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ORIGINAL ARTICLE

Association between environmental tobacco smoke exposure and dementia syndromes

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ABSTRACT

Objectives Environmental tobacco smoke (ETS) has a range of adverse health effects, but its association with dementia remains unclear and with dementia syndromes unknown. We examined the dose–response relationship between ETS exposure and dementia syndromes.

Methods Using a standard method of GMS, we interviewed 5921 people aged ≥60 years in five provinces in China in 2007–2009 and characterised their ETS exposure. Five levels of dementia syndrome were diagnosed using the Automated Geriatric Examination for Computer Assisted Taxonomy instrument. The relative risk (RR) of moderate (levels 1–2) and severe (levels 3–5) dementia syndromes among participants exposed to ETS was calculated in multivariate adjusted regression models.

Results 626 participants (10.6%) had severe dementia syndromes and 869 (14.7%) moderate syndromes. Participants exposed to ETS had a significantly increased risk of severe syndromes (adjusted RR 1.29, 95% CI 1.05 to 1.59). This was dose-dependently related to exposure level and duration. The cumulative exposure dose data showed an adjusted RR of 0.99 (95% CI 0.76 to 1.28) for >0–24 level years of exposure, 1.15 (95% CI 0.93 to 1.42) for 25–49 level years, 1.18 (95% CI 0.87 to 1.59) for 59–74 level years, 1.39 (95% CI 1.03 to 1.84) for 75–99 level years and 1.95 (95% CI 1.34 to 2.83) for ≥100 level years. Significant associations with severe syndromes were found in never smokers and in former/current smokers. There were no positive associations between ETS and moderate dementia syndromes.

Conclusions ETS should be considered an important risk factor for severe dementia syndromes. Avoidance of ETS may reduce the rates of severe dementia syndromes worldwide.

What this paper adds

- Environmental tobacco smoke (ETS) increases the risks of cancer, and respiratory and cardiovascular diseases, but its association with dementia remains unclear.
- No study has previously investigated the dose–response relationship between ETS and dementia syndromes.
- The risk of severe dementia syndromes was dose-dependently increased with ETS exposure.
- The effect was similar between never smokers and smokers, and was predominately due to ETS exposure at work.
- ETS should be considered an important risk factor for severe dementia syndromes.

BACKGROUND

Dementia syndromes are comprehensive chronic mental disorders, the main clinical features being cognitive decline and varying degrees of personality change. They comprise Alzheimer's disease, vascular dementia and other rarer conditions. Dementia syndromes are relatively common, increasing in prevalence, and the largest cause of disability, particularly disability that affects self-care and the ability to carry out domestic tasks.[1] They are one of the world's biggest health problems and a major public health challenge that is increasing as populations age.[2]

Previous studies have shown that cigarette smoking substantially increases the risk of Alzheimer's disease and all types of dementia.[3 4] This has stimulated speculation that environmental tobacco smoke (ETS), also known as second-hand smoke or passive smoking, may also have a role. In a recent study, Llewellyn *et al*[5] reported a significant association between ETS and cognitive impairment (defined by the lowest 10% of scores on a battery of neuropsychological tests) in a UK population aged ≥50. In Italy, Orsitto *et al*[6] observed that both mild cognitive impairment and dementia were related to ETS in 856 patients aged ≥65 who were consecutively admitted to a geriatric unit. In the USA, however, Barnes *et al*[7] did not find a significant relationship between ETS and risk of dementia in a cohort of 970 older people. The uncertain association between ETS exposure and risk of dementia is compounded by lack of data, urging further investigation. In this study, we examine the dose–response relationship between ETS exposure and dementia syndromes (as opposed to dementia cases).

METHODS

Study populations were derived from a four-province study of dementia,[8] and also from the third wave survey of the Anhui study,[9] to increase the study power.

