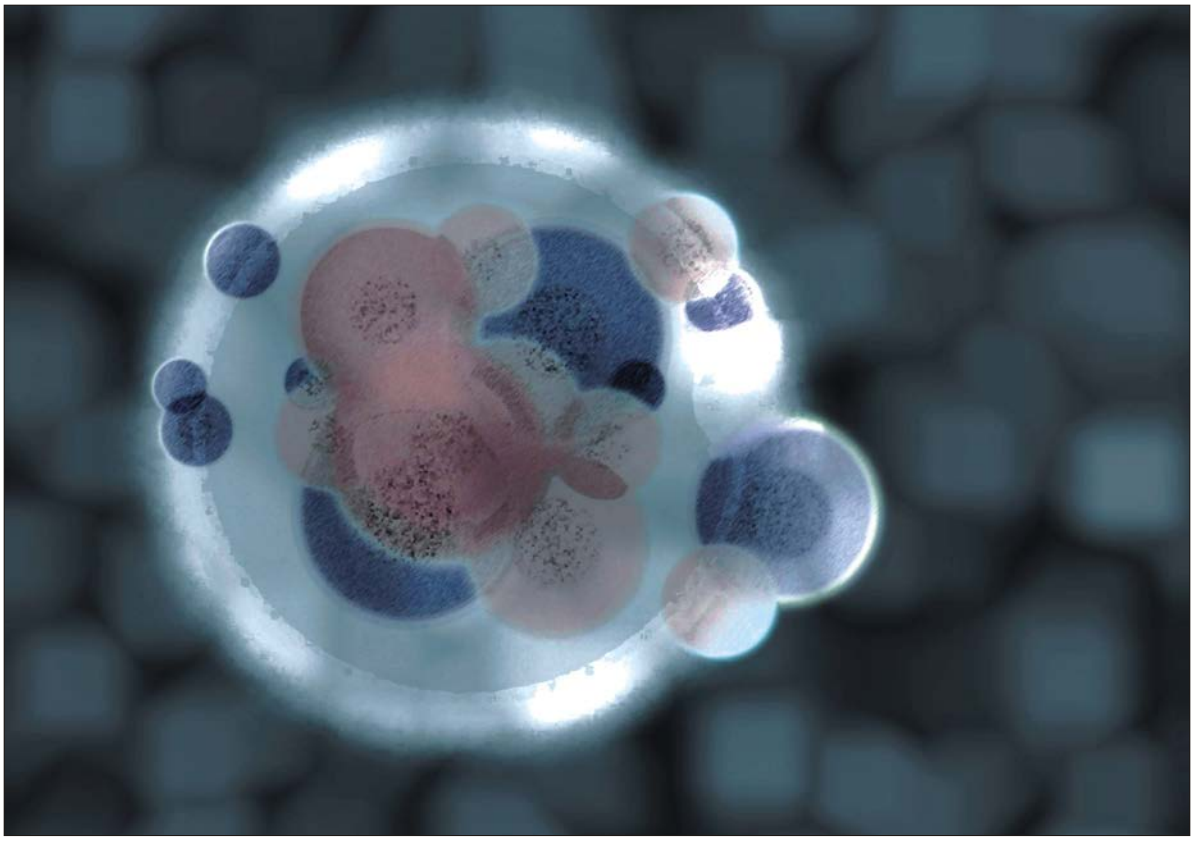

Journal of Biological Sciences

ISSN 1727-3048

science alert

ANSInet
an open access publisher
http://ansinet.com

Journal of Biological Sciences 10 (8): 773-778, 2010
ISSN 1727-3048

Perinatal Exposure to Weak Magnetic Fields Delays the Asymmetry Ontogeny of Astroglia in the Parasolitary Nucleus: Implications for Sudden Infant Death

J. Hu, G.H. Parker and M.A. Persinger
Behavioural Neuroscience Laboratory,
Department of Biology, Laurentian University, Sudbury, Ontario P3E 2C6, Canada

