

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

松本・東京地下鉄サリン事件の医学的影響の長期フォローに必要な調査項目についての研究

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研究要旨 松本・東京地下鉄サリン事件の被害者における長期的な健康被害は、今もなお続いている。そのため、長期フォローの際に必要な調査項目を検討した。Pubmedを用いて網羅的に検索し、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から、総説論文や急性サリン中毒によって死去した剖検例の報告を除いて27編を同定した。同定した論文の内容を検討して調査項目をリストアップした。

### A. 研究目的

松本・東京地下鉄サリン事件の被害者における長期的な健康被害は、今もなお続いている。そのため、長期フォローの際に必要な調査項目を挙げる。

医学的観点からみても同事件は、単一で特定された化学兵器への暴露という国際的にも稀有な事件であり、長期的調査によって次世代にその記録・知見をつなぐことは国内的にも国際的にも責務がある。

### B. 研究方法

2020年7月に本事業の研究分担者として横山らが体系的に概観して同定した116編に追加して、その後の2022年3月18日までに発表された文献をPubmedでSarin AND Tokyoで検索して追加した。

その上で、同定した文献を基に、被害者の長期フォローに関して、含めるべき調査項目を検討した。また、調査項目をカバーするための医療費を概算した。

### C. 研究結果

PubmedでSarin AND Tokyoで検索し、2020年7月以降に発表されていた23編の文献が該当した。このうち、松本・東京地下鉄サリン事件とは関係のない文献と総説論文を除き、1編の文献を同定した（Sugiyama et al., 2020）。この1編と、2020年に横山らが同定した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33編について内容を検討し、さらに総説5編と急性サリン中毒によって死去した剖検例の報告2編を除いた27編について、表1に概要をまとめた。

これらの27編の報告で含まれていた調査項目をまとめると表2のように要約出来た。

Impact of event scale revised, Clinician-administered PTSD scale, Mini-international Neuropsychiatric interview, Stait-Trait Anxiety Inventory, Questionnaires developed by St. Lukus Hospital teamなどの、多くの報告に含まれている基礎的な臨床的評価項目や背景情報にあたるものを除くと、16の評価項目について、サリン暴露の有無やPTSDの有無に関連した有意な結果が報告されていた。このうち、同一の調査データに基づく複数の報告を除くと、Cholinesterase level、P3 event related potential、General Health Questionnaireの3つの項目については2つ以上の調査によって有意な結果が報告されていた。

### D, E. 考察と結論

今回の調査結果に基づくと、Impact of event scale revised（診療点数80点）、Clinician-administered PTSD scale（同450点）、Mini-international Neuropsychiatric interview、Stait-Trait Anxiety Inventory（同80点）、Questionnaires developed by St. Lukus Hospital teamなどの、多くの報告に含まれている基礎的な臨床的評価項目や背景情報に加えて、Cholinesterase level（同144点）、P3 event related potential、General Health Questionnaire（同80点）を長期フォローの際の調査項目をすることが考えられる。これらのうちで診療報酬点数がついている項目の合計は834点となる。

一方で、被害者に多く認められる眼に関連した症状については、文献は1編のみであるが眼科的検査で多くの所見が報告されており（岩佐ら2012）、被害者個々の症状に合わせて眼科的検査や神経学的検査や頭部MRIなどを行えることが望ましいと考えられる。

## **F. 健康危機情報**

総括研究報告書にまとめて記入

## **G. 研究発表**

1. 論文発表  
該当なし
2. 学会発表  
該当なし

## **H. 知的財産権の出願・登録状況**

(予定を含む。)

