 5-AVA decreased both LMA and myoclonia during the compression and the beginning of the holding time at 8 MPa, and no epileptic seizure was observed. These data confirm the participation of the GP in the development of LMA and myoclonia at pressure. They indicate also that this structure can modulate the convulsive seizure occurrences evoked by pressure. Consequently, our data report that GABAa and GABAb neurotransmission have different roles in the severity of behavioral disorders induced by pressure in rats.

At normal pressure, several studies have reported the participation of GP in seizures. Marked metabolic activation was seen at the GP level in a rat model of self-sustaining status epilepticus (SSSE; Pereira de Vasconcelos et al., 1999) or in models of cholinergic convulsions (Scremin et al., 1998). Additionally, it is noted that GP lesion exerts a pronounced antiepileptic effect on the development of the neocortical epileptic activity complexes. In contrast, the GP stimulation has been reported to enhance the neocortex interictal seizure activity (Makulkin et al., 1992). Our data report that a higher dose of gabazine (50 nmol) evoked epileptic seizures at normal pressure. These convulsions are probably in relation to a sustained increase of GP activity as previously described by Makulkin et al. (1992). The fact that pallidal administration of gabazine, at lower doses, which did not induce convulsion at normal pressure, decreased the threshold of pressure-evoked convulsion suggests that pressure may disrupt the GABAa neurotransmission in the GP of rats. This finding is in agreement with previous studies performed at pressure, supporting the view that the enhancement of GABAa neurotransmission decreases the severity of the HPNS in mice (Bichard and Little, 1982) and in rats (Rostain et al., 1986). They also suggest that the GP is probably involved, at least in part, in the protective effects of GABAa antagonist against pressure-evoked convulsion. However, at normal pressure, recent data have suggested that the disruption of GABAa receptor activity at several levels in the neural axis can produce myoclonus (Matsumoto et al., 2000). These results may partially explain the origin of the myoclonia at pressure, which have been reported to relate to an excitability increase in the GP (Darbin et al., 2000). In this view, the fact that pallidal gabazine administration decreased myoclonia at the end of compression and during the holding time at 8 MPa is unlikely a direct consequence of GABAa receptor blockage but more probably a consequence of the premature convulsion occurrences.

Little is known about the effect of pressure on GABA receptors. In vitro, pressure has been reported to be without effect on GABA response in cervical ganglion and on the potentiation of the GABA caused by pentobarbitone (Little and Thomas, 1986). These data support the view that GABAa neurotransmission disruption at pressure may not be related to a direct effect of pressure on the GABAa receptor. Interestingly, ketamine (a NMDA antagonist) has been reported to reduce GABA response of cervical ganglion at normal condition and at pressure (Little, 1982), supporting the view that pressure does not alter NMDA–GABAa interaction. NMDA hyperactivity has been demonstrated in vitro, in mammalian excitatory receptors expressed in *Xenopus* oocytes (Daniels et al., 1991) and in rat hippocampal slices (Zinebi et al., 1991) exposed to pressure and has been suggested in vivo (Darbin et al., 1999, 2000, 2001). Consequently, it is reasonable to suggest that GABAa neurotransmission disruption in the GP could be in relation to the pallidal NMDA hyperactivity (Darbin et al., 2000).

In contrast to gabazine, 5-AVA administration (GABAa/GABAb antagonist) (Luzzi et al., 1985) reduced the severity of the HPNS in rats. Since gabazine was found to enhance the effects of pressure, the protective effects of 5-AVA can be related to its binding on GABAb receptors in the extern GP. In the primate, Charara et al. (2000) reported that most GABAb-containing terminals (as well GP intern and substantia nigra pars reticulata) displayed the ultrastructural features of glutamatergic buttons. In agreement with these observations, the application of baclofen was found to decrease the efflux of glutamate in the rat GP in vivo (Singh, 1990). Consequently, the protective effects of 5-AVA against the behavioral disorders induced by pressure are probably related, at least in part, to the enhancement of glutamate efflux in this

structure through GABAb presynaptic heteroreceptors. The fact that pressure-induced LMA and myoclonia are decreased by pallidal inhibition of glutamate uptake (Abraini et al., 1999) reinforces this hypothesis. Nevertheless, NMDA neurotransmission is probably not involved in these protective effects since pallidal NMDA antagonist administration reduces the severity of the HPNS (Darbin et al., 2000).