Abstract: The aim of the study was to discern if Sudden Infant Death Syndrome (SIDS) reflects a transient vulnerability to stimuli during anomalous ontogeny of normal cellular interaction within brain stem structures such as the parasolitary (Psol) nucleus. Perinatal exposure equivalent to the strength and frequency of a magnetic field configuration correlated with SIDS was utilized to produce alterations in cellular asymmetry within the Psol nucleus. The numbers of neurons and nuclei of astroglia and oligodendroglia from n = 40, 5 and 15 day old rats that had been exposed to a 0.5 Hz, 5 to 10 nT magnetic field between -3 to +7 days of birth and were counted at 1000 X. A robust and significant interaction (explaining 30% of the variance) between numbers of astroglia nuclei in the right vs. the left side of the nucleus, age and exposure to the field was demonstrated. These results indicate exposure to this specific intensity and frequency may delay the normal ontogeny of asymmetry-to-symmetry in cell numbers that affect the blood brain barrier and neuronal function. Greater attention to neuroaxial asymmetry in post-mortem measures of SIDS cases may be warranted.

Key words: SIDS, astroglia numbers, ELF magnetic fields, brain stem

INTRODUCTION

The sudden mortality of human infants Sudden Infant Death Syndrome (SIDS), between the ages of 2 and 6 months (Waters *et al*., 1999; Moon *et al*., 2007) suggests a transient period of vulnerability coupled to ontogeny. The level of the solitary nucleus is one of the most frequent brain stem areas for which changes in measures of neuronal, glial, or receptor subtypes have been found (Kawai and Senba, 2000; Sawaguchi *et al*., 2003). Patterns of synaptic currents involved with respiratory neurons in this area are not stable but change during early postnatal life (Zec and Kinney, 2003). We have been pursuing the hypothesis that disruptions by subtle environmental stimuli of the normal ontogeny of structural asymmetry (and consequently function) within the brain stem nuclei may contribute to neuroelectrical transients and sporadic autonomic crisis. Transgenic mice with reversible but excessive serotonin autoinhibition within the brain stem have been recently shown (Audero *et al*., 2008) to display sporadic bradycardia that frequently progressed to death.

Geomagnetic activity has been considered both a predisposing and precipitating factor for SIDS (Eckert, 1992). Daily and monthly levels of global geomagnetic activity and the numbers of cases of SIDs are moderately and positively correlated (O'Connor and Persinger, 1997, 1999; Persinger and O'Connor, 2001). The primary association involves numbers of days with specific bands of variation in geomagnetic intensities around 1 to about 10 nT. Experiments by Dupont *et al*. (2005) demonstrated fewer live births (M = 14.1, SD = 2.1) in rats exposed for two days before birth to 0.5 Hz, 5 to 10 nT magnetic fields compared to sham-field controls (M = 16.2, SD = 2.7). The proportions of death were actually greater than for rats exposed to 500 nT fields of the same frequency. In other studies (Dupont *et al*., 2004) brains of 21 day old rats exposed perinatally for 3 days before to 7 days after birth to a variable range of 0.5 Hz intensities between 4 and 13 nT showed fewer neurons within the parasolitary (Psol) nucleus.

In the present study we selected this low intensity (5 to 10 nT) and frequency (0.5 Hz) as primary parameters because of their frequent presence on days in which SIDS occur (O'Connor and Persinger, 1997, 1999). In addition 0.5 Hz is within the range of stimulation rates that evoke reliable volleys in brain stem neurons involved with vestibular, respiratory and cardiovascular responses (Barmack and Yahknitsa, 2000) and with a specific prediction from a theoretical model involving proton

Corresponding Author: Dr. M.A. Persinger, Behavioural Neuroscience Laboratory, Department of Biology, Laurentian University, 935 Ramsey Lake Road, Sudbury ON, P3E 2C6, Canada
Tel: 705-675-4824 Fax: 705-671-3844

resonance (Persinger, 2006). Weak, extremely low frequency magnetic fields can interact with unstable states (Whissell and Persinger, 2007a) and interact with Nitric Oxide (NO) functions (Whissell and Persinger, 2007b). Persinger *et al.* (2005) had shown that 50 nT but neither weaker (10 nT) nor stronger (500 nT) experimentally generated 7 Hz magnetic fields whose amplitudes were continuously increased and decreased in 14 steps every 6 min (0.3 mHz) increased sudden cardiac death in adult rats during the first 24 h following induction of epileptic seizures.