The four-province study

The methods employed in the four-province study have been fully described before.[8] In brief, in 2008–2009, following our previous studies in Anhui province,[10 11] we chose one urban and one rural community from each of four provinces (Guangdong, Heilongjiang, Shanghai and Shanxi) as the study fields and sought to recruit 500 or

more participants from each community. We employed a cluster random sampling method to select residential communities from each of the four provinces (detailed location data are available on request). The target population consisted of residents aged ≤60 years who had lived in the area for at least 5 years. Ethics approval for the study was obtained from the Research Ethics Committee, University College London, UK, and the local governments in China. Based on the residency lists of the district and village committees, we recruited a total of 4314 participants, with an overall response rate of 93.8%. Permission for interview and informed consent were obtained from each participant or, if that was not possible, from the closest responsible adult. The participants were interviewed at home by each local survey team from Guangzhou, Harbing and Shanxi Medical Universities, and the School of Public Health of Fudan University. Two researchers from each team were trained at Anhui Medical University, where we had completed several surveys of mental illness in older people and had a skilled and experienced interview team.[9–11] Researchers then returned to their own centres, passed on their skills to local research teams and re-trained the interviewers. The main interview materials were a general health and risk factors questionnaire[9] and the Geriatric Mental State Examination (GMS)—a comprehensive semi-structured mental state interview.[8 12] According to standard procedures,[13 14] we measured systolic and diastolic blood pressure, and weight and waist circumference in all participants.

The third wave survey of the Anhui study

The methods employed in the different wave surveys of the Anhui study have been described previously.[8 9] In brief, in 2001–2003 we examined a random sample of 3336 men and women aged ≤60 years in urban and rural Anhui, China (wave 1) using the standard GMS method.[12] After completing the wave 2 interview in the year following the baseline investigation,[15] we carried out the third wave survey during 2007–2009 and successfully re-interviewed 1757 participants, obtaining a response rate of 82.4% of surviving cohort members.[9] The third wave interview protocol was similar to that in the four-province study mentioned above, and was described in a previous publication.[9]

Assessment of dementia syndromes

A computer program-assisted diagnosis system, the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT),[12] was used to analyse the information from the GMS to identify the principal mental disorders in the study participants. AGECAT was developed using a theoretical model and tested on sample populations diagnosed by psychiatrists. It first attempts to replicate the process by which a psychiatrist diagnoses a syndrome, and then offers a differential diagnosis. GMS symptoms are combined into 150 'symptom components'. In stage I, the symptom components are assembled into groups that characterise the major symptoms of each syndrome. The scores on these individual groups determine the confidence of the diagnosis of the syndrome level. Thus the system uses both quantitative and qualitative measures to determine levels of confidence and utilises numerous clinical decisions to allocate symptom components to syndrome levels. Levels of confidence of diagnosis (0–5) for individual participants are assigned for each of the eight diagnostic syndromes: organic disorder, depression, mania, schizophrenia and paranoia, obsession, phobia, hypochondria, and general anxiety.[16] In stage II the various syndrome levels are compared with each other to derive a final differential diagnosis and a level of confidence of diagnosis (0–5). A level of ≥3 in most circumstances designates a 'case level', which corresponds with what psychiatrists usually recognise as 'a case for intervention' for organic mental disorder. The GMS-AGECAT diagnosis has been validated in a variety of populations,[12] including older Chinese populations.[12 17]

Definition of ETS exposure

We asked the participants for information on smoking habits and ETS exposures, using a questionnaire similar to that employed in the Scottish MONICA surveys.[18 19] Current smokers were those who gave a positive answer to the question 'Do you smoke cigarettes now?' and provided additional information including the number of cigarettes smoked each day, the maximum number smoked each day in the last 2 years, and the duration of the smoking habit. If not currently smoking, participants were asked about their smoking history and related information. We defined 'never smokers' as those who gave negative answers to both enquiries. After giving details of smoking status, all participants were required to provide the answers '*yes*' or '*no*' relating to exposure to ETS. Three sources of ETS exposure were given; home, workplace, and other places, and respondents were given three choices: *no, none at all; yes, some; or yes, a lot*. All participants were asked how many years they were exposed to each of three sources of ETS.

Statistical analysis

The four-province data were combined with the Anhui wave 3 data for analysis (waves 1 and 2 did not have ETS data available). Of 6071 participants, 5962 reported smoking status, of whom 5928 had data on ETS exposure available. Exclusion of seven participants who did not have GMS-AGECAT data, left 5921 for analysis in this study. We defined levels 1–2 organic disorder syndromes as moderate dementia syndromes and levels 3–5 as severe syndromes.[16 20] We employed a Cox regression model used previously[21 22] to calculate the RR of increased dementia syndromes among participants with ETS compared to those without. Moderate and severe syndromes were compared individually to each of the other syndromes. In the analysis we adjusted for age, sex, smoking status, urban/rural location, educational level, occupational class, annual income, marital status, religion, current drinking, visiting children or relatives, hypertension, stroke and depressive syndromes, and accounted for the clustering effect of the five-province geographical area in the model. We further investigated the RR for different sources of ETS exposure (at home, at work and in other locations) and their durations in relation to the excess of dementia syndromes. We scored the three exposure levels ('No, none at all', 'Yes, some' and 'Yes, a lot') as 0, 1 and 2, respectively, and calculated cumulative exposures by multiplying each score by exposure duration. We included cumulative exposure in the analysis. All analyses were performed in Stata V.11 (StataCorp, College Station, Texas, USA).

