厚生労働科学研究費補助金（厚生労働科学特別研究事業）
分担　研究報告書
東京地下鉄サリン事件による健康被害に関する研究の状況

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PubMed でキーワード sarin AND Tokyo で検索、該当 155 文献のうち東京地下鉄サリン事件被害者に起きた慢性影響に関する研究を検討した。同定された 51 論文のうち 33 が事件 2～３か月後から 20 年後までの長期影響に関するものであった。大部分は少数例を対象とした研究であり、PTSD に焦点を置いたものが目立った。サリンによる長期かつ非顕性の影響を総合的に明らかにするには大規模な科学的調査が必要と思われる。

A. 研究目的

平成 7（1995）年 3 月 20 日朝の通勤時間帯に、東京・霞ケ関駅を通過する３つの地下鉄路線を走る５つの車両に、オウム真理教信者によりサリンが散布され、死者 13 人を含め 5800 人以上に甚大な健康被害がもたらされた。筆者らは、事件６～８か月後に被害者の調査を行い、急性中毒回復後も心的外傷後ストレス障害（PTSD）とともに中枢神経影響の遷延を報告した。これらは、サリンを含む急性有機リン中毒による慢性神経学的後遺症に関するこれまでの報告と一致し、中枢神経系の不可逆的変化を示唆していた。一方では、朝鮮戦争退役軍人での観察のように精神・心理的症状の残存を示した。

今回は、東京地下鉄サリン事件被害者に起きた慢性影響に関する研究の状況を把握するために研究を行った。

B. 研究方法

PubMed でキーワード sarin AND Tokyo で検索（2020 年 7 月 17 日）、該当した 155 文献の内容を検討した。

C. 研究結果

東京地下鉄サリン事件と関係ないものを除いた 116 文献（表２）から、被害者の心身影響について 51 論文が同定された（表１、総説や既報のまとめは除く）。うち 33 が事件 2～３か月後（文献 21）から 20 年後（同 32）までの長期影響（表１）、18 が短期影響（直後から数日後）に関するものであった。長期影響に関する論文の大部分は少数例を対象としたものであり、PTSD／精神影響に焦点を置いたものが半数以上であった。51 論文以外は、実験研究、テロリズム対策に関するものや総説等であった。

D. 考察

サリンは強力な神経毒であり、その後遺症は多彩であると予想されるが、調査研究の範囲は部分的である。

E. 結論

サリンによる長期かつ非顕性の長期影響を総合的に明らかにするには大規模な科学的調査が必要と思われる。

G. 研究発表

横山和仁：東京地下鉄サリン事件による健康被害に関する研究の状況. 第 91 回日本衛生学会学術総会、富山、2021 年３月６～８日

表１　東京地下鉄サリン事件被災者の長期心身影響に関する研究論文

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付表２　東京地下鉄サリン事件被害者の心身影響に関する 51 論文					
	Authors (year)	**Study subjects**	**Serum ChE just after the attack (mean ±SD)**	**Time elapsed after attack**	**Major findings**
1.	Suzuki T., Morita H., Ono K., et al. (1995)	58 patients (36 males and 22 females, mean [SD] age 33.4 [13.6]) were brought to the University of Tokyo Hospital	Severe 174.5±85.1 Mild 492.0±104.9	During the sarin incident in Tokyo	Reduced consciousness levels, miosis, marked fasciculations, flushing, tachycardia, raised blood pressure, respiratory distress, and flaccid paralysis. Patients with mild poisoning complained of headaches, dizziness, nausea, chest discomfort abdominal cramps, and showed marked miosis. Nicotinic-dominant responses
2.	Nozaki H, Aikawa N, Shinozawa Y, et al. (1995)	113 patients after exposure to sarin on the Tokyo subway; 1 was dead on arrival, 15 were admitted and the others are being treated as outpatients.		During the sarin incident in Tokyo	Neurological and pulmonary dysfunction after exposure to sarin.
3.	Masuda N., Takatsu M., Morinari H., et al. (1995)	71 patients attended Tokyo Teisin Hospital, and 43 were admitted. Of these, 39 were secondarily exposed emergency medical technicians, 25 of whom received treatment as inpatients.	182 to 804 IU/L (normal 300-750) RBC ChE 0.3-2.0 U (normal 1.2-2.0)	During the sarin incident in Tokyo	Local symptoms, such as eye pain, cough, tightness in throat, nausea, miosis and ataxia.