Recently, St-Pierre *et al.* (2007) reported a doubling of mortality following inductions of epileptic seizures in 21 to 25 day old (weanling) rats if they had been exposed perinatally to a 5 nT, 7 Hz magnetic field. The mortality of rats that had been exposed to different windows of strengths below or above (up to 500 nT) this narrow window did not differ from controls. We report here that perinatal exposure to 0.5 Hz, 5 to 10 nT magnetic fields produced a specific delay in the asymmetry of astroglia but not oligodendroglia or neurons within the Psol nucleus. It was selected, of the many possible regions that have been shown to display pathophysiology, because of its proximity to and sometimes interposition with the solitary nucleus with which it shares and receives projections (Barmack *et al.*, 1998).

MATERIALS AND METHODS

Animals: A total of 40 male and female albino Wistar rats that had been born in the laboratory within the various experimental conditions served as subjects. All procedures were completed in 2006 under approved research protocols at the Paul Field Animal Care Facility at Laurentian University, Sudbury, ON, Canada.

Procedure: In four separate blocks of experiments over a one year period a total of 20 Wistar pregnant females were exposed singly in plastic cages approximately two to three days before expected birth (as inferred by sperm plugs) to seven days after birth to a coil in which a 5 to 10 nT, 0.5 Hz sine wave magnetic field was generated or to an orthogonally-oriented, non-activated coil in the same room. We selected the sine-wave rather than square-wave option because of the similar morphology to Pc1 (continuous pulsations) generated during specific conditions within the geomagnetic field. Characteristics of the coil have been published elsewhere (McKay *et al.*, 2003; Dupont *et al.*, 2005; St-Pierre *et al.*, 2007). The light:dark cycle was 12:12 with the onset of light at 08:00 h. Temperature was maintained within 1 deg of 21°C.

The field was generated in the E-W direction for two blocks of experiments and in the N-S direction for two blocks. The activated coil (and hence orientation) was alternated with each block. A MEDA FM-300 Vector magnetometer placed in the coil and coupled to a laptop computer maintained a continuous record of the normal geomagnetic (background) and experimental fields. During the period between 3 days before birth to 7 days after birth the experimental field was discontinued for 30 min once every 4 h (hence 21 h of field exposure per day) because we have found that 30 min of no field following protracted presentations can be as effective as 30 min of field presentation in adults for producing analgesic effects (Martin *et al.*, 2004). Similar observations have been found for analgesia (Prato *et al.*, 2005) in adult mice. The induced field within the perpendicular coil employed as a reference in any given block was not detectable by instrumentation (less than 1 nT).

On postnatal days 5 and 15 (8 days after the termination of the field exposures) one pup from each litter was randomly selected. The brain was removed within four min and fixed in ethanol-formalin-acetic acid (Persinger, 1983). After processing and paraffin embedding 10 μm coronal sections were obtained from the medulla at the level of the easily identifiable Psol nucleus. The sections were stained with toluidine blue O. The numbers of neurons and nuclei of astroglia and oligodendroglia were counted at 1000 X within a 0.1 mm by 0.1 mm grid (containing 6×6 smaller squares) that was focused at the center of the Psol nucleus for two non-consecutive slides for the left and right side of the brainstem. The cytometrist was blind to the experimental conditions of the rats.

Statistical analysis: Four way analyses of variance with three between subject levels: treatment (sham field vs. 5 to 10 nT), gender (male vs. female), age (5 vs. 15 days) and one within subject measure (left vs. right parasolitary nucleus) were completed for each of the cell types. Post hoc analyses involved combinations of paired t-tests and Tukey's set at $p<0.05$. All analyses involved SPSS software on a VAX 4000 computer.