1. 特許取得  
該当なし
2. 実用新案登録  
該当なし
3. その他  
特になし

表1 サリン事件被害者の健康状態についての長期的な調査結果の研究報告リスト

Papers	Subjects	Timepoint	Outcome measures	Major findings
Yokoyama et al., 1998a	18 exposed, 15 non-exposed	Sep-Nov 1995	Neurobehavioural tests and questionnaires	Lower performance on digit symbol and Higher scores on GHQ, Fatigue, and PTSD tendency
Yokoyama et al., 1998b	18 exposed, 15 non-exposed	Sep-Nov 1995	Neurobehavioural tests, questionnaires, Brain evoked potentials, Computerized static posturography, ECG	Overlap with Yokoyama et al., 1998 and Murata et al., 1997
Li et al., 1998	9 exposed males and 39 un-exposed males	May-June 1995	Sister chromatid exchanges,	Higher flecuency of sister chromatid exchanges in exposed compared with un-exposed males
Murata et al., 1997	18 exposed and 18 non-exposed	Sep-Nov 1995	P3, Visual evoked potential, brainstem auditory evoked potential, ECG, ChE	The prolonged latencies of P3 and visual evoked potential in the exposed subjects compared with the non-exposed controls. The R-R inteerval variability at 6 months later was correlated with ChE level at exposure.
Kadokura et al., 2000	459 exposed subjects	Sep-95	GHQ, SDS, Questionaires	7.8% of the participants possibly satisfy PTSD diagnosis, and showed higer GHQ and SDS scores.
Nishiwaki et al., 2001	56 exposed males and 52 un-exposed males	1998	Neurobehavioural tests	A tendency for lower performance on backward digit span test in the exposed compared with non-exposed controls.
Tochigi et al., 2002	34 exposed (8 PTSD)	2000	CAPS, STAI, T-Cho, HDL-Cho, UA, ChE	Lower ChE level in PTSD subjects than in non-exposed subjects
Simizu et al., 2002	37 exposed (11 PTSD)	2000	CAPS, IESR, STAI, WMSR, Questionaires developped by St. Lukus Hospital team	Overlap with Tochigi et al., 2004
Asukai et al., 2002	658 exposed subjects	2000	IESR	Testing reliability and validity of Japanese version of IESR
Yokoyama et al., 2002	9 females with exposure	Sep-Nov 1995	Computerized static posturography	Included in Yokoyama et al., 1998
Matsuo et al., 2003a	34 exposed (8 PTSD)	2000	CAPS, STAI, WMNS-R, NIRS	Lower attention and concentration in WMSR and OxyHb in NIRS and their correlation in PTSD subjects compared with non-PTSD exposed subjects
Matsuo et al., 2003b	34 exposed (8 PTSD)	2000	CAPS, STAI, Skin conductance response, NIRS	Increased prefrontal oxygenated hemoglobin during trauma-related exposed and decreased deoxygenerated hemoglobin and increased skin conductance response during trauma-related image in exposed subjects with PTSD.
Yamasue et al., 2003	36 exposed (9 PTSD)	2000	CAPS, STAI, ChE, 3D-T1 MRI	Lower ACC gray matter density correlated with CAPS score not with ChE level at exposure in exposed subjects with PTSD compared with those without PTSD.
Otani et al., 2003	115 exposed subjects	2001	IESR, Questionaires developped by St. Lukus Hospital team	Various symptoms were also recognized at the study point.
Li et al., 2004	52 exposed males and 44 un-exposed males	1998	Sister chromatid exchanges,	Higher flecuency of sister chromatid exchanges in exposed compared with un-exposed males and their correlation with ChE decreases at the exposure
Tochigi et al., 2004	34 exposed (11 PTSD)	2000	CAPS, IESR, STAI, WMSR, Questionaires developped by St. Lukus Hospital team	Higher stait and trait anxiety and lower performane on visual memory in the victims with PTSD compared with those without PTSD.
Araki et al., 2005	21 exposed (8 PTSD)	2000	CAPS, STAI, P3	Lower P3 amplitude and its correlation with ACC gray matter density
Tochigi et al., 2005	34 exposed (8 PTSD)	2000	CAPS, STAI, T-Cho, HDL-Cho, UA, ChE	The ChE level both at exposure and 2000 showed correlations with CAPS scores.
Miyaki et al., 2005	80 exposed	1998 and 2002	Neurobehavioural tests	Lower psychomotor performance in exposed subjects than in un-exposed subjects
Okumra et al., 2005	303 exposed subjects	1996	Questionaires developped by St. Lukus Hospital team	Highly prevalent residual symptoms especially eye symptoms
Kawana et al., 2005	Totally 1722 exposed subjects	2000-2003	IESR, Questionaires developped by St. Lukus Hospital team	Various time-couse of posttraumatic symptoms
Kawada et al., 2005	161 exposed subjects	2003	Questionaire	Various types of insominia were recognized amongd the participants.
Abe et al., 2006	36 exposed (9 PTSD)	2000	CAPS, DTI	Increased FA in cingulum in exposed subjects with PTSD compared with non-PTSD exposed subjects.

