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Chapter 13

Stress, childhood trauma, and cognitive functions in functional neurologic disorders

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Abstract

Conversion disorder (CD) has traditionally been ascribed to psychologic factors such as trauma, stress, or emotional conflict. Although reference to the psychologic origin of CD has been removed from the criteria list in DSM-5, many theories still incorporate CD as originating from adverse events.

This chapter provides a critical review of the literature on stressful life events in CD and discusses current cognitive and neurobiologic models linking psychologic stressors with conversion symptomatology. In addition, we propose a neurobiologic stress model integrating those cognitive models with neuroendocrine stress research and propose that stress and stress-induced changes in hypothalamus–pituitary–adrenal (HPA) axis function may result in cognitive alterations, that in turn contribute to experiencing conversion symptoms. Experimental studies indeed suggest that basal as well as stress-induced changes in HPA axis responding lead to alterations in attentional processing in CD. Although those changes are stronger in traumatized patients, similar patterns have been observed in patients who do not report a history of traumatic events.

We conclude that, whereas adverse events may play an important role in many cases of CD, a substantial proportion of patients do not report a history of traumatization or recent stressful events. Studies integrating effects of stress on cognitive functioning in CD are scarce. We propose that, instead of focusing research on defining etiologic events in terms of symptom-eliciting events, future research should work towards an integrated mechanistic account, assessing alterations in cognitive and biologic stress systems in an integrated manner in patients with CD. Such an account may not only serve early symptom detection, it might also provide a starting point for better-targeted interventions.

INTRODUCTION

Medically unexplained neurologic symptoms have been observed in over 30% of patients presenting in specialized neurologic clinics (Carson et al., 2000). The official rates for conversion disorder (CD) are lower: only 5% of referrals to neurology clinics are diagnosed with CD, and the incidence in the general population is estimated to be 2–5 per 100 000 per year (American Psychiatric Association, 2013). This discrepancy is in part due to scarce psychiatric evaluation and underreporting in nonpsychiatric settings (Akagi and House, 2002; Nicholson et al., 2011). Given the prevalence and because conversion symptoms are associated with individual suffering and excessive public health costs, it is highly relevant to gain more insight into the underlying etiologic mechanisms (Konnopka et al., 2012).

CD has traditionally been ascribed to psychologic stress factors such as trauma, adverse life events, or emotional conflicts. Until the introduction of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5: American Psychiatric Association,

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2013) this etiologic factor even belonged to the main criteria for the diagnostic entity of CD, stating that the symptom initiation or exacerbation should be preceded by conflicts or other stressors (fourth edition, text revision: American Psychiatric Association, 2000). Because the DSM is a descriptive manual and because it is extremely difficult, if not impossible, to prove that a psychologic event has a causal relationship with the onset or exacerbation of a symptom, this criterion has now been removed from the current DSM-5. The presence of psychologic stressors is now handled as a specifier that can be added to the diagnosis. Note that in the revised 10th version of the *International Classification of Diseases* (ICD-10: World Health Organization, 2010), CD is still assumed to be "associated closely in time with traumatic events, insoluble and intolerable problems, or disturbed relationships" (article F44).

Not only diagnostic manuals but also traditional theories on CD have been dominated by the view that the symptoms would be caused by a psychologic stressor or an emotional conflict. Throughout history, philosophers like Plato, physicians such as Breuer, neurologists such as Freud, and pioneer psychiatrists such as Janet have tried to explain how conversion symptoms could arise from such stress factors. Before describing current theories on conversion symptoms, we will first present an overview of the literature on comparative studies that reported on the occurrence of stressful life events or trauma in the history of patients diagnosed with CD. Thereafter, we will present explanatory models, mostly of cognitive nature. Finally, those models will be integrated with recent neurobiologic findings in CD and we will end with setting an agenda for research needed to advance this emerging and interesting field of medically unexplained somatic symptoms.