However, evidences for dendritic GABAb receptors have been reported in the rat GP (Stefani et al., 1999) and in the GP extern of the primate (Charara et al., 2000). Electrophysiological studies also have reported that GABAb receptors mediate an inhibition of calcium current in a subset of pallidal neurons (Stefani et al., 1999). Therefore, it is reasonable to suggest that protective effects of pallidal 5-AVA administration against HPNS may be linked, at least in part, to a decrease of GABA-evoked inhibition through postsynaptic GABAb receptors located on dendrites of this subset pallidal output neurons. Pharmacological and anatomical characterizations of this subset pallidal output neurons appear to be required to increase our knowledge of pallidal GABAb neurotransmission functions.

The hypothesis that higher pressure induces a disruption of GABAa neurotransmission remains to be established more directly (i.e. patch clamp) but could partially explain previous data obtained on NMDA neurotransmission. The GABAa neurotransmission is believed to control the spreading of excitability (Avoli, 1996). In this view, the putative disruption of GABAa neurotransmission at pressure may facilitate the spreading of excitability along the cortico-cortical pathways and explain that NMDA antagonists have protective effects against HPNS at every level in the basal ganglia (e.g. striatum, GP, entopedoncular nucleus, substantia nigra or thalamus; Millan et al., 1989, 1990; Darbin et al., 1999), especially in the GP (Darbin et al., 2000). Despite a lack of information on the magnitude of excitation mediated by 5-AVA, we believe that protective effects of this GABAb antagonist may be related to a moderate increase in the activity of inhibitory output pathways of the GP. Some increases of GABA release into the output structures of the GP (i.e. SN and thalamus) may also decrease the spread of excitability into the cortico-cortical loop. Nevertheless, the paradoxal effects of GABAa and GABAb at pressure remain to be clarified by further electrophysiological studies.

In conclusion, our data report that pallidal GABAa and GABAb neurotransmission have opposing effects on HPNS in rats. They also suggest that a disruption of GABAa neurotransmission may enhance the spread of pressure-evoked excitability along the cortico-cortical pathways. Further experiments are required to better understand the role of the GP in the spread of excitability in cortico-cortical pathways at pressure and its involvement in the behavioral components of HPNS.

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## References

Abraini JH, Rostain JC. Pressure-induced striatal dopamine release correlates hyperlocomotor activity in rats exposed to high pressure. J Appl Physiol 1991;71:638–643.

Abraini JH, Tomei C, Rostain JC. Role of dopamine receptors in the occurrence of behavioral motor disturbances in rats exposed to high pressure. Pharmacol Biochem Behav 1991;39:773–779.

Abraini JH, Kriem B, Rostain JC. Administration of the glutamate uptake inhibitor L-*trans*-PDC in the globus pallidus and the substantia nigra, but not in the striatum, attenuates the psychostimulant effect of high helium pressure on locomotor activity in the rat. Neurosci Res 1999;35:273–279.

Avoli M. GABA-mediated synchronous potentials and seizure generation. Epilepsia 1996;37:1035–1042.

Bichard AR, Little HJ. Drugs that increase gamma-aminobutyric acid transmission protect against the High Pressure Neurological Syndrome. Br J Pharmacol 1982;76:447–452.

Charara A, Heilman TC, Levey AI, Smith Y. Pre- and postsynaptic localization of GABA(B) receptors in the basal ganglia in monkeys. Neuroscience 2000;95:127–140.

Daniels S, Zhao DM, Inman N, Price DJ, Shelton CJ, Smith EB. Effects of general anesthetics and pressure on mammalian excitatory receptors expressed in *Xenopus* oocytes. Ann NY Acad Sci 1991;625:108–115.

Darbin O, Risso JJ, Rostain JC. A new system analysis of motor and locomotor activities associated with a microdialysis study of pressure-induced dopamine increase in rats. Physiol Behav 1997a;62:367–371.

Darbin O, Risso JJ, Rostain JC. Pressure induces striatal serotonin and dopamine increases: a simultaneous analysis in free-moving microdialysed rats. Neurosci Lett 1997b;238:69–72.

Darbin O, Risso JJ, Rostain JC. The full expression of locomotor and motor hyperactivities induced by pressure requires both striatal dopaminergic and *N*-methyl-D-aspartate receptor activities in the rat. Neurosci Lett 1999;267:149–152.

Darbin O, Risso JJ, Rostain JC. High pressure enhanced NMDA activity in the striatum and the globus pallidus: relationships with myoclonia and locomotor and motor activity in rat. Brain Res 2000;852:62–67.

Darbin O, Risso JJ, Rostain JC. High pressure induced striatal glutamate increase: a microdialysis study in free-moving rat. Neurosci Lett 2001;297:37–40.