RESULTS

There were no statistically significant differences between treatments (all Fs = 1,30) for the numbers of neurons except for the significantly greater density within the 5 day old pups compared to the 15 day old pups ($F(1,30) = 7.09$, $p = 0.01$; 19% of variance explained). The means and standard deviations for the numbers of neurons 0.01 mm^{-2} of the two ages were 28.5 and 5.1 and

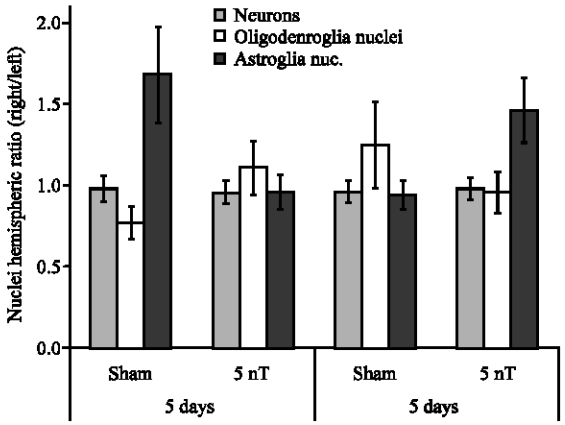

Fig. 1: Right/Left Side Ratios of Numbers of neurons, nuclei of oligodendroglia and nuclei of astroglia in rats that had been exposed to either the 5 to 10 nT, 0.5 Hz magnetic field or reference setting at 5 days (8 days of field exposure) or 15 days (8 days after termination of field exposure) of age. Vertical bars indicate standard errors of the mean

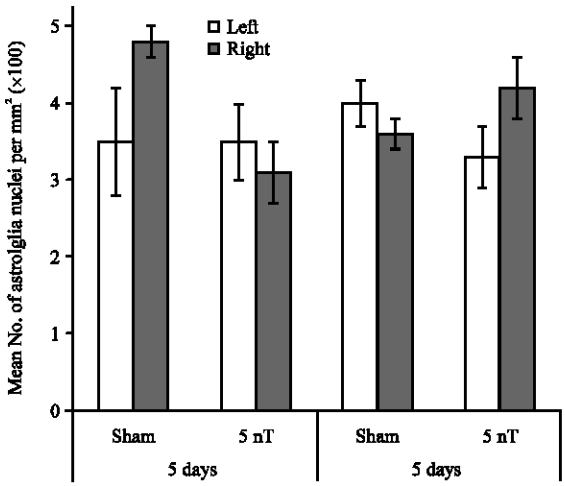

Fig. 2: Mean numbers of nuclei of astroglia per mm^2 (×100) within the left and right parasolitary nucleus of rats exposed to either a 5 to 10 nT, 0.5 Hz field or reference condition at 5 days (8 days of field exposure) or 15 days (8 days after termination of field exposure) of age. Vertical bars indicate standard errors of the mean

25.6 and 5.4, respectively. None of the within subject (left vs. right side) and between subject interactions were statistically significant. There were also no statistically significant effects for the differences between groups or the two-way interactions for the numbers of nuclei of oligodendroglia or astroglia.

However, there was a strong statistically significant interaction ($F(1,30) = 9.91$, $p<0.01$; 25% of variance explained) between exposure to the magnetic field, age of the brain (5 vs. 15 days) and the numbers of astroglia within the left and right Psol nuclei. Post hoc analyses, as shown in Fig. 1, indicated that the primary source of this interaction was due to the elimination of the asymmetry in the numbers of astroglia between the right and left sides of the Psol nuclei in the rats exposed to the magnetic field compared to controls at 5 days of age (after 8 days of continuous exposure to this field configuration). However by the time the rats were 15 days of age (8 days after the termination of the field), the rats that had been exposed demonstrated the right-sided increase of astroglia cells whereas the controls showed equal numbers.