TRAUMA AND LIFE EVENTS IN CONVERSION DISORDER: A LITERATURE REVIEW

Literature on life adversities generally distinguishes between trauma and recent stressful events (e.g., Roelofs et al., 2005; Reuber et al., 2007; Bakvis et al., 2009b). For trauma it is common to further distinguish between emotional, physical, and sexual abuse (e.g., Alper et al., 1993; Bakvis et al., 2009b, 2010a; Baslet, 2011; Almis et al., 2013; Baker et al., 2013). In the present literature review we will follow these distinctions, resulting in four subcategories of life adversities (physical abuse, sexual abuse, emotional abuse/neglect, and life events). Some studies report specifically on childhood trauma; if this was the case, it will be reported in the review. Because the literature only reports on retrospective studies on life adversities in CD and because the reliability of various retrospective assessment methods may vary, we decided to indicate the assessment method (interview, questionnaire, or both) in our literature review. In addition, we excluded studies with fewer than 10 subjects in the experimental group and studies that did not have a control group. Following these criteria, we conducted a literature review in online databases (PsycINFO and Medline 1990–September 2014), using a range of keywords describing variants of CD (conversion, hysteria, hysterical, functional, pseudoneurologic, pseudoepileptic, psychogenic or medically unexplained symptoms or disorders) combined with variants of traumatic experiences (trauma, life event, adverse event, abuse, neglect, assault). In addition, the reference lists of the found studies were explored to detect other relevant citations. Please note that we did not include a systematic quality assessment and do not claim that this review is complete. The results of the literature review are presented in Table 13.1. Articles that report on stressful life events without specifically referring to trauma are not included in the table, but are discussed below in the section on Life events. Depending on the availability of data and results, trauma rates (in percentages) and/or the significance of differences between subsamples (in *p*-value) have been reported.

Trauma rates in conversion disorder

A total of 32 studies was selected. Most studies distinguished between various subtypes of trauma; physical and sexual abuse were common categories. Trauma was measured using a structured interview, questionnaire, or a clinical (unstructured) interview. The outcome of the present literature overview gives no indication of systematic variance related to use of assessment instrument.

In 22 studies, total trauma rates for CD patients were compared to those in a control sample. Fifteen of those studies reported total trauma percentages, ranging from 14% to 100% for CD samples (and 9–66% for controls; organic, psychiatric, or healthy). At first sight, the trauma rates for CD seem higher than those in the normal population, where estimates of trauma exposure vary between 14.2% and 56% (Breslau et al., 1991; Kessler et al., 1995; Perkonigg et al., 2000). In 18 of the 22 studies the group differences in trauma rates were statistically tested (using occurrence rates or questionnaire scores). In 17 of these 18, total trauma experience was significantly higher in the CD sample than in the control sample. One study found no significant difference (no. 18). In the remaining four studies, that provided no formal statistical testing of group differences, the pattern was in the same direction. Below we detail findings for separate trauma categories: physical, sexual, and emotional abuse.

Table 13.1

Review of the literature on the occurrence rates of (childhood) trauma and recent stressful events in different conversion disorder samples

	Article	Measurement instrument	L/C*	Sample characteristics	Physical abuse		Sexual abuse	Emotional abuse/ neglect		Total trauma†	Recent life events‡
1	Almis et al. (2013)	Structured Clinical Interview for DSM-IV	C	22 PNES, 100% female, age 25	5%		9%			14%	
				22 healthy controls, 100% female, age 25	5%		5% $p = 0.550$			9% (abuse)	
2	Alper et al. (1993)	Structured Clinical Interview for DSM-IV	C	71 PNES, 73% female, age 32	16%		24%			32%	
				140 epilepsy, 51% female, age 32	3%		7%			9% (abuse)	
3	Arnold and Privitera (1996)	Own instrument	L	14 PNES, 64% female, age 33	43%		0%			86%	
				27 ES, 48% female, age 35	0%		11% (incl. physical)			33% (any trauma) $p = 0.004$	
4	Akyuz et al. (2004)	Childhood Abuse and Neglect Questionnaire	C	33 PNES, 100% female, age 28	79%		33%	61%	42%		
				30 ES, 100% female, age 28	17% $p < 0.001$		7% $p = 0.009$	13% (abuse) $p < 0.001$	27% (neglect) $p = 0.190$	(abuse and neglect) $p < 0.001$	
5	Baker et al. (2013)	Life Events and Difficulties Schedule	L	73 functional voice disorder, 100% female, age 47	41%	14%	32%			49%	74%
				55 organic voice disorder, age 48	29%	7%	18%			33%	22%
				66 nonrandom control group, age 47	14% (violence) $p = 0.002$	2% (strangulation) $p = 0.025$	11% $p = 0.008$			21% (abuse) $p = 0.002$	14% (severe events) $p < 0.001$
6§	Bakvis et al. (2009b)	Traumatic Experiences Checklist	L	19 PNES, 79% female, age 28	63%		74%	74%		89%	
				20 healthy controls, 90% female, age 22	5% $p < 0.001$		5% $p < 0.001$	11% $p < 0.001$		11% (interpersonal) $p < 0.001$	
7§	Bakvis et al. (2010a)	Traumatic Experiences Checklist	L	18 PNES patients, 61% female, age 32	33%		39%	44%		61%	
				19 healthy controls, 47% female, age 35	16% $p = 0.021$		11% $p = 0.044$	21% (abuse) $p = 0.129$		26% (interpersonal) $p = 0.033$	