4.	Nozaki H., Aikawa N. (1995)	The same as 2		During the sarin incident in Tokyo	Nicotinic-dominant responses on the cardiovascular system, pronounced miosis and dim vision.
5.	Yokoyama K., Ogura Y., Kishimoto M., et al. (1995)	A 45-years-old woman among 230 patients were seen at Toranomon Hospital.	129.6 IU/L (noemal > 227 IU/L)	2 hours after the attack	Deep coma, shallow respirations, and blood pressure measurement of 160/80 mmHg. Coarse crepitations were heard throughout both lung fields, pupillary constriction and pulmonary edema.
6.	Nozaki H., Hori S., Shinozawa Y., et al. (1995)	15 doctors treating victims of a terrorist attack with sarin in the Tokyo subways on the day of the attack.	Within the normal ranges	On the day of the attack	Among 11 doctors (73%) who complained of dim vision, the pupils were severely miotic (< 2mm) in 8 (73%). Other symptoms included rhinorrhea in eight (53%), dyspnea or tightness of the chest in 4 (27%), and cough in 2 (13%).
7.	Inoue N. (1995)	A middle aged man who inhaled sarin in a train in a subway station in Tokyo.	Remarkably decreased.	At 8:35 a.m. Match 20, 1995.	Muscle weakness, dyspnea, unconsciousness of sudden onset, marked miosis, delirium consisting of visual hallucination, insomnia and irritability at mid-night for more than seven days.
8.	Okumura T., Takasu N., Ishimatsu S., et al. (1996)	640 patients were presented, 395 (61.7%) were males, mean age 35.0, the range was 8 to 65. years, on the day of the attack.		On the day of the attack	111 patients (17.3%) were admitted. 528 discharged from ED, mild cases (82.5%). 2 were dead. Mild: only eye signs or symptoms (e.g. miosis, eye pain, dim vision, decreased visual acuity) Moderate: systemic signs and symptoms (e.g. weakness, difficult breathing, fasciculations, convulsions.) but specifically did not require mechanical ventilation. Severe: those requiring emergency respiratory support (e.g. intubation and ventilation support)

9.	Matsui Y., Ohbu S., Yamashina A. (1996)	As in reference 10 with detailed explanation of actions by St Luke's International Hospital.			Almost all patients showed miosis. Although those signs and symptoms disappeared within a few weeks, psychological problems associated with posttraumatic stress disorder persisted longer.
10.	Yokoyama K., Yamada A., Mimura N. (1996)	213 patients (139 males and 74 females) pretended to Toranomon Hospital	Normal (>227 IU/L) in most patients. The use of cholinesterase activity as an index of the severity of sarin poisoning appears unreliable.		Coughing, nasal discharge, and pupillary construction, symptoms associated with cholinesterase inhibition. Pupillary constriction was the most common.
11.	Ohbu S., Yamashina A., Takasu N., et al. (1997)	As in reference 10 with detailed explanation of actions by St Luke's International Hospital.			Although these physical signs and symptoms disappeared within a few weeks, psychologic problems associated with posttraumatic stress disorder persisted longer. Also, secondary contamination of the house staff occurred, with some sort of physical abnormality in more than 20%.