The effect was still evident when the measures were expressed as right side/left side ratios for numbers of astroglia nuclei within the nucleus. This statistically significant interaction between age and treatment ($F(1,30) = 10.98$, $p<0.01$) explained 30% of the variance in this ratio. After initial covariance for the ratio of neurons and nuclei of oligodendroglia in the left vs. right side of the Psol nucleus, the statistically significant interaction between treatment and age ($F(1,28) = 13.49$, $p<0.001$) remained. For comparison, the right-to-left sided ratios for neurons and nuclei for oligodendroglia and astroglia in the Psol nucleus are shown in Fig. 2. There were no statistically significant differences in asymmetry for neurons or nuclei of oligodendroglia as a function of treatment or age. The major effect involved only the astroglia.

DISCUSSION

The results of this study indicated that 8 days of exposure to 0.5 Hz, 5 nT magnetic fields during development from three days before birth to 7 days after birth in the rat did not affect the numbers of neurons within the Psol nucleus. Instead the exposure affected the ratio of astroglia cells on the right vs. left side of the structure. After about 8 days of continuous exposure to the 5 nT, 0.5 Hz magnetic field configuration the asymmetry (right side dominance) of astroglial cells displayed by the reference group was not observed. By 8 days after the termination of the exposure this asymmetry (right side dominance) was present.

We interpret this age-dependent pattern as the consequence of the delaying effect of the 5 nT, 0.5 Hz magnetic field upon normal development in this area. Our interpretation would be compatible with the conclusions of Rodriguez *et al.* (1994) who found a decrease in asymmetry of dopaminergic neurons in the midbrain

during postnatal development. On the basis of altered catecholamingeric dendritic development in SIDS cases, Takashima and Becker (1991) also suggested a delay in neuronal maturation manifested as subtle decreases in neurotransmitter interactions. One example was the alpha-2 adrenergic receptors (Ozawa *et al*., 2003). Such transient asymmetry in microstructure and function between the left and right side of the brain stem could contribute to positive feedback loops (Barmack and Yakhnitsa, 2000) from a variety of precipitating stimuli that could lead to sudden cardiac death or respiratory cessation following over stimulation of vestibular input from a number of direct and indirect afferents.

Unlike the experiment by Dupont *et al*. (2004) we did not find a significant difference in the numbers of neurons within the parasolitary nucleus. However, the brains of the rats in that study were 21 days old compared to 5 and 15 days in the present study. Although, their (Dupont *et al*., 2004) effect may be related to the additional slow amplitude-variations of their 0.5 Hz field, the reduced neuronal density may also reflect the long term consequences of disruption of the normal alterations of asymmetry in astroglial numbers. Numbers of astroglia affect neuronal density as well as synaptogenesis (Ullian *et al*., 2001). It may be relevant that more spontaneous neonatal deaths were noted as well within the nanoTesla fields of that study (Dupont *et al*., 2004) compared to much higher (microTesla) intensities.

The Psol nucleus has been described as a new vestibular nucleus located dorsal to the nucleus solitarius and tractus solitarius. Many of the structures implicated in SIDS postmortems send inputs to the Psol nucleus. It receives ipsilateral secondary vestibular afferent projections from vestibular nuclei, bilateral descending projections from the fastigial nuclei and cerebellar Purkinje cells located in the ipsilateral uvula-nodulus. It also receives input from the posterior hypothalamus (Cavdar *et al*., 2001) and serotonin-mediated vasopressor inputs from the midline medulla (Potas *et al*., 2003). Serotonergic neurons are sensitive sensors of CO_2 that maintain pH. An increase or decrease in blood concentration of a little as 100 nM of free protons can be fatal (Richerson, 2004).

Cytometric patterns characterized as active astrogliosis in the dorsal vagal and solitary nuclei have often been reported in the medulla of SIDS infants compared to controls (Sawaguchi *et al*., 2003). Recent research has shown that astrocytes are more than a passive syncytium and play a significant if not major role in information processing. For example blocking astroglial responses increased the neuronal response to stimulation in the visual cortices (St-Pierre *et al*., 2008).