RESULTS

Of 5921 participants, 2153 (36.4%) were exposed to ETS (1159 (30.8%) of 3769 never smokers, and 994 (46.2%) of 2152 former/current smokers) (table 1). In comparison to those without ETS exposure, ETS-exposed participants were significantly younger, and more likely to have smoked, live in a rural area, have lower education and occupational class, be married (versus widowed), have a religious belief, drink alcohol and visit children (table 1). There were no significant differences between exposed and non-exposed groups regarding body mass index, annual income, hypertension, diabetes, stroke and depressive syndrome. However, participants exposed to ETS had a significantly increased risk of dementia syndromes (table 1).

Table 1 Basic characteristics and dementia syndromes of participants with and without environmental tobacco smoke (ETS) exposure in the five-province study, China

Variable	ETS exposure				
	No (n=3768)		Yes (n=2153)		
	n	%	n	%	p Value
Age					
Mean (SD)	72.99	7.53	72.02	7.43	<0.001
Sex					
Men	1640	43.5	953	44.3	0.581
Women	2128	56.5	1200	55.7	
Body mass index (kg/m^2)					
<25	2692	74.9	1546	74.9	0.971
25–29.9	765	21.3	436	21.1	
≥30	137	3.8	81	3.9	
Smoking status					
Never	2610	69.3	1159	53.8	<0.001
Former	367	9.7	361	16.8	
Current	791	21.0	633	29.4	
Urban/rural					
Urban	1986	52.7	783	36.4	<0.001
Rural	1782	47.3	1370	63.6	
Educational level					
College/university	234	6.2	88	4.1	<0.001
High secondary school	409	10.9	141	6.6	
Secondary school	579	15.4	259	12.0	
Primary school	900	23.9	598	27.8	
Illiterate	1643	43.6	1064	49.5	
Main occupation					
Official/teacher	683	18.1	243	11.3	<0.001
Manual labourer	694	18.4	340	15.8	
Business	23	0.6	16	0.7	
Housewife	327	8.7	153	7.1	
Other	291	7.7	122	5.7	
Farmer	1748	46.4	1278	59.4	
Annual income					
Very satisfactory	343	9.1	179	8.3	0.519
Satisfactory	1617	43.0	943	43.9	
Average	1518	40.4	849	39.6	
Poor	281	7.5	175	8.2	
Marriage					
Married	2519	66.9	1622	75.4	<0.001
Widow	1126	29.9	476	22.1	
Divorced	19	0.5	10	0.5	
Never married	101	2.7	44	2.0	
Having a religious belief					
No	3227	85.8	1740	81.0	<0.001
Yes with religious activity	368	9.8	282	13.1	
Yes without religious activity	168	4.5	125	5.8	
Current drinking					
No	3258	86.6	1745	81.0	<0.001
Yes	505	13.4	408	19.0	
Visiting children or relatives					
Every day	1564	41.6	945	44.0	<0.001
1–3/week	1287	34.2	611	28.4	
≤1/month	908	24.2	592	27.6	
Hypertension					
No	1586	43.2	866	41.1	0.114
Yes	2082	56.8	1241	58.9	
Diabetes					
No	3514	93.4	2015	93.8	0.499

Continued

Table 1 Continued

Variable	ETS exposure				
	No (n=3768)		Yes (n=2153)		
	n	%	n	%	p Value
Yes	250	6.6	133	6.2	
Stroke					
No	3621	96.2	2065	96.3	0.893
Yes	143	3.8	80	3.7	
Depressive syndrome (level)					
0	3351	88.9	1883	87.5	0.214
1–2	214	5.7	143	6.6	
3–5	203	5.4	127	5.9	
Dementia syndrome (level)					
No	2903	77.0	1523	70.7	<0.001
1–2	531	14.1	338	15.7	
3–5	334	8.9	292	13.6	

