A review of psychosocial factors and stroke : A new public health problem

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Abstract

The role of psychosocial factors (PSF) in increased risk of stroke is a novel public health challenge, but unclear definitions for PSF and the multiple stroke subtypes have led to inconsistent reports. A review of this issue is therefore warranted.

Methods

Several databases were used for this narrative systematic review (Medline, Embase and Cochrane Library). Two independent reviewers evaluated articles from between 2001 and 2018 on the themes of PSF and stroke / transient ischemic attack (TIA). PSF criteria were job strain, psychological interpersonal and behavioral stress, and social deprivation. Ischemic and hemorrhagic stroke and TIA subtypes were also identified.

Results

Forty-seven cohorts, seven case-control studies and two meta-analyses were included. Despite mixed results, PSF were associated with an increased risk of ischemic and hemorrhagic stroke in populations of all ages, and more predominantly in women.

Conclusion

This broad review shows that the presence of PSF is associated with an increased risk stroke and TIA. As such, PSF must figure in both public health policy and stroke prevention programs, similar to other established metabolic and environmental factors.

Key-words

Stroke, TIA, Psychosocial factors, stress, risk factors, environmental factors

Introduction

Stroke is the primary cause of motor handicap in adulthood, the second cause of cognitive decline after Alzheimer disease and the second cause of death in both women and men, making it a major public health problem [1-4].

Along with ischemic heart disease, stroke is a disease for which the risk factors have been clearly identified: 10 risk factors are responsible for 90 % of strokes [1,5]. Psychosocial factors (PSF), whose influence on myocardial infarction is well known [6], have an unclear role in stroke risk [7] for several reasons. Stroke is an umbrella term for five diseases : large-artery atherosclerosis, cardioembolism, small-artery occlusion (lacune), stroke of other determined causes, and stroke of undetermined causes [8]. Classical psychosocial stressors are perceived factors such as job strain, psychosocial stress, behavioral characteristics, interpersonal problems and social deprivation.

Job strain or work-place stress are increasingly recognized as societal issues [9-13] with two parameters measuring the well-being of employees: their self-satisfaction status and their adaptation to the work. To the other side, it has been demonstrated that the incidence rates for stroke is increasing in active professionals aged less than 55 years [2,14,15].

The objective of the present study was to conduct a narrative systematic review to establish whether PSF increases the risk of stroke and transient ischemic attacks (TIA).

Methods

We explored articles from between 2001 and June 2018 indexed in Medline, Embase, and Cochrane Library. We limited our search to articles with the following keywords in the title: psychological factors (depression, mood, anger, anxiety, distress, stress, self-esteem, life satisfaction); behavioral factors (ambition, coping); interpersonal relationships (emotion, social activity, isolation, happy and sad life events, quality of family life, quality of leisure); occupational factors (type of work, job satisfaction, working duration, shift work, education level); and social deprivation.

We retained studies that used a standard definition of stroke and TIA [1,2,8,9,16] for ischemic and hemorrhagic stroke, subarachnoid hemorrhage, and which reported on recognized vascular risk factors (high blood pressure, diabetes, hypercholesterolemia, smoking, atrial fibrillation, obesity) [1,5,17].

Studies were included if they adhered to the abovementioned criteria. Articles were excluded if they did not use the usual criteria for stroke and PSF or were in the form of conference abstracts.

Two investigators (MGr, MGi) independently evaluated all retrieved studies for eligibility and performed data extraction. Any discordance between investigators was resolved through discussion.

Results

Overall, 56 studies were retained: 47 cohort studies, 7 case-control studies and 2 meta-analyses.

Twenty-four cohort studies investigated psychological risk factors [18-41], 13 of them occupational risk factors [11,13,35,40,42-50] (Table 1), 8 of them interpersonal risks [24,40,42,48,51-54], and 2 of them behavioral risks [55,56] (Table 2).

The case-control study by O'Donnell et al. [5] was the first to demonstrate a strong, statistically significant positive relationship between overall PSF and stroke (OR 2.20, 99% CI 1.78-2.72), among the classical risk factors for stroke.

Among the case-control studies, 2 focused on psychological risks [57,58], 2 interpersonal risks [59,60], 2 social deprivation [61,62] and 1 looked at overall psychological risks [5] (Table 3).

The 2 meta-analyses [9,10] provided data on global psychosocial risk factors for stroke (Table 4).

Most of the studies demonstrated a significant positive association between PSF and stroke risks, and 22 of the 56 studies found a positive but not significant association (Tables 1-4).

Some discrepancies were observed related to a problem of small number of patients. One study [27] observed a non-significant positive association in patients older than 65 years. Five studies [13,33,45,46,59] observed a non-significant positive association in women, while 2 [37,47] observed a non-significant association in men.