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Table 13.1

Continued

	Article	Measurement instrument	L/C*	Sample characteristics	Physical abuse	Sexual abuse	Emotional abuse/ neglect	Total trauma†	Recent life events‡
8	Berkhoff et al. (1998)	Own interview	C	10 PNES, 50% female, age 44	10%	20%			
				10 ES, 50% female, age 43	0% $p = 0.317$	0% $p = 0.179$			
9	Betts and Boden (1992)	Case history	C	96 PNES, 85% female, age ?		54%			
				132 ES, 61% female, age ?		25%			
				87 psychiatric control, 67% female, age ?		32%			
10	Binzer and Eisemann (1998)	Own memories of childrearing experiences	C	30 PMD, 60% female, age 39		3.3%			
				30 neurological motor disorder, 70% female, age 34		0% $p > 0.05$			
11	Binzer et al. (2004)	Own memories of childrearing experiences	C	20 PNES, 75% female, age 27		30%			(year prior to onset) $p < 0.001$
				20 ES, 60% female, age 27		5% (incest) $p = 0.090$			
12	Bowman and Markand, (1996)	Own trauma experience checklist	C	45 PNES, 78% female, age 38	67%	69%		84% (any trauma) $p < 0.001$	
				Unspecified comparable sample		38% (females) $p < 0.010$			
13	Dikel et al. (2003)	Life Events Checklist	L	17 PNES, 76% female, age 39		71%		100%	
				34 ES, 50% female, age 35		32% (childhood) $p = 0.010$		67.6% (any assault) $p = 0.008$	
14	Jawad et al. (1995)	Own interview	C	46 PNES, 100% female, age 29		9%			
				50 psychiatric control, age 32		8% $p = 0.900$			

15	Kaplan et al. (2013)	Childhood Trauma Questionnaire	C	91 PNES, 90% female, age 42	35%	38%	44%	30%		
				81 ES, 68% female, age 40	20% $p = 0.030$	25% $p = 0.050$	30% (abuse) $p = 0.054$	17% (neglect) $p = 0.005$		
16	Kozlowska et al. (2011)	Linguistic analysis of interview	C	76 conversion, 70% female, age 13	15%	7%	13% (neglect)		75%,	27% (bereavement)
				76 healthy controls, matched for age and sex					12% (unresolved loss/trauma) $p < 0.001$	
17	Kranick et al. (2011)	Childhood Trauma Questionnaire	C	64 PMD, 72% female, age 45	$p = 0.090$	$p = 0.700$	$p < 0.050$		(abuse and neglect) $p < 0.001$	
				39 focal hand dystonia, 74% female, age 4939 healthy controls, 74% female, age 49						
18	Kuyk et al. (1999)	Trauma Questionnaire	L	27 PNES, 77% female, age 29	26%	33%	37%		44%	
				47 temporal-lobe epilepsy (TLE), 36% female, age 39	6%	4%	23%		26%	
				25 non-TLE , 38% female, age 35	16% PNES vs. other: $p = 0.053$	0% PNES vs. other $p < 0.001$	16% PNES vs. other: $p > 0.05$		24% (abuse) PNES vs. other: $p > 0.05$	
19	Litwin and Cardeña (2000)	Dissociative Disorders Interview Schedule	L	10 PNES, 100% female, age 31	50%	60%				
				31 ES, 45% female, age 35	29% $p > 0.050$	13% $p < 0.005$				
20	McDade and Brown (1992)	Own interview	C	18 PNES, 38% female, age 34		17%				
				18 ES, 44% female, age 32		5%				
21	Mökleby et al. (2002)	MINI International Neuropsychiatric Interview	L	23 PNES, 83% female, age 32					30%	
				23 other somatoform disorder, 83% female, age 32					17%	
				23 healthy controls, 83% female, age 30					0% (abuse)	