Gerfen CR. The neostriatal mosaic: multiple levels of compartmental organization in the basal ganglia. Annu Rev Neurosci 1999;15:285–320.

Hu XT, White FJ. Dopamine enhances glutamate-induced excitation of rat striatal neurons by cooperative activation of D1 and D2 class receptors. Neurosci Lett 1997;224:61–65.

König JFR, Klippel R. The rat brain: a stereotaxic atlas. Krieger, NY: Krieger, 1967.

Little HJ. Effects of ketamine and of high pressure on the responses to gamma-aminobutyric acid of the rat superior cervical ganglion in vitro. Br J Pharmacol 1982;77:209–216.

Little HJ, Thomas DL. The effects of anaesthetics and high pressure on the responses of the rat superior cervical ganglion in vitro. J Physiol 1986;374:387–399.

Luzzi S, Maggi CA, Spagnesi S, Santicioli P, Zilletti L. 5-Aminovaleric acid interactions with GABAA and GABAB receptors in guinea-pig ileum. J Auton Pharmacol 1985;5:65–69.

Makulkin RF, Novytskyi SA, Korniienko TV. Role of globus pallidus in mechanisms of antiepileptic caudate-cortical effects. Fiziol Zh 1992;38: 3–9.

Matsumoto RR, Truong DD, Nguyen KD, Dang AT, Hoang TT, Vo PQ, Sandroni P. Involvement of GABA(A) receptors in myoclonus. Mov Disord 2000;15(Suppl 1):47–52.

Meldrum BS, Wardley-Smith B, Halsey MJ, Rostain JC. 2-Amino-phosphoheptanoic acid protects against the high pressure neurological syndrome. Eur J Pharmacol 1983;87:501–502.

Millan MH, Wardley-Smith B, Halsey MJ, Meldrum BS. Studies on the role of NMDA receptor in the substantia nigra pars reticulata and entopeduncular nucleus in the development of the high pressure neurological syndrome in rats. Exp Brain Res 1989;78:174–178.

Millan MH, Wardley-Smith B, Halsey MJ, Meldrum BS. Effect of NMDA and 2-amino-7-phosphonoheptanoate focal injection into the ventrolateral thalamic nucleus on the high pressure neurological syndrome in the rat. Brain Res 1990;507:354–356.

Pereira de Vasconcelos A, Mazarati AM, Wasterlain CG, Nehlig A. Self-sustaining status epilepticus after a brief electrical stimulation of the perforant path: a 2-deoxyglucose study. Brain Res 1999;838: 110–118.

Requin M, Risso JJ. Effects of high pressure on striatal dopamine release in freely-moving rats: a microdialysis study. Neurosci Lett 1992;146: 211–214.

Rostain JC. The nervous system: man and laboratory mammals. In: Macdonald AG, editor. Advance in comparative and environmental physiology: effects of high pressure on biological systems, vol. 17. Berlin: Springer-Verlag, 1993. pp. 197–238.

Rostain JC, Wardley-Smith B, Forni C, Halsey MJ. Gamma aminobutyric acid and the high pressure neurological syndrome. Neuropharmacology 1986;25:545–554.

Scremin OU, Shih TM, Li MG, Jenden DJ. Mapping of cerebral metabolic activation in three models of cholinergic convulsions. Brain Res Bull 1998;45:167–174.

Seutin V, Scuvee-Moreau J, Dresse A. Evidence for a non-GABAergic action of quaternary salts of bicuculline on dopaminergic neurones. Neuropharmacology 1997;36:1653–1657.

Siegel S, Castellan NJ. Non parametric statistics for the behavioral science. New York: McGraw-Hill, 1989 (399 pp.).

Singh R. GABAb receptors modulate glutamate release in the rat caudate and globus pallidus. Soc Neurosci Abstr 1990;16:1041.

Stefani A, Spadoni F, Giacomini P, Lavaroni F, Bernardi G. The modulation of calcium current by GABA metabotropic receptors in a sub-population of pallidal neurons. Eur J Neurosci 1999;11:3995–4005.

Wardley-Smith B, Meldrum BS. Effect of excitatory amino acid antagonists on the high pressure neurological syndrome in rats. Eur J Pharmacol 1984;105:351–354.

Wardley-Smith B, Wann KT. The effects of non-competitive NMDA receptor antagonists on rats exposed to hyperbaric pressure. Eur J Pharmacol 1989;168:107–112.

Zinebi F, Fagni L, Hugon M. Excitatory and inhibitory amino acids involved in the high pressure nervous syndrome: epileptic activity and hyperexcitability. Amino Acids 1991;1:47–56.