To the opposite, 2 studies reported a significant association between PSF and stroke for women [37,43] and 5 for men [32,43,45,46,59]. One study [11] observed a significant positive association for ischemic stroke, but not for hemorrhagic stroke. Three studies observed a paradoxical protective effect for psychological risk [33], occupational risk in women [46] or behavioral risk [55].

Finally, the 2 available meta-analyses [9,10] and the cohort-study by O'Donnell et al. [5] found a significant positive association between overall psychosocial risks and stroke.

The meta-analysis by Booth et al. [10] pooled the data from 14 studies. They found that the adjusted effect estimate for overall risk of stroke in patients exposed to work stress or to stressful life events was 1.33 (95 % confidence interval [CI] 1.17-1.50, $P < 0.00001$). Psychosocial stress was associated with an increased risk of fatal stroke (hazard ratio [HR] 1.45, 95 % CI 1.19-1.78, $P = 0.002$) and ischemic stroke (HR 1.40, 95 % CI 1.00-1.97, $P > 0.0001$). They observed a higher risk of stroke in women (HR 1.90, 95 % CI 1.40-2.56, $P < 0.0001$) than in men (HR 1.24, 95 % CI 1.12-1.36, $P < 0.0001$).

In 2017, Lightbody et al. [9] evaluated 41 cohort studies and 5 case-controls studies. Overall pooled adjusted estimates showed that psychosocial risk factors were an independent risk factor for stroke: they reported that psychological stress increased the risk of stroke by 39 % (HR 1.39, 95% CI 1.27-1.51), occupational stress by 35 % (HR 1.35, 95% CI 1.20-1.51), and interpersonal stress by 16 % (HR 1.16, 95% CI 1.03-1.31), whereas the effects of behavioral factors were not significant (HR 0.94, 95 % CI 0.20-4.31).

Unusual factors, mainly social deprivation, were analyzed in a number of other studies [42,43,50,61-63]. Stroke incidence was found to increase with social deprivation (OR 1.34; $P = 0.003$) [61]. After discharge, age- and gender-adjusted mortality gradually increased with social deprivation, as measured by the Townsend Deprivation Score (HR 2.08 ; 95 % CI 1.07-4.02) [63]. The most deprived patients presented a significantly higher risk of both mild and moderate/severe stroke (OR 1.44, 95 % CI 1.09-1.92) [62].

Discussion

Studies that have focused on modifiable risk factors for acute stroke without factoring in PSF [1] may underestimate the influence of personal, psychological, behavioral, social deprivation and occupational burden on stroke risk [5].

Our review of 56 studies, which includes 47 cohort-studies, 7 case-control studies and 2 meta-analyses, brings together the data from more than 10.000 strokes. The studies seen here demonstrate a statistically positive association between PSF and both ischemic and hemorrhagic stroke, in men and women. This positive association was seen in cohort studies, case-control studies and meta-analyses. The robust latest results of Lightbody et al. [9] demonstrated that psychological factors increased the risk of stroke by 39 %, occupational risks by 35 %, interpersonal risk by 16 %. In addition, our team has previously demonstrated that social deprivation are associated with increased risk of stroke [61], stroke severity [62] and mortality [63].

Despite a marked heterogeneity ($I^2 \geq 60$ %), the sensitivity analyses conducted by Lightbody et al. [9] which were adjusted for the heterogeneous study types and various PSF, demonstrated that the risk estimates were significant. Some limitations may explain this heterogeneity.

The first bias is related to the confounders. While Lightbody et al. [9] included studies that have adjusted to potential cofounders, some studies adjusted for only 4 cofounders [43], and others adjusted for 16 [48,54,56].

Another limitation is the definition of PSF, psychological, occupational and interpersonal factors, whose scopes are more or less broad according to the studies. In this review, we added social deprivation to psychological, occupational, interpersonal and behavioral factors because it is another robust risk factor for stroke.

Other PSF such as long working hours [64-66], short sleep cycles [67], and social deprivation [50,61-63] were sometimes added. All of these factors, which may further influence occupational stress, life satisfaction and quality of life, were found to increase the risk of stroke.

The use of a single question, subjective responses, the length of exposure to PSF, the type of PSF, the burden of job strain [11-13] or negative life events, depression [68-70] and atrial fibrillation [65,66], may worsen the heterogeneity of the results.

Age is another significant bias. The age groups in the studies ranged from 18 [78] to 100 years [27], meaning that there were variations in stroke incidence. Duration of exposition to PSF varied between 5 to 30 years [10]. Eight cohort studies included only men or women [19,25,36,38,42,49,50,55].