Continued

Table 13.1

Continued

	Article	Measurement instrument	L/C*	Sample characteristics	Physical abuse		Sexual abuse		Emotional abuse/ neglect		Total trauma†	Recent life events‡
22	Ozcetin et al. (2009)	Childhood Trauma Questionnaire	C	56 PNES, 100% female, age 34 59 healthy controls, 100% female, age 34	$p < 0.001$		$p < 0.001$		$p < 0.001$		(abuse and neglect) $p < 0.001$	
23	Plioplys et al. (2014)	Children's Hassles Scale	C	55, 71% female, age 15 35 healthy siblings, 51% female, age 14	13% 6% $p = 0.300$		15% 3% $p = 0.200$		42% 17% (abuse) $p = 0.010$		(adversities) $p = 0.020$	
24	Proença et al. (2011)	Childhood Trauma Questionnaire	C	20 PNES 20 ES No significant differences in age or gender	$p = 0.144$		$p = 0.123$		$p > 0.05$ for every subcategory		(abuse) $p = 0.014$	
25	Reilly et al. (1999)	Medical History Questionnaire	L	40 PNES, 73% female, age 34	53%	18%	53%	18%	60%	45%		
				40 ES, 60% female, age 34	40%	23%	40%	23%	45%	33%		
				40 medically unexplained gastrointestinal symptoms, 75% female, age 41	13% (childhood) PNES vs. other $p < 0.001$	0% (adulthood)	13% (childhood) PNES vs. other $p < 0.010$	0% (adulthood)	23% (childhood) PNES vs. other $p < 0.001$	13% (adulthood)		
26	Roelofs et al. (2002a)	Structured Trauma Interview	C	54 conversion, 83% female, age 38	28%		24%				44%	
				50 affective disorder, 82% female, age 36	20% $p = 0.280$		14% $p = 0.85$				24% (abuse) $p < 0.050$	
27	Salmon et al. (2003)	Medical History Questionnaire Parental Bonding Instrument	L	81 PNES, 69% female, age 35	36%	14%	31%	32%	53%	31%		
				81 ES, 69% female, age 35	21% (childhood) $p < 0.050$	4% (adulthood) $p < 0.050$	16% (childhood) $p < 0.050$	15% (adulthood) $p < 0.001$	32% (childhood) $p < 0.010$	26% (adulthood) $p > 0.050$		

28	Şar et al. (2009)	Own interview (A-criterion DSM-IV)	C	274 conversion symptoms	12%	3%		37%	43%	
				32 somatization with conversion	19%	9%		63%	66%	
				322 no conversion	5%	1%		15%	32%	
				total sample: 100% female, age 35	$p = 0.001$	$p = 0.019$		$p < 0.001$	(abuse and neglect) $p < 0.001$	
29	Scévola et al. (2013)	Structured Clinical Interview for DSM-IV	L	35 PNES, 77% female, age 38	14%	26%			49%	
				49 ES, 59% female, age 35	12% (incl. other violence) $p = 0.410$	4% $p = 0.007$			25% (any trauma) $p = 0.020$	
30	Steffen et al. (2015)	Early Trauma Inventory Life Events Questionnaire	L	45 FND (excl. PNES), 71% female, age 40	$p > 0.050$	$p > 0.050$		$p < 0.001$	(general trauma) $p < 0.010$	(in past year) $p < 0.001$
				45 healthy controls, 69% female, age 45						
31	Tojek et al. (2000)	Life Events Checklist	L	25 PNES, 88% female, age 44	(adulthood) $p = 0.030$	(childhood) $p = 0.350$	(adulthood) $p = 0.100$		44%	$p < 0.050$
				33 ES, 91% female, age 40					33% (abuse)	
32	Van Merode et al. (2015)	Childhood Trauma Questionnaire	C	40 PNES, 65% female, age 49					(abuse and neglect) $p = 0.030$	
				138 ES, 50% female, age 35						