12.	Murata K., Araki S., Yokoyama K., et al. (1997)	18 passengers (9 males and 9 females)	13-131 IU/L	6-8 months	Prolonged latencies of event-related and visual evoked potentials (P300 and P100); no effects on brainstem auditory evoked potentials and ECG RR interval variabilities
13.	Nozaki H., Hori S., Shinozawa Y., et al. (1997)	80 patients who were exposed to sarin in a terrorist attack in Tokyo subways.		Lower than normal in 32 patients (64.0%)	Pupil size and AchE activity on the day of exposure were measured. Among the 80 patients, the pupils were miotic (< 3 mm) in 50 patients (62.5%), while AchE activity was below the normal range (< 1.2 U) in 34 patients (42.5%). AchE was significantly lower in the miotic group than in the group with normal pupils (1.0 ± 0.5 U vs 1.5 ± 0.3 U, $p < 0.01$). Systemic poisoning is apparently less likely to develop of the patient's pupil size is normal on arrival at the hospital.
14.	Murayama S. (1997)	A 51-year-old man who inhaled sarin in the attack of Tokyo subway.			Fell into vegetative state and was passively maintained for 13 months. Peripheral sensory nerve showed typical pattern of dying back-type distal peripheral axonopathy.
15.	Li Q., Minami M., Clement JG., Boulet CA. (1998)	The exposed group included 9 male victims (age: 35-52 years) exposed to sarin and hospitalized at the Nippon Medical School Hospital. The control group included 39 healthy males (age: 30-58 years)		2-3 months after the exposure.	The frequency of SCEs was significantly higher in the victims than in the control group. The victims were exposed to not only sarin per se, but by-products of sarin synthesis, i.e. diisoropyl methylphosphonate (DIMP), diethyl methylphosphonate (DEMP) and ethyl isopropyl methylphosphonate (EIMP).
16.	Yokoyama K., Araki S., Murata K., et al. (1998)	18 passengers (9 males and 9 females)	13-131 IU/L	6-8 months	Decreased performance in digit symbol test; high PTSD scores with mood changes and psychiatric complaints

17.	Yokoyama K., Araki S., Murata K., et al. (1998)	18 passengers (9 males and 9 females)	13-131 IU/L	6-8 months	Vestibulo-cerebellar effects as indicated by stabilometry
18.	Minami M., Hui DM., Wang Z., et al. (1998)	4 seriously intoxicated patients hospitalized in ICU of Nippon Medical School (NMS)		Just after	Marked miosis, decreased serum cholinesterase activity, transient increase of serum CPK activity after 3 days of the exposure, diisoropyl methylphosphonate (DIMP), ethyl methylphosphonate fluoridate (EMPF, or ethylsarin), diethyl methylphosphonate (DEMP) and ethyl isopropyl methylphosphonate (EIMP). Isopropanol (IPA) and ethanol (EtOH) were detected of large quantities in the urine samples, and were thought to be derived from sarin and the sarin counterpart, EMPE, DIMP, DEMP and EIMP. Higher sister chromatid exchange (SCE) rate (5.00±1.48/cell) than the control (3.81±0.697/cell), because dialkyl methylphosphonates seemed to have alkylating activity and producing DNA adducts.
19.	Himuro K., Murayama S., Nishiyama K., et al. (1998)	one male	8 IU/L	15 months	Distal sensory axonopathy; died due to pneumonia
20.	Noort D., Hulst AG., Platenburg DH., et al. (1998)	11 victims in Tokyo incident 7 victims in Matsumoto incident			Quantitative analysis of O-isopropyl methlphosphonic acid in serum samples of Japanese citizens allegedly exposed to sarin: estimation of internal dosage. The internal and exposure doses of the victim were estimated. In several cases, the doses appeared to be substantially higher than the assumed lethal doses in man. 曝露レベルの推定
21.	Kamimura M., Katoh O., Kawata H., et al. (1998)	A 72-years-old man		Despite these	Eye discomfort, chest tightness, headache and weakness of the lower limbs and oropharyngeal muscles. Muscle weakness disappeared 8

				symptoms, he visited a hot spring on the same day with his family.	days after exposure to sarin, but respiratory failure rapidly developed, necessitating artificial ventilation within 4 days after hospitalization on March 28th. Bronchitis caused by Legionellosis.
22.	Kadokura M., Ogawa Y., Shimizu H., et al. (2000) [in Japanese]	228 male and 180 female victims	-	6 months	Thirty-two subjects (17 males and 15 females) showed PTSD with increased depressive (Zung scale), psychiatric (GHQ) and physical symptoms by questionnaires
23.	Nishiwaki Y., Maekawa K., Ogawa Y., et al. (2001)	27 male rescue team staffs and 30 male police officers	-	34-45 months	Less well performance in digit span test; no effects on stabilometry and vibration perception threshold
24.	Yamada Y., Takatori T., Nagao M., et al. (2001)	10 sarin poisoning victims int the Tokyo subway terrorist attack.			7 of the victims expressed the PON1 phenotype with high sarin hydrolyzing activity and 3 with low sarin hydrolyzing activity. The main factor contributing to the tragedy of the Tokyo subway terrorist attack was the high toxicity of sarin rather than the rase-dependent genetic difference in the Arg192PON1 polymorphism.
25.	Hood E. (2001)	56 exposed subjects from the Tokyo fire and police departments, 52 nonexposed subjects of similar backgrounds from the same departments.		3 years after the exposure.	Backward digit portion of the test that uncovered significant memory loss in the exposed subjects. Causality between the sarin attack and memory disturbance.