Table 2 Dementia syndromes in participants with and without environmental tobacco smoke (ETS) exposure by exposure sources and duration in the five-province study, China

Source of ETS exposure	Dementia syndrome level						
	0 (n=4426)		1–2 (n=869)		3–5 (n=626)		
	n	%	n	%	n	%	p Value
Exposure level							
At home							
None	2903	65.6	531	61.1	334	53.4	<0.001
No	432	9.8	54	6.2	33	5.3	
Yes*	1091	24.6	284	32.7	259	41.4	
At work							
None	2903	65.6	531	61.1	334	53.4	<0.001
No	840	19.0	220	25.3	175	28.0	
Yes*	683	15.4	118	13.6	117	18.7	
In other locations							
None	2903	65.6	531	61.1	334	53.4	<0.001
No	735	16.6	191	22.0	137	21.9	
Yes*	788	17.8	147	16.9	155	24.8	
Above 3 combined							
None	2903	65.6	531	61.1	334	53.4	<0.001
Some (1–2)†	1212	27.4	287	33.0	230	36.7	
A lot (3–6)†	311	7.0	51	5.9	62	9.9	
Exposure duration (years)							
At home							
None	2903	65.6	531	61.1	334	53.4	<0.001
No	432	9.8	54	6.2	33	5.3	
>0–19	246	5.6	64	7.4	37	5.9	
20–39	535	12.1	112	12.9	101	16.1	
≥40	310	7.0	108	12.4	121	19.3	
At work							
None	2903	65.6	531	61.1	334	53.4	<0.001
No	840	19.0	220	25.3	175	28.0	
>0–19	118	2.7	28	3.2	22	3.5	
20–39	382	8.6	51	5.9	49	7.8	
≥40	183	4.1	39	4.5	46	7.3	
In other locations							
None	2903	65.6	531	61.1	334	53.4	<0.001
No	735	16.6	191	22.0	137	21.9	

Continued

Table 2 Continued

	Dementia syndrome level						
	0 (n=4426)		1–2 (n=869)		3–5 (n=626)		
Source of ETS exposure	n	%	n	%	n	%	p Value
>0–19	274	6.2	40	4.6	35	5.6	
20–39	373	8.4	62	7.1	66	10.5	
≥40	141	3.2	45	5.2	54	8.6	
Above 3 combined score‡							
None	2903	65.6	531	61.1	334	53.4	<0.001
1	196	4.4	48	5.5	32	5.1	
2	480	10.8	96	11.0	56	8.9	
3–4	465	10.5	105	12.1	100	16.0	
5–9	382	8.6	89	10.2	104	16.6	
Cumulative dose score (level×duration)§							
None	2903	65.6	531	61.1	334	53.4	<0.001
0–24	330	7.5	63	7.2	41	6.5	
25–49	403	9.1	106	12.2	68	10.9	
50–74	350	7.9	63	7.2	59	9.4	
75–99	223	5.0	54	6.2	44	7.0	
≥100	217	4.9	52	6.0	80	12.8	

*Including any participants indicating 'yes, some' or 'yes, a lot' of ETS exposure.
†Each participant had an overall score for total exposure from all three ETS sources. Exposure levels of 'no, none at all', 'yes, some' and 'yes, a lot' were scored as 0, 1 and 2, respectively. Therefore, a participant exposed to ETS 'no, none at all' at home, 'yes, a lot' at work and 'yes, some' in other locations would have a total score of 3 (0+2+1).
‡Participants with ETS exposure durations of 0, >0–19, 20–39 or ≥40 years were scored as 0, 1, 2 or 3 for each exposure source. Overall scores were the sum of the individual scores for the three sources of exposure.
§Cumulative dose score calculated by multiplying exposure level by exposure duration (years) for each ETS source, and then combining the results for the three sources of exposure. Therefore, a participant exposed to ETS 'yes, some' at home for 20 years, 'yes, a lot' at work for 15 years, and 'yes, some' in other locations for 10 years, would have total score of 60 years (1×20+2×15+1×10).
"None" means "no ETS at all". "No" means "not ETS exposure at either home, work or other places"