DSM-IV: *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn (American Psychiatric Association, 2000); PNES, psychogenic nonepileptic seizures; ES, epileptic seizures; PMD, psychogenic motor disorder; FND, functional neurological disorder.

Empty cells: type of trauma was not assessed or figure was not reported. Red marking: group difference was significant; blue marking: group difference was non-significant; white: group difference was not statistically tested.

*L/C: specifies the investigated period of trauma occurrence, with L standing for "at any point in lifetime" and C standing for "anywhere during childhood" (before age 18).

†The "total trauma" category follows the definition as cited in the respective paper.

‡The "stressful events" category includes bereavement and other loss, accidents, change in health or employment status, and interpersonal conflict.

§Please note that some overlap in the patient samples of these two articles could not be ruled out.

Physical abuse

In 22 studies, physical abuse rates for CD patients were compared to those in a control sample. Absolute physical abuse rates (based on 19 of those studies) ranged from 5% to 79% for CD samples and rates from 0% to 40% for control samples. Ten out of 19 studies that statistically tested for group differences in physical abuse rates found significantly higher rates or scores in the CD group. In the other nine studies, there were no significant differences. In two out of the three final studies (nos. 1–3) that did not test for significant differences, physical abuse rates followed the pattern of being higher in CD samples than in controls. In 11 of the 22 studies that reported on physical abuse, specific rates were provided for childhood abuse (before age 18). In six out of those 11 studies, a significantly higher rate was found in CD compared to controls. In three of the remaining five, the difference did not reach significance (nos. 9, 17, and 24). In the final two no formal statistical testing was provided, but the physical abuse rates showed the pattern of being higher in CD than in control samples (nos. 1 and 2).

Sexual abuse

Thirty studies reported on sexual abuse. The rates of sexual abuse ranged between 0% and 74% in CD samples and between 0% and 40% in controls (based on 25 studies). In 13 out of the 26 studies that statistically tested for group differences, rates of sexual abuse were significantly higher in CD compared to at least one control group. When specifically looking at childhood sexual abuse, seven out of 18 studies that statistically tested for group differences found a significant difference, with higher rates of childhood sexual abuse in CD patients than in at least one control group. In the other 11, no significant differences were found. Three studies (nos. 2, 8, and 20) did not test for significance, but did report childhood sexual abuse rates, and those followed the pattern of being higher in the CD samples than in controls.

Emotional abuse or neglect

A total of 14 studies looked into emotional abuse and/or neglect. Rates for the total category or of abuse or neglect only were 30–74% for CD samples and 11–63% for control samples (based on nine studies). Thirteen of the 14 studies statistically tested the difference in rates between CD and control samples, with 10 finding a significant effect for the total category or at least one subcategory of emotional abuse and neglect. One study (no. 18) found a significant difference in the opposite direction, with rates being higher in the psychiatric control group than in CD. Six studies found no significant differences in the total category or in a subcategory. In 10 of the 14 studies, the occurrence of neglect/emotional abuse in childhood (under age 18) was under investigation. Of those studies, nine tested for group differences in this category. Eight of those found significantly higher rates in CD samples compared to controls, although in two the rates were only significantly higher in CD for some subtype of emotional abuse or neglect (nos. 4 and 15). One study (no. 24) showed no significant difference and the final study only reported an occurrence rate for their CD sample (no. 16).