(表1 つづき)

Yamasue et al., 2007	38 exposed, 76 non-exposed	2000	CAPS, WMSR, ChE, DTI, 3D-T1 MRI, Questionnaires developed by St. Lukus Hospital team	Smaller insular and surrounding white matter and hippocampus and lower FA in an extensive area in exposed compared with non-exposed. The reduced volumes were correlated with somatic complaints and ChE levels in 1995.
Rogers et al., 2009	25 exposed (9 PTSD)	2000	CAPS, STAI, ChE, 3D-T1 MRI	Smaller amygdala volume correlated with lower ACC gray matter intensity and CAPS score in exposed subjects with PTSD compared with those without PTSD.
Iwasa et al., 2012	305 exposed subjects	2002-2010	Eye position, pupil, eye movements, visual acuity, accommodation, refraction, intraocular pressure, slit-lamp biomicroscopy, and funduscopy	Various eye symptoms were recognized especially the following with high prevalence: asthenopia, visual loss, blurred vision, photophobia, and ocular pain.
Sugiyama et al., 2020	747 exposed subjects	2000-2009	IESR, Questionnaires developed by St. Lukus Hospital team	60-80 % reported somatic symptoms; 35.1 % reported traumatic stress symptoms; and has not decreased

Abbreviations: PTSD: post-traumatic stress disorder; CAPS: Clinician-administered PTSD scale; STAI: Stait-Trait Anxiety Inventory; GHQ: General Health Questionnaire; IESR: Impact of event scale revised; SDS: Self-Rating Depression Scale; ECG: Electrocardiography; ChE: Cholineesterase; WMSR: Wechsler Memory Scale Revised; P3: P300 event related potential; DTI: Diffusion tensor imaging; ACC: anterior cingulate cortex; NIRS: Near Infrared spectroscopy; FA: Fractional anisotropy; UA: Uretic acid

表2 調査項目のリスト	
Measures	Papers reporting positive findings
<b>Outcome measures</b>	
Cholineesterase level	Murata et al., 1997; Tochigi et al., 2002 (Yamasue et al., 2003; Yamasue et al., 2007); Li et al., 2004
P3 event related potential	Murata et al., 1997; Araki et al., 2005
General Health Questionnaire	Yokoyama et al., 1998a; Kadokura et al., 2000
Wechsler Memory Scale Revised	Matsuo et al., 2003a (Shimizu et al., 2002; Tochigi et al., 2004; Yamasue et al., 2007)
Sister chromatid exchanges	Li et al., 1998; 2004
Digit symbol test	Yokoyama et al., 1998a
Digit span test	Nishiwaki et al., 2001
Visual evoked potential	Murata et al., 1997
Computerized static posturography	Yokoyama et al., 1998b
Ophthalmic tests	Iwasa et al., 2012
Electrocardiography	Murata et al., 1997
Skin Conductance Response	Matsuo et al., 2003b
Prefrontal Oxygenated hemoglobin	Matsuo et al., 2003a (2003b)
Prefrontal deoxygenated hemoglobin	Matsuo et al., 2003b
3D-T1 MRI	Yamasue et al., 2003 (2007)
Diffusion tensor imaging	Abe et al., 2006 (Yamasue et al., 2007)
brainstem auditory evoked potential	
<b>Clinical and background assessments</b>	
Impact of event scale revised	
Clinician-administered PTSD scale	
Mini-international Neuropsychiatric interview	
Stait-Trait Anxiety Inventory	
Questionnaires developed by St. Lukus Hospital team	