The age-sex adjusted analysis accounting for the clustering effect of the five-province geographical data showed a significantly increased relative risk for severe dementia syndromes (1.61, 95% CI 1.30 to 1.98; p<0.001) but not for moderate syndromes (1.14, 95% CI 0.89 to 1.45; p=0.305). After further adjustment for smoking status, urban/rural location, educational level, occupation, income, marital status, religion, current drinking, visiting children or relatives, hypertension, stroke and depressive syndrome, the RR was 1.29 (95% CI 1.05 to 1.59; p=0.014) and 0.96 (95% CI 0.84 to 1.09; p=0.502), respectively. The corresponding figures for the four-province study were 1.33 (95% CI 0.98 to 1.81) and 1.08 (95% CI 0.94 to 1.24), and for the Anhui third wave survey 1.29 (95% CI 0.99 to 1.68) and 0.97 (95% CI 0.78 to 1.22).

Separate data analysis for never smokers and former/current smokers showed similar results: an increased risk of severe syndromes of 1.33 (95% CI 1.01 to 1.74) in never smokers and 1.23 (95% CI 1.02 to 1.49) in former/current smokers, with corresponding figures for moderate syndromes of 1.06 (95% CI 0.78 to 1.45) and 0.81 (95% CI 0.57 to 1.17), respectively.

Table 2 shows the numbers and percentages of participants with dementia syndromes in relation to different sources of ETS, exposure duration and cumulative exposure. The dementia syndromes were significantly related to ETS exposure across different sources, exposure duration and cumulative exposure. It appears that the more severe the syndrome, the stronger the association with ETS.

Table 3 shows the RR of severe syndromes in relation to different sources of ETS and cumulative exposures. The increased RR for all participants was consistent across different sources of exposure. The risk was significantly increased with duration of exposure at home, at work and in other locations, and with cumulative dose. A pattern of slightly increased RRs was seen in never smokers (table 3). Significant associations were also found in former/current smokers. However, the data for moderate syndromes showed no such relationships (data available on request).

DISCUSSION

In this large population-based study of dementia in China, we observed a significant increase in the risk of severe dementia syndromes among participants exposed to ETS. The impact of ETS was dose-dependent, and significantly affected both never smokers and former/current smokers.

China is the largest producer and consumer of tobacco in the world: 30% of the world's cigarettes are consumed by China's 350 million smokers.[23] A 1996 national survey showed that the prevalence rate for ever smokers was 66.9% for men and 4.2% for women over the age of 15 years, and that 53.5% of non-smokers were regularly exposed to ETS.[23] In 2002, ever-smoking rates in males and females aged 15 and over were 66.0% and 3.1%, respectively, and the prevalence of ETS in non-smokers was 51.9%.[24] Since the World Health Organization Framework Convention on Tobacco Control (FCTC) came into force in January 2006, the Chinese government has actively promoted the introduction of smoke-free environments in hospitals, in schools, on public transportation and in other public places.[25] However, the implementation of such policies, and their impact, has been far from satisfactory. Recent data show that the prevalence of ETS among never smokers has not reduced significantly, with 52.5% exposed to ETS daily.[26] ETS exposure has many detrimental effects on the cardiovascular system, including increased coagulability of blood platelets, endothelial dysfunction, decreased coronary flow velocity reserves and accelerated atheroma genesis.[27] Moreover, endothelial dysfunction may be related to reduced

Table 3 Relative risk of severe dementia syndrome according to different sources of ETS exposure and cumulative exposure in the five-province study, China