Prenatal exposures to very weak (10 to 200 nT) physiologically-patterned magnetic fields produced long term changes in blood chemistry and subtle anomalies in cellular organization with the hippocampus (Schummers *et al*., 2008). Prolonged exposures to weak, physiologically-patterned magnetic fields affect NO (nitric oxide) levels (Akdag *et al*., 2007). NO reduces blood pressure in the solitary nucleus (Lin *et al*., 1999; Wu *et al*., 2002) within which there is reciprocal regulation of NO and glutamate (Lin *et al*., 2000); NO is directly (as is adenosine) involved with hypoxia induced vasodilation (Sharp and Bernaudin, 2004). Weak magnetic, time-varying, pulsed magnetic fields also affect mu opiate receptors (Thomas *et al*., 1997) which may be relevant considering the association between opiate usage in mothers and SIDS (Kinney *et al*., 1998) and the recent discovery of endomorphic neurons and mu-receptors within the Psol and solitary nuclei (Wang *et al*., 2002).

Although, the biophysical mechanism by which such weak magnetic fields could affect cellular function must still be elucidated, Persinger (2006) has suggested that proton resonance may be sensitive to specifically tuned intensities and frequencies. The reason 5 nT was selected in the present study was because of the solution from this resonance equation. The resonance frequency for a 5×10^{-9} T field influencing a charge of 1.6×10^{-19} Coulombs divided by the mass of a proton (1.6×10^{-27} kg) is 0.5 Hz. It may be relevant that the average intensity of the interplanetary magnetic field embedded within the solar wind, whose fluctuations in density and velocity are the major correlates of geomagnetic activity, is between 5 and 10 nT. The voltage gradient if reconnecting flux lines in the geomagnetic field is about a microV/cm, well within the range of detection by some biological systems (Adey, 1988).

Proton channels are present within neurons, microglia, granulocytes, connective tissue and a variety of epithelium (Decoursey, 2003). We suggest that protracted modulation of proton channels by chronic exposure to frequency and intensity-tuned magnetic fields during ontogenesis could affect the expression of neuroaxial asymmetries and transiently alter the microstructure and function within vital regions of the brain stem. Because sudden unexpected death in infants involves less than 1% of the age-range population during the critical period, there are obviously several variables that must converge before a fatality occurs.

ACKNOWLEDGMENTS

Thanks to Mr. Mathew D. Hunter for his technical support and contributions. Portions of this research was supported by grants from the Canadian Foundation

for the Study of Infant Deaths for the years 2004 and 2000 (Dr. S. Segal Research Grant).

REFERENCES

Adey, W.R., 1988. Cell membranes: The electromagnetic environment and cancer promotion. Neurochem. Res., 13: 671-677.

Akdag, M.Z., M.H. Bilgin, S. Dasdag and C. Tumer, 2007. Alteration of nitric oxide production in rats exposed to a prolonged, extremely low-frequency magnetic field Electromagn. Biol. Med., 26: 99-106.

Audero, E., E. Coppi, B. Mlinar, T. Rossetti and A. Caprioli *et al*., 2008. Sporadic autonomic dysregulation and death associated with excessive serotonin autoinhibition. Science, 321: 130-133.

Barmack, N.H., B.J. Fredette and E. Mugnaini, 1998. Parasolitary nucleus: a source of GABAergic vestibular information to the inferior olive of rat and rabbit. J. Comp. Neurol., 392: 352-372.

Barmack, N.H. and V. Yakhnitsa, 2000. Vestibular signals in the parasolitary nucleus. J. Neurophysiol., 83: 3559-3569.

Cavdar, S., F. Onat, R. Aker, U. Sehirli, T. San and H.R. Yananli, 2001. The afferent connections of the posterior hypothalamic nucleus in the rat using horseradish peroxidase. J. Anat., 198: 463-472.

Decoursey, T.E., 2003. Voltage-gated proton channels and other proton transfer pathways. Physiol. Rev., 83: 475-579.

Dupont, M.J., B.E. McKay, G. Parker and M.A. Persinger, 2004. Geophysical variables and behavior: XCIX. Reductions in numbers of neurons within the parasolitary nucleus in rats exposed perinatally to a magnetic pattern designed to imitate geomagnetic continuous pulsations: implications for sudden infant death. Percept. Mot. Skills, 98: 958-966.