26.	Romano JA Jr., King JM. (2001)				Chronic health effects from this acute exposure, including CNS or behavioral changes that were inextricably linked to post-traumatic stress disorder (PTSD) were observed.
27.	Shimizu et al (2002) [in Japanese]	37 victims (21 males and 16 females, mean [SD] age 43.9 [13.31])	-	5 years	History of PTSD in 11 subjects (8 males and 3 females) revealed by an interview; increased psychiatric symptoms (Impact of Event Scale-Revised, IES-R) in PTSD group as compared with non-PTSD subjects. そのうち 6 名は他の精神疾患も合併
28.	Tochigi et al (2002)	34 victims of the Tokyo subway sarin poisoning (20 males and 14 females, age range: 21-69 years, mean [SD] age 43.8 [13.4]) The same number of age-matched and mostly sex-matched volunteers was enrolled in the study as controls (18 males and 16 females, age range: 24-70 years, mean [SD] 43.7 [12.5])	313±77 IU/I, 276±47 and 324±81 IU/L for PTSD and non-PTSD subjects,	5 years of the sarin attack	No significant relationship was observed between PTSD and serum cholesterols or uric acid. Serum cholinesterase level was significantly reduced in the victims with the development of PTSD. PTSD developed in 8 victims after the attack; increased IES-R and STAI scores in PTSD group as compared with non-PTSD subjects; decrease in serum ChE activities in PTSD group
29.	Yokoyama K., Araki S., Nishikitani M., et al. (2002)		Plasma cholinesterase (ChE) activities of 13-95 (mean 68) IU/I on the	6-8 months before the study (Tokyo Subway Sarin	The chronic (long-term) effect on the vestibulocerebellar function persisted in acute sarin poisoning.

			day of poisoning	Poisoning, March 20, 1995)	
30.	Okudera H. (2002)	Citizens in the city of Matsumoto. About 600 people including residents and rescue staff			58 victims were admitted to hospitals and 7 died. Miosis was the most common finding in the affected people. In cases with severe poisoning, organophosphate may affect the central nervous system and cause cardiomyopathy
31.	Asukai N., Kato H., Kawamura N., et al. (2002)	658 survivors of sarin attack (367 males, mean [SD] age 48.5 [12.3] and 291 females, mean [SD] age 35.7 [11.0])		5 years	Japanese-language version of the Impact of Event Scale-Revised (IES-R-J). Female patients indicated higher scores than male patients.
32.	Otani T., Iwanami A., Shimizu H., et al. (2003) [in Japanese]	55 male and 30 female victims (participation rate = 12.9%)	-	6 years	A variety of psychiatric and physical symptoms such as blurred vision and memory disturbance related to scores on IES-R; PTSD assessed by a structured interview
33.	Yamasue H., Kasai K., Iwanami A., et al. (2003)	15 male and 10 female victims	110±29 and 141±32 IU/L for PTSD and non-PTSD subjects, respectively	5 years	Gray-matter volume reduction in the left anterior cingulate cortex in PTSD group demonstrated by voxel-based analysis of MRI