	Severe dementia syndromes					
	All participants (n=5921)			Never smokers (n=3769)		
ETS exposure	RR*	95% CI	p Value	RR*	95% CI	p Value
Exposure source						
At home						
None	1.00			1.00		
No	1.01	0.67 to 1.51	0.978	0.89	0.43 to 1.81	0.739
Yes†	1.35	1.11 to 1.64	0.002	1.39	1.08 to 1.79	0.010
At work						
None	1.00			1.00		
No	1.15	0.94 to 1.40	0.161	1.11	0.76 to 1.64	0.585
Yes†	1.59	1.02 to 2.48	0.039	1.98	1.21 to 3.24	0.006
In other locations						
None	1.00			1.00		
No	1.19	1.08 to 1.31	0.001	1.20	0.90 to 1.60	0.210
Yes†	1.41	1.00 to 1.98	0.051	1.53	0.97 to 2.39	0.065
Above 3 combined‡						
None	1.00			1.00		
Some (1–2)‡	1.22	1.06 to 1.40	0.005	1.22	0.94 to 1.57	0.130
A lot (3–6)‡	1.67	1.25 to 2.24	0.001	2.02	1.59 to 2.58	<0.001
Exposure duration (years)						
At home						
None	1.00			1.00		
No	1.00	0.67 to 1.49	0.999	0.88	0.44 to 1.78	0.724
>0–19	1.12	0.84 to 1.48	0.440	1.32	0.88 to 1.98	0.177
20–39	1.20	1.00 to 1.43	0.049	1.17	0.92 to 1.48	0.196
≥40	1.65	1.21 to 2.27	0.002	1.70	1.28 to 2.27	<0.001
At work						
None	1.00			1.00		
No	1.15	0.95 to 1.40	0.153	1.12	0.76 to 1.64	0.581
>0–19	1.35	0.92 to 1.97	0.129	1.69	0.78 to 3.68	0.186
20–39	1.42	0.84 to 2.40	0.189	1.86	0.97 to 3.54	0.060
≥40	2.05	1.32 to 3.19	0.001	2.39	1.52 to 3.76	<0.001
In other locations						
None	1.00			1.00		
No	1.20	1.08 to 1.33	0.001	1.21	0.90 to 1.61	0.203
>0–19	1.10	0.76 to 1.59	0.630	1.48	1.10 to 1.99	0.009
20–39	1.32	0.86 to 2.04	0.209	1.18	0.54 to 2.59	0.682
≥40	1.93	1.37 to 2.72	<0.001	2.21	1.53 to 3.18	<0.001
Above 3 combined score§						
None	1.00			1.00		
1	1.17	0.79 to 1.72	0.433	1.29	0.73 to 2.30	0.381
2	0.96	0.78 to 1.18	0.707	0.85	0.56 to 1.31	0.475
3–4	1.31	1.03 to 1.69	0.031	1.33	0.95 to 1.86	0.097
5–9	1.66	1.21 to 2.28	0.002	1.98	1.52 to 2.59	<0.001
Cumulative dose (level×duration)¶						
None	1.00			1.00		
>0–24	0.99	0.76 to 1.28	0.919	0.94	0.60 to 1.50	0.809
25–49	1.15	0.93 to 1.42	0.199	1.11	0.82 to 1.51	0.502
50–74	1.18	0.87 to 1.59	0.281	1.16	0.76 to 1.79	0.488
75–99	1.39	1.03 to 1.84	0.028	1.34	0.76 to 2.36	0.305
≥100	1.95	1.34 to 2.83	<0.001	2.55	1.67 to 3.90	<0.001

*Adjusted for age, sex, smoking status, urban/rural location, educational level, occupation, income, marital status, religion, current drinking, visiting children or relatives, hypertension, stroke and depressive syndrome, and taking account of the five-province geographical area clustering.

†Including participants with 'yes, some' or 'yes, a lot' of ETS exposure.

‡Each participant had an overall score for total exposure from all three ETS sources. Exposure levels of 'no, none at all', 'yes, some' and 'yes, a lot' were scored as 0, 1 and 2, respectively. Therefore, a participant exposed to ETS 'no, none at all' at home, 'yes, a lot' at work and 'yes, some' in other locations, would have a total score of 3 (0+2+1).

§Participants with ETS exposure durations of 0, >0–19, 20–39 or ≥40 years were scored as 0, 1, 2 or 3 for each exposure source. Overall scores were the sum of the individual scores for the three sources of exposure.

¶Cumulative dose score calculated by multiplying exposure level by exposure duration (years) for each ETS source, and then combining the results for the three sources of exposure. Therefore, a participant exposed to ETS 'yes, some' at home for 20 years, 'yes, a lot' at work for 15 years, and 'yes, some' in other locations for 10 years, would have total score of 60 years (1×20+2×15 +1×10).

"None" means "no ETS at all". "No" means "not ETS exposure at either home, work or other places"

clearance of β-amyloid protein, which is considered to be implicated in the pathogenesis of Alzheimer's disease.[28] Thus it is not surprising that exposure to ETS was found to increase the risk of dementia syndromes in this study.