Dupont, M.J., G. Parker and M.A. Persinger, 2005. Reduced litter sizes following 48-h of prenatal exposure to 5 nT to 10 nT,0.5 Hz magnetic fields: implications for sudden infant deaths. Int. J. Neurosci., 115: 713-715.

Eckert, E.E., 1992. Magnetic influences on fetus and infant as reason for sudden infant death syndrome: a new testable hypothesis. Med. Hypotheses, 38: 66-69.

Kawai, Y. and E. Senba, 2000. Postnatal differentiation of local networks in the nucleus of the tractus solitarius. Neuroscience, 100: 109-114.

Kinney, H.C., J.J. Filiano, S.F. Assmann, F. Mandell and M. Valdes-Dapena *et al*., 1998. Tritiated-naloxone binding to brainstem opioid receptors in the sudden infant death syndrome. J. Auton. Nerv. Syst., 69: 156-163.

Lin, H.C., F.J. Wan, K.K. Cheng and C.J. Tseng, 1999. Nitric oxide signaling pathway mediates the L-arginine-induced cardiovascular effects in the nucleus tractus solitarii of rats. Life Sci., 65: 2439-2451.

Lin, H.C., B.H. Kang, F.J. Wan, S.T. Huang and C.J. Tseng, 2000. Reciprocal regulation of nitric oxide and glutamate in the nucleus tractus solitarii of rats. Eur. J. Pharmacol., 407: 83-89.

Martin, L.J., S.A. Koren and M.A. Persinger, 2004. Thermal analgesic effects from weak, complex magnetic fields and pharmacological interactions. Pharmacol. Biochem. Behav., 78: 217-227.

McKay, B.E., S.A. Koren and M.A. Persinger, 2003. Behavioral effects of combined perinatal L-NAME and 0.5 Hz magnetic field treatments. Int. J. Neurosci., 113: 119-139.

Moon, R.Y., R.S. Horne and F.R. Hauck, 2007. Sudden infant death syndrome. Lancet, 370: 1578-1587.

Ozawa, Y., S. Takashima and H. Tada, 2003. Alpha2-adrenergic receptor subtype alterations in the brainstem in the sudden infant death syndrome. Early Hum. Dev., 75: 129-138.

O'Connor, R.P. and M.A. Persinger, 1997. Geophysical variables and behavior: LXXXII. A strong association between sudden infant death syndrome and increments of global geomagnetic activity-possible support for the melatonin hypothesis. Percept. Mot. Skills, 84: 395-402.

O'Connor, R.P. and M.A. Persinger, 1999. Geophysical variables and behavior: LXXXV. Sudden infant death, bands of geomagnetic activity and pc1 (0.2 to 5 HZ) geomagnetic micropulsations. Percept. Mot. Skills, 88: 391-397.

Persinger, M.A., 1983. Degranulation of brain mast cells in young albino rats. Behav. Neural Biol., 39: 299-306.

Persinger, M.A. and R.P. O'Connor, 2001. Geophysical variables and behavior: CIII. Days with sudden infant deaths and cardiac arrhythmias in adults share a factor with PC1 geomagnetic pulsations: Implications for pursuing mechanism. Percept. Mot. Skills, 92: 653-654.

Persinger, M.A., B.E. McKay, C.A. O'Donovan and S.A. Koren, 2005. Sudden death in epileptic rats exposed to nocturnal magnetic fields that simulate the shape and the intensity of sudden changes in geomagnetic activity: an experiment in response to Schnabel, Beblo and May. Int. J. Biometeorol., 49: 256-261.

Persinger, M.A., 2006. A potential multiple resonance mechanism by which weak magnetic fields affect molecules and medical problems: the example of melatonin and experimental 'multiple sclerosis'. Med. Hypotheses, 66: 811-815.