Medical history was inconsistent, and key data regarding blood pressure, atrial fibrillation, diabetes, smoking, sleep habits and working hours was often lacking.

Psychological factors are a cluster of symptoms from panic attacks to schizophrenia to depression [35,68-70]. These factors may induce a bias even if localized in the right category and, additionally, measures of psychosocial exposure are not homogeneous: less than 50 % of the studies evaluate exposure with a validated tool [9].

We can also observe that repeated measures were not performed, thus limiting the reliability of the results.

However, O'Donnell et al.'s case-control study [5] and the 2 meta-analyses [9,10] were able to reduce the number of biases, confirming the importance and the depth of the interaction between PSF and stroke.

The strength of this review is based on the number of validated studies summarized in the systematic review and meta-analyse of Lightbody et al. [9], and the multiple sources of the homogeneous studies. The reality of this association is demonstrated by the prospective work of Becher et al [71] which demonstrated the efficacy of a psychosocial safety climate compared to an usual psychosocial policy.

Biological mechanisms of the PSF-stroke association

These results indicate a need to improve the understanding of the underlying mechanisms of PSF. For instance, it is already known that PSF may trigger autonomic nervous system reactions [9,10,72].

Possible processes, though not fully validated, are vascular inflammation, oxidative stress [10], activation of hypothalamic axis, catecholamine and cortisol release, stress-induced auricular fibrillation [12,73], hypertension, hippocampal stimulation [72], C-reactive protein and interleukin release [9]. Behavioral risk (alcohol, cannabis and tobacco abuse) may also be influenced by underlying mechanisms [73]. It has also been postulated that each PSF may have a specific independent impact on stroke risk [12,56]. A further understanding of such mechanisms may provide important advances for the prevention of stroke.

Identification of at-risk populations

This review highlights a population at risk of stroke. Both the research and prevention should turn their attention to those who experience occupational stress and shift work, stress at home, depression, anxiety, long working hours and short sleep cycles, social deprivation, with particular attention paid to

the presence of proven stroke factors like high blood pressure, smoking, alcohol, diabetes, and atrial fibrillation [1,12,74-76].

Recommendations for future research

Further prospective epidemiological studies are required to determine associations between PSF and stroke subtypes, both for the risk of first-ever and recurrent stroke. Future studies should identify the effects of the accumulation of various PSF subtypes and the role of each, the mechanisms of the cause-effect associations, possible synergistic effects of PSF and classical risk factors for stroke, and the respective place of acute and chronic exposure to PSF.

Recommendations for practice

As it is not possible to identify a threshold between safe and dangerous levels of PSF, health policy must work towards raising awareness in the workplace about the role of PSF as a risk factor for stroke.

Conclusion

Though the true amplitude of the issue is not yet known, this review brings attention to a novel public health problem by demonstrating that PSF are independent risk factors for stroke. Further studies are needed to understand the direct mechanisms underlying this association and to confirm the causal links necessary to promote primary and secondary prevention.

This problem is particularly important in developed countries where the incidence rates of stroke are increasing in relatively young populations who are still fully engaged in occupational and personal pursuits.

The results of this review could have a public health impact if the reported association is seen as a serious but modifiable vascular risk factor.

Indeed, awareness of this association should be included in public health policy and in primary and secondary stroke prevention programs [9,10,74,77,78] and psychological health must be promoted in the workplace more specifically [71].

We can conclude that there is an existing link between PSF and the risk of stroke [5,9,10], but it will not be possible to establish the level of risk until more data becomes available.

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Table 1: Characteristics of cohort studies