In the current study, definitions of dementia syndromes were based on symptoms reflecting cognitive impairment consistent with a diagnosis of dementia.[12] A score of ≥3 on the GMS-AGECAT indicates an 'organic state' which may also include acute confusional states. The large number of studies which have used GMS-AGECAT[29] indicate that acute confusional states are common in hospital-based practice. However, the probable rate of 0.5–1% in the community is small enough to be ignored in most studies of dementia; usually such individuals die or recover and are consequently not included in analysis in multiphase epidemiological studies of dementia. In the Chinese community, severe dementia syndromes diagnosed by the GMS-AGECAT predicted the risk of dementia being diagnosed by psychiatrists. In the Anhui cohort which was followed up over 7.5 years,[9] those with baseline severe dementia syndromes had an increased risk of incident dementia; after adjusting for age, sex, annual income and hypertensive status, the hazards ratio was 2.36 (95% CI 1.02 to 5.47). In the earlier data analysis of women in the four-province study, we observed that ETS exposure was also significantly associated with severe dementia diagnosed by the GMS-AGECAT.[30]

Strengths and weaknesses of the study

The main contribution of this study is that it provides information on the dose–response relationship between ETS exposure and severe dementia syndromes. China has had high levels of both active and passive smoking,[23 31] and also has the highest number of dementia sufferers in the world,[2] with increasing rates of dementia in the future suggested,[16] allowing the association between ETS exposure and dementia syndromes to be examined. A second strength is that we included a relatively large number of study participants and the response rate was high. Although the nature of the study and response rate in the third wave survey in Anhui differed from those in the four-province study, separate data analysis of results from the four-province study and the Anhui study demonstrated similar findings. In addition to increasing study power, inclusion of the Anhui study data in the analysis allowed us to investigate whether the onset of dementia rendered participants more liable to ETS exposure (reverse causality). Of 1694 participants examined in this study, 116 had severe dementia syndromes at baseline, 219 had moderate syndromes and 1359 did not have dementia, and their prevalences of ETS exposure at wave 3 were 30.2%, 35.2% and 31.0%, respectively ($p=0.444$). The findings showed no association between baseline dementia syndromes at wave 1 and follow-up ETS exposure at wave 3. A third strength is that we adjusted for 14 important variables, minimising the residual effect of confounding. In addition to accounting for the geographical clustering effect in analysis, we directly calculated the RR of dementia syndromes in relation to ETS, avoiding its conversion from the OR.[32] We did not use a logistic regression model as it is likely to overestimate the association when the outcome prevalence is common (>10%).

Our study has several limitations. First, the study was cross-sectional and the causal relationship found between ETS exposure and severe dementia syndromes needs to be confirmed by longitudinal follow-up studies. However, it is unlikely that the data on ETS status were affected by differential reporting bias in non-dementia versus dementia cases as ETS was determined before a diagnosis was established. Most Chinese people are unaware of the potential relationship between dementia and ETS exposure. Thus, bias resulting from over-reporting of exposure in patients with dementia syndromes and their carers was unlikely. Furthermore, we have excluded the possibility of reverse causality with ETS exposure resulting from the onset of dementia syndromes in the Anhui cohort data. Second, we did not measure cotinine level to quantify ETS exposure, which is a major limitation. Self-reported ETS may underestimate exposure,[33] although previous research has indicated that it satisfactorily differentiates between relative levels of exposure.[34] Our previous studies[18 19] suggest the combination of the questionnaire and cotinine level measurement increases the statistical power. Thus the association between ETS and dementia symptoms as found in this study may be a conservative estimate.

In conclusion, as far as we know, our study is the first to investigate the relationship between ETS exposure and dementia syndromes. A significant association between ETS exposure and severe dementia syndromes was found. The relationship is dose-independent, and ETS significantly affects never smokers and former/current smokers. The similarity of effects of ETS in smokers and never smokers is consistent with findings in a population-based study in the UK,[5] suggesting that ETS exposure is a strong risk factor for severe dementia syndromes in the general population. The findings from this study, while needing confirmation from prospective longitudinal research, strengthen the case for public health measures to protect people from exposure to ETS. The increased risk of severe dementia in those exposed to ETS is similar to increased risk of coronary heart disease,[35] suggesting that urgent preventive measures should be taken. At present 93% of the world's population live in countries not fully covered by smoke-free public health regulations.[36] More campaigns against ETS exposure and tobacco use in the general population will help decrease the risk of severe dementia and reduce the dementia epidemic worldwide.

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