Potas, J.R., K.A. Keay, L.A. Henderson and R. Bandler, 2003. Somatic and visceral afferents to the vasodepressor region of the caudal midline medulla in the rat. Eur. J. Neurosci., 17: 1135-1149.

Prato, F.S., J.A. Robertson, D. Desjardins, J. Hensel and A.W. Thomas, 2005. Daily repeated magnetic field shielding induces analgesia in CD-1 mice Bioelectromagnetics, 26: 109-117.

Richerson, G.B., 2004. Serotonergic neurons as carbon dioxide sensors that maintain pH homeostasis. Nat. Rev. Neurosci., 5: 449-461.

Rodriguez, M., L. Martin and C. Santana, 1994. Ontogenic development of brain asymmetry in dopaminergic neurons. Brain Res. Bull., 33: 163-171.

Sawaguchi, T., F. Patricia, H. Kadhim, J. Groswasser, M. Sottiaux, H. Nishida and A. Kahn, 2003. Clinicopathological correlation between brainstem gliosis using GFAP as a marker and sleep apnea in the sudden infant death syndrome. Early Hum. Dev., 75: 3-11.

Schummers, J., H. Yu and M. Sur, 2008. Tuned responses of astrocytes and their influence on hemodynamic signals in the visual cortex. Science, 320: 1638-1643.

Sharp, F.R. and M. Bernaudin, 2004. HIF1 and oxygen sensing in the brain. Nat. Rev. Neurosci., 5: 437-448.

St-Pierre, L.S., G.H. Parker, G.A. Bubenik and M.A. Persinger, 2007. Enhanced mortality of rat pups following inductions of epileptic seizures after perinatal exposures to 5 nT, 7 Hz magnetic fields. Life Sci., 81: 1496-1500.

St-Pierre, L.S., A. Mazzuchin and M.A. Persinger, 2008. Altered blood chemistry and hippocampal histomorphology in adult rats following prenatal exposure to physiologically-patterned, weak (50 to 500 nanoTesla range) magnetic fields. Int. J. Rad. Biol., 84: 325-335.

Takashima, S. and L.E. Becker, 1991. Delayed dendritic development of catecholaminergic neurons in the ventrolateral medulla of children who died of sudden infant death syndrome. Neuropediatrics, 22: 97-99.

Thomas, A.W., M. Kavaliers, F.S. Prato and K.P. Ossenkopp, 1997. Antinociceptive effects of a pulsed magnetic field in the land snail, Cepaea nemoralis. Neurosci. Lett., 222: 107-110.

Ullian, E.M., S.K. Sapperstein, K.S. Christopherson and B.A. Barres, 2001. Control of synapse number by glia. Science, 291: 657-661.

Wang, Q.P., J.E. Zadina, J.L. Guan and S. Shioda, 2002. Morphological studies of the endomorphinergic neurons in the central nervous system. Jpn. J. Pharmacol., 89: 209-215.

Waters, K.A., B. Meehan, J.Q. Huang, R.A. Gravel, J. M ichaud and A. Cote, 1999. Neuronal apoptosis in sudden infant death syndrome. Pediatr. Res., 45: 166-172.

Whissell, P.D. and M.A. Persinger, 2007a. Developmental effects of perinatal exposure to extremely weak 7 Hz magnetic fields and nitric oxide modulation in the Wistar albino rat. Int. J. Dev. Neurosci., 25: 433-439.

Whissell, P.D. and M.A. Persinger, 2007b. Emerging synergisms between drugs and physiologically-patterned weak magnetic fields: Implications for neuropharmacology and the human population in the twenty-first century. Curr. Neuropharmacol., 5: 278-288.

Wu, W.C., Y. Wang, L.S. Kao, F.I. Tang and C.Y. Chai, 2002. Nitric oxide reduces blood pressure in the nucleus tractus solitarius: a real time electrochemical study. Brain Res. Bull., 57: 171-177.

Zec, N. and H.C. Kinney, 2003. Anatomic relationships of the human nucleus of the solitary tract in the medulla oblongata: A DiI labeling study. Auton. Neurosci., 105: 131-144.