34.	Matsuo K., Taneichi K., Matsumoto A., et al. (2003a)	21 male and 13 female victims	-	5-6 years	Near-Infrared spectrometry (NIRS) showed lower Oxygenated hemoglobin (OxyHb) in the prefrontal cortex in PTSD group (n=8) as compared with non-PTSD during verbal frequency test
35.	Matsuo K., Kato T., Taneichi K., et al. (2003b)	21 male and 13 female victims	-	5-6 years	Higher OxyHb in the prefrontal cortex during the trauma-related stimuli by video image as compared with controls, as measured by NIRS; skin conductance response was also increased in PTSD group
36.	Li Q., Hirata Y., Kawada T., et al. (2004)	27 male fire fighters and 25 male police officers (secondary exposure)	0-90% inhibition	3 years	Elevated frequency of sister chromatid exchanges of lymphocytes, which were related to %ChE inhibitions
37.	Ohtani T., Iwanami A., Kasai K., et al. (2004)	St. Luke's International Hospital sent a letter to the 565 persons who were the victims of the Tokyo subway attack and were consequently treated at emergency wards for acute sarin intoxication. A total of 170 persons replied, with 64 of them consenting to undertake the survey. . In total, 34 victims (20 males and 14 females; age range, 21–69 years) joined in the study at Tokyo University. The mean age of the subjects was 43.9 (SD		5 years after the attack	Not only post-traumatic stress disorder (PTSD) but also non-specific mental symptoms persisted in the victims at a high rate. A total of 11 victims were diagnosed with current or lifetime PTSD according to CAPS. Victims with PTSD showed higher anxiety levels and more visual memory impairment. A significant correlation between the total score of Impact of Event Scale-Revised (IES-R) and CAPS was found.

		13.3) years (male, 50.2 (SD 11.9) years; female, 39.6 (SD 10.4) years).			
38.	Kawana N., Ishimatsu S., Matsui Y., et al. (2005)				
39.	Miyaki K., Nishiwaki Y., Maekawa K., et al. (2005)	In order to make the effects of sarin more evident with higher statistical power, the data of this study and a previous study were combined together, and re-analyzed. The number of the combined study subjects was 80 exposed subjects, who were subway workers, rescue staff and police officers, consisting of 30 high-exposure and 50 low-exposure subjects, and 65 referents.	-	3 and 7 years after the attack	The exposed group performed significantly less well in the psychomotor function test (tapping). Using merged data, this phenomenon was also observed in a dose-dependent manner and the exposed group performed significantly less well in the backward digit span test. Chronic decline of psychomotor function and memory function still exist 7 year after the sarin exposure.
40.	Kawada T., Katsumata M., Suzuki H., et al. (2005)	161 participants		8 years after the attack	The high prevalence of insomnia and insomnia-related factors for victims especially under 50 years of age.
41.	Okumura T., Hisaoka T., Naito T., et al. (2005)	On March 20, 1995, 640 victims of the Tokyo subway sarin attack were treated at St. Luke's International Hospital. Subsequently, a total of 1410 victims presented for treatment.			The most prominent sign was miosis. Headache, dyspnea, nausea, eye pain, blurred vision, visual darkness, and vomiting were also

					noted. The most prominent abnormal lab value was low plasma ChE activity.
42.	Araki T., Kasai K., Yamasue H., et al. (2005)	13 male and 8 female victims (8 with PTSD)	110.8±29.2 and 150.3±20.5 IU/L for PTSD and non-PTSD subjects, respectively	5-6 years	Lower amplitude of P300 in victims with PTSD as compared with those without PTSD
43.	Tochigi M., Otani T., Yamasue H., et al. (2005)	20 male and 14 female victims	276±47 and 324±81 IU/L for PTSD and non-PTSD subjects, respectively	5 years	Scores on Clinician-Administered PTSD scale were significantly correlated with ChE
44.	Tokuda Y., Kikuchi M., Takahashi O., et al. (2006)			1 year	The most common acute symptoms and signs were miosis and associated visual darkness. Other major signs and symptoms were headache, dyspnea, nausea, ocular pain, blurred vision, vomiting, coughing, muscle weakness, and agitation. Approximately 1 year after the Tokyo subway sarin attack, the hospital sent follow-up questionnaires to 606 patients. Of 303 respondents, 46% still had either physical or psychological symptoms: 18.5% had eye symptoms, 11.9% had easy fatigability, and 8.6% had headache. For