In conclusion, the reported trauma rates are generally found to be higher for CD compared to healthy and organic disorder control groups. Studies specifically targeting childhood experiences reported comparable findings to those investigating adverse events during adulthood or any time in life. Note that only three studies included a psychiatric control group. Two of those studies reported slightly higher childhood trauma rates in CD (nos. 14 and 26), but the third failed to find this (no. 9). Only two studies compared CD directly to other somatoform disorders and found trauma rates to be higher in the former samples. Finally, it is important to realize that if 14–100% of CD patients have experienced trauma, the remaining 0–86% have not. Concluding, in general trauma rates (childhood or adult) appear to be higher in CD than in healthy or organic disorder control groups, but this is not universally so, and more research is needed to determine whether trauma rates in CD are elevated in comparison to other psychiatric disorders, too.

Life events

Of all studies focused on traumatic events reviewed in Table 13.1, only five studies reported separately on life events (adverse events, not necessarily traumatic, that have typically preceded the onset of symptoms: nos. 5, 11, 16, 30, and 31). Four of those studies reported significantly higher life event rates/scores for CD compared to a control group. The last one did not report comparison rates and did not test for statistical differences. Apart from the articles reviewed above, other studies have specifically focused on stressful life events. These studies are not reported in Table 13.1 as it reviews studies on trauma, but they will be briefly discussed below. In these studies life events are typically defined as “change” events that have occurred within a year prior to symptom onset or assessment time. They include changes in health, relationships, housing, or employment status. It is often found that CD patients have experienced more of such events than controls (Grattan-Smith et al., 1988; Binzer et al., 1997; Roelofs et al., 2005; Bodde et al., 2013). However, other studies failed to find this (e.g., Voon et al., 2010; Czarnecki and Hallett, 2012; Testa et al., 2012).

The relation between life events and CD seems to be not so clearcut. For example, one study (Binzer et al., 2004) found no group differences between psychogenic nonepileptic seizures (PNES) and epileptic seizures (ES) patients in the number of events in the 3 months prior to symptom onset, but did so when accounting for events during the whole year prior to symptom onset. One older study (House and Andrews, 1988) found that women with functional dysphonia had not experienced more stressful events in general, but did experience more "conflicts over speaking out." In another study, among 40 subjects with PNES compared to 60 without, Testa et al. (2012) found that PNES patients did not experience higher frequency or severity of stressful life events, although they did rate them as more distressing. Testing 54 patients with CD, Roelofs et al. (2005) did find a link between severity of life events and conversion symptoms. In addition and most critically, they showed that the relationship between childhood trauma and the severity of conversion symptoms was mediated by the occurrence of recent stressful events (Roelofs et al., 2005).

To conclude, a large percentage (14–100%) of CD patients report having experienced some traumatic event in their history. In addition, they also report relatively more recent stressful life events, that may mediate the link between trauma and CD. Although adverse life events may have occurred in a large number of CD patients, it is important to note that many other patients do not report trauma (0–86%) or stressful life events. Also, note that all studies relied on retrospective reports for measuring life adversities. Underreporting and overreporting may have biased the results.

OTHER VULNERABILITY FACTORS

Life adversity will not result in psychopathology in everyone: multiple factors will determine vulnerability (e.g., Belsky and Pluess, 2009). As risk factors for psychopathology, gender, socioeconomic status (SES), social support, personality and genetic factors have been identified (for an overview, see Rolf and Garmezy, 1992). In CD, some of these factors have been confirmed to play a role. In particular, female gender (Bodde et al., 2009) and low SES (Stefánsson et al., 1976) have been identified as predisposing risk factors. In addition, avoidant and borderline personality have been reported as risk factors (e.g., Reuber et al., 2004; Bodde et al., 2009), though only once (to our knowledge) in a prospective study (Binzer et al., 2004). Genetic factors are still unknown, although scarce evidence in mixed samples of somatoform disorders seems to indicate a role for serotonergic pathway genes (Hennings et al., 2009; Koh et al., 2011). As for precipitating factors, context variables as social support are relevant to take into account when considering the effects of adverse events (e.g., Mehnert et al., 2010). Unfortunately, in only one of the above-reported studies (Table 13.1) was social support taken into account (no. 4). Importantly, this study found social support to be lower in the CD sample.

In sum, besides life adversities, other predisposing and precipitating factors (such as gender, SES, genetics, social context) as well as their interactions should be considered. There is a lack of studies that have tested these factors and their interactions in CD. Nevertheless it is relevant to consider how adversities could lead to CD. The next section describes relevant cognitive and neurobiologic models of conversion symptoms and explores whether and how adverse life events can be linked to conversion symptomatology.