Psychological risks		Occupational risks	
Author (year) (ref)	Risk estimation HR (95 % CI)	Author (year) (ref)	Risk estimation HR (95 % CI)
1) Ohira et al (2001) ¹⁸	1.90 (1.10-3.50)	1) Kuper et al (2007) ⁴²	1.50 (1.00-2.20)
2) May et al (2002) ¹⁹	1.26 (0.85-1.85)	2) Li et al (2008) ⁴³	
3) Truelsen et al (2003) ²⁰	1.13 (0.85-1.50)	men	1.29 (1.06-1.58)
4) Ohlin et al (2004) ²¹	1.29 (1.04-1.60)	women	1.75 (1.36-2.25)
5) Nilsson et al (2004) ²²	1.22 (1.06-1.41)	3) Mac Fadden et al (2009) ⁴⁴	2.55 (1.34-4.85)
6) Curkendall et al (2004) ²³	1.50 (1.20-2.00)	4) Tsutsumi et al (2011) ⁴⁵	
7) Araki et al (2004) ²⁴	2.70 (1.10-6.80)	men	2.80 (1.20-6.40)
8) Smoller et al (2007) ²⁵	1.98 (0.75-5.24)	women	1.30 (0.60-3.00)
9) Lin et al (2007) ²⁶	2.05 (1.73-3.54)	5) Veronesi et al (2011) ⁴⁶	
10) Salaycik et al (2007) ²⁷		men	2.18 (1.26-3.78)
< 65 years	3.43 (1.60-7.36)	women	0.40 (0.20-0.85)
> 65 years	0.78 (0.46-1.34)	6) Gillum et al (2012) ⁴⁷	
11) Arbelaiez et al (2007) ²⁸	1.25 (1.02-1.53)	white men	0.80 (0.57-1.12)
12) Surtees et al (2008) ²⁹	1.08 (0.67-1.75)	black people	0.70 (0.46-1.08)
13) Lee et al (2008) ³⁰	5.43 (3.47-8.51)	7) Tsai et al (2012) ³⁵	1.16 (1.01-1.33)
14) Bos et al (2008) ³¹	1.21 (0.80-1.83)	8) Yan et al (2013) ⁴⁸	1.14 (0.86-1.52)
15) Shirai et al (2009) ³²		9) Mejia-Lancheros et al (2014) ⁴⁰	1.83 (1.09-3.09)
men	1.22 (1.01-1.47)	10) Schioler et al (2015) ⁴⁹	1.13 (0.95-1.34)
women	1.09 (0.86-1.37)	11) Honjo et al (2015) ⁵⁰	1.05 (0.90-1.23)
16) Nabi et al (2010) ³³	0.52 (0.29-0.93)	12) Fransson et al (2015) ¹¹	
17) Lahti et al (2012) ³⁴	1.69 (0.90-3.16)	ischemic stroke	1.24 (1.05-1.47)
18) Tsai et al (2012) ³⁵	1.13 (1.06-1.22)	hemorrhagic stroke	1.01 (0.75-1.36)
19) Majed et al (2012) ³⁶	1.41 (0.95-2.11)	13) Huang et al (2015) ¹³	
20) Feller et al (2013) ³⁷		men	1.33 (1.04-1.69)
men	1.40 (0.89-2.19)	women	1.26 (0.69-2.27)
women	1.69 (1.05-2.73)		
21) Bergh et al (2014) ³⁸	1.16 (1.04-1.29)		
22) Eurelings et al (2014) ³⁹	1.74 (0.89-3.38)		
23) Mejia-Lancheros et al (2014) ⁴⁰	0.66 (0.38-1.15)		
24) Hamano et al (2015) ⁴¹	1.22 (1.08-1.38)		

Table 2. Characteristics of cohort studies

Interpersonal risks		Behavioral risks	
Author (year) (ref)	Risk estimation HR (95 % CI)	Author (year) (ref)	Risk estimation HR (95 % CI)
1) Araki et al (2004) ²⁴	3.20 (1.30-7.80)	1) Eng et al (2003) ⁵⁵	0.42 (0.20-0.88)
2) André-Peterson et al (2007) ⁵¹	1.80 (1.05-3.10)	2) Everson-Rose et al (2014) ⁵⁶	2.00 (1.15-3.47)
3) Kuper et al (2007) ⁴²	1.30 (0.90-1.80)		
4) Ikeda et al (2008) ⁵²	1.11 (0.89-1.37)		
5) Kornerup et al (2010) ⁵³	1.32 (0.77-2.25)		
6) Yan et al (2013) ⁴⁸	1.02 (0.98-1.07)		
7) Mejia-Lancheros et al (2014) ⁴⁰	0.56 (0.28-1.12)		
8) Nagayoshi et al (2014) ⁵⁴	1.44 (1.02-2.04)		

Table 3. Characteristics of case-control studies

	Author (year) (ref)	Risk estimation HR (95 % CI)
Psychological risks	Jood et al (2009) [57]	2.51 (1.42-4.44)
	Riaz et al (2015) [58]	4.14 (1.54-11.09)
Interpersonal risks	Engstrom et al (2004) [59] men	1.23 (1.03-1.50)
	Engstrom et al (2004) [59] women	0.98 (0.84-1.20)
	Egido et al (2012) [60]	3.84 (1.91-7.70)
Social deprivation	Grimaud et al (2011) [61]	2.08 (1.07-4.02)
	Béjot et al (2017) [62]	1.39 (1.06-1.84)
Whole psychosocial risks	O'Donnell et al (2016) [5]	2.20 (1.78-2.72)

Table 3: Meta-analyses

Author (year) (ref)	Risk estimation HR (95 % CI)
Lightbody et al (2017) ⁹	1.35 (1.20-1.51)
Booth et al (2015) ¹⁰	1.33 (1.17-1.50)