					psychological symptoms, 12.9% felt fear for subways, 11.6% had fear concerning escape from the attack, 10.6% reported flashbacks, 7.9% had depression and 7.6% had lack of concentration.
45.	Abe O., Yamasue H., Kasai K., et al. (2006)	5 male and 4 female victims with PTSD and 16 matched victims of the same traumatic event without PTSD	"the subject characteristics have been described in detail previously (Yamasue et al. 2003)."	5-6 years	The voxel-based analysis showed a significant fractional anisotropy increase in the left anterior cingulum, subjacent to the left ACC gray matter where we previously found a volume decrement, in PTSD subjects.
46.	Yamasue H., Abe O., Kasai K., et al. (2007)	21 male and 17 female victims and 76 matched healthy control subjects	120±46 IU/mL among victims	5-6 years	Serum ChE levels (mean±SD) were 308±62 IU/mL at the day of the MRI scan. The voxel-based morphometry exhibited smaller than normal regional brain volumes in the insular cortex and neighboring white matter, as well as in the hippocampus in the victims. The reduced regional white matter volume correlated with decreased serum cholinesterase levels and with the severity of chronic somatic complaints related to interoceptive awareness. Voxel-based analysis of diffusion tensor magnetic resonance imaging further demonstrated an extensively lower than normal fractional anisotropy in the victims. All these findings were statistically significant (corrected $p < 0.05$).

47.	Rogers MA., Yamasue H., Abe O., et al. (2009)	25 people (10 females) who experienced the Tokyo subway sarin attack in 1995	-	5–6 years	The group with a history of PTSD had significantly smaller mean bilateral amygdala volume than did the group that did not develop PTSD. Furthermore, left amygdala volume showed a significant negative correlation with severity of PTSD symptomatology as well as reduced gray matter density in the left anterior cingulate cortex.
48.	Iwasa M., Inoue K., Wakakura M. (2012) [in Japanese]	154 male and 151 female patients	-	7-15 years	The most common symptom was asthenopia, followed by visual loss, blurred vision, photophobia and ocular pain. Effects of sarin poisoning were strongly suspected in 54 patients （19%）. Described in detail are 3 severely affected cases （miosis, horizontal smooth pursuit eye movement disorder, accommodative insufficiency）
49.	Iwanami A. (2016) [in Japanese]	299 victims and the bereaved (n = 18)	-	20 years	The prevalences of ocular fatigability, dimness of sight, weakness, easy fatigability, vertigo, headache, and PTSD symptoms were 76%, 71%, 57%, 63%, 44%, 42%, and 29% (among the victims), respectively. Forty-eight percent of the respondents felt intimidated by approaching subways or the spot of the accident.
50.	Ishimatsu S. [in Japanese] (2016)	640 patients on the same day. 事件当日の受診者総数：640名			事件から数年後の後遺症は、身体的後遺症、眼科的後遺症、精神的後遺症に分けることができる。後遺症と認定されている眼症状、PTSD をはじめとする精神症状以外での身体症状では、「からだがだるい」1 年後 7.3%、5 年後 16.0%、10 年後 43.4%、20 年後 39.6%、「からだが疲れやすい」は 1 年後 11.9%、5 年後 23.1%、10 年後 56.3%、20 年後 47.5%、「頭痛」は 1 年後 8.6%、5 年後 12.5%、10 年後 44.7%、20 年後

					28.3%、「下痢をしやすい」は 1 年後 1.0%、5 年後 11.9%、10 年後 18.6%、20 年後 14.6%であった。「手足のしびれ」は 12 年後の時点で 42.2%と実に半数近くが症状を訴えていたが、16 年後は 26.4%、20 年後には 25.8%となった。
51.	Sugiyama A., Matsuoka T., Sakamune K., et al. (2020)	747 survivors (12% of the total) who responded to the annual questionnaire once or more during the study period.		5 to 14 years	Posttraumatic stress response (PTSR). The prevalence of somatic symptoms, especially eye symptoms, was 60–80% and has not decreased. PTSR prevalence was 35.1%, and again there was no change with time. The multivariate Poisson regression model results revealed “old age” and “female” as independent risk factors, but the passage of time did not decrease the risk of PTSR. The Recovery Support Center (RSC), a non-profit organization, is the largest organization that has been providing support to the victims of the two Aum Shinrikyo sarin gas attacks; the aforementioned incident in the Tokyo subway in 1995, and a previous one in Matsumoto in 1994 that killed 8 citizens and injured about 660.