EXPLANATORY MODELS

Historic models of conversion and dissociation

Freud and Breuer) were the first to propose that hysteric symptoms could arise when affect related to psychologic stress factors or conflicts was "converted" into somatic symptoms (Breuer and Freud, 2009). Those stress factors or conflicts could be subconscious and were assumed to be often sexual or aggressive in nature. Although very influential, this theory and later modifications of it have been criticized for circular reasoning and for being untestable (e.g., Miller, 1999; Brown, 2004). Also, evaluation of the original conversion hypothesis does not suggest that psychologic distress symptoms are successfully converted into somatic symptoms: CD patients still experience a lot of psychologic discomfort (e.g., Lader and Sartorius, 1968; Brown, 2004).

Instead of "direct" conversion as described by Freud, Janet proposed dissociation as a mechanism that could explain conversion symptoms (Janet, 1907). According to dissociation theories, sensory processing that occurs via different sensory channels can be modified via attentional mechanisms that may block processing of some channels, but not the processing of other sensory channels. Later modifications of dissociation theory by Kihlstrom (1992) and Oakley (1999) integrated these attentional accounts with current hierarchic cognitive models (Norman and Shallice, 1986) and suggested that CD is an autosuggestive disorder that may lead to dissociative symptoms that are characteristic of conversion but also of hypnotic states (e.g., Oakley, 1999; Bell et al., 2010). Original conversion and dissociation accounts have been largely abandoned, but dissociation as a descriptive cognitive phenomenon referring to state, characterized by a dissociation between implicit and explicit information processing, still plays an important role in many modern explanatory models of CD.

Cognitive hierarchic models

One of the first cognitive hierarchic models of CD was described by Brown (2004). Like Oakley (1999), Brown based his model on the hierarchic attention model of Norman and Shallice (Norman and Shallice, 1986; Shallice, 1988), adopting the view that there is a supervisory attentional system and a more automated "contention-scheduling" system that generates reflex-like actions based on learned schemata. Schemata or representations on motor and/or sensory functions would be altered in CD. This would lead to altered allocation of attentional function to certain sensory states, resulting in activation of dysfunctional hypotheses about sensory and motor outcome (e.g., "I will not be able to move my leg"; "I'll experience pain in that leg") and eventually feeding back into dysfunctional mental representations. Brown called these altered mental representations mental "rogue" representations. He proposed that these "rogue" representations could be formed through various routes, including autosuggestion (see Oakley, 1999), the presence of examples or "models" in the environment, but also via earlier experiences (e.g., by re-experiencing physical symptoms initially experienced during trauma exposure). There is indeed accumulating evidence suggesting that attention can alter actual sensory processing, and that participants reporting medically unexplained somatic symptoms pay more attention to hypotheses they have about sensorimotor processes and are less responsive to actual sensory input (Bogaerts et al., 2008; Brown et al., 2010; Miles et al., 2011; Pareés et al., 2012; Schaefer et al., 2012).

Building on this line of reasoning, Edwards et al. (2012) further specified the role of attentional processes on sensory gating in CD by applying a Bayesian computational view based on the free-energy theory of Friston et al. (2006). In this predictive coding model, neuronal prediction units predict the outcome of a particular sensory (perception) or motor system (action). Lower-order units feed back a prediction error if the expectation did not come true. According to the free-energy principle, the brain will always try to minimize prediction error. Therefore, the subject will alter his or her prediction ("prior"). The prediction error feeds back into the prediction system of the subject. In some situations, however, it makes more sense to change the motor action or the perception itself instead of the prior prediction. Now the prediction error feeds forward into motor action.

According to Edwards, these feedback and feedforward processes, that play a role in many situations, are disturbed in CD patients. A problem in feedback processes may, for example, arise when an individual experiences a "real" somatic symptom, for example, is not able to lift his or her hand for a moment. The person may start to belief that he or she will never be able to lift the hand and, instead of feeding forward the prediction error and changing the outcome (lifting the hand), it is fed back and the prior is changed (paralysis belief). Feedforward problems in CD may arise when priors about outcome of behavior or sensation are given too much attention. To prevent prediction error, motor action or perception is adapted to what was expected. This, in turn, will reinforce the prior and result in a self-sustaining circle. Although this Bayesian predictive coding theory is particularly valuable in specifying how attention beliefs may eventually lead to actual symptoms in CD, it does not specify how stress may amplify this system.

Neurobiologic stress models

Neurobiologic stress models (Vuilleumier, 2005; Roelofs and Spinhoven, 2007; Kozlowska, 2013) of CD propose a link between major biologic stress/emotion systems and somatic symptoms. For example, Kozlowska (2005) applied the somatic marker theory of Damasio (1994) to explain conversion symptoms. According to this hypothesis, some emotional stimulus activates neural emotion-processing systems, which leads directly to a "body map," a representation of body state. Such a body map becomes part of an "as-if" loop, in which the body state associated with some emotion is directly produced, without real evaluation of the body. This system could be distorted in CD patients in such a way that false associations between emotional and bodily states arise in the as-if loop. For example, it may be that there is some innate or learned link between an emotion and a motor response (e.g., trembling or freezing), and an automatically processed emotion may involuntarily give rise to that same response or body map, immediately resulting in, for example, trembling or freezing. Accordingly, increased emotional reactivity (Roberts and Reuber, 2014) could give rise to a high motor readiness to respond with tremors or spasms to emotional stimuli (Kozlowska, 2013).

Vuilleumier et al. (2001) indeed found altered function of striatothalamocortical brain circuits during sensory stimulation in patients with CD. These circuits are known to be implicated in intentional movement and sensory processing and receive input from the limbic (emotional) structures in the brain (Vuilleumier, 2005). The authors proposed that affective and stress-related factors can result in conversion symptoms through reflexive alertness processes and interactions between limbic and sensorimotor networks. Although these neural circuits may provide a mechanism through which emotions may affect sensory and/or motor representations in CD, few studies have attempted to integrate these findings with findings on neurobiologic stress systems such as

the hypothalamic–pituitary–adrenal (HPA) axis or on cognitive processes in CD. The next sections will describe cognitive dysfunctions in CD and the way these may interact with stress factors and alterations in major neurobiologic stress systems such as the HPA axis.

Cognitive dysfunction in CD: empiric support

Studies on general neuropsychologic function in CD have not resulted in a clear explanatory model of CD. Many studies have reported neuropsychologic impairments in CD patients (e.g., Kalogjera-Sackellares and Sackellares, 1999; Drane et al., 2006; Binder and Salinsky, 2007; Almis et al., 2013; Bodde et al., 2013; Demir et al., 2013). Some studies find intelligence to be somewhat lower, too (Kalogjera-Sackellares and Sackellares, 1999; Van Beilen et al., 2010). However, these impairments are not worse in psychogenic neurologic disorders than in organic neurologic disorders (Binder et al., 1998; Van Beilen et al., 2010; Heintz et al., 2013).

Evidence for abnormalities in voluntary attention is more unequivocal. Impairment in higher-order, voluntarily controlled attention came, for example, from a study using exogenous and endogenous cueing tasks, showing that patients with CD have reduced attentional guiding by endogenous cues, indicative of impaired voluntary attention, but show no problem in automatic exogenous cueing of attention (Roelofs et al., 2003; Pareés et al., 2013).

Self-focused attention, in particular, may be enhanced in patients with motor CD. Several event-related potential and functional magnetic resonance studies have shown increased action monitoring and heightened prefrontal cortex activity (mainly stemming from the anterior cingulate and medial prefrontal cortices) during voluntary motor processes, consistent with amplified self-directed attention to affected limbs in CD (Roelofs et al., 2006; De Lange et al., 2008, 2010; Cojan et al., 2009; Van Beilen et al., 2010). CD patients also show reduced motor excitability during explicit motor performance compared to implicit motor tasks (Liepert et al., 2011). This may explain why several studies have indicated that, whereas mental movements can be elicited implicitly (by task requirements), there are problems when (mental) movements are under explicit control (Roelofs et al., 2002b; Roelofs et al., 2003; Pareés et al., 2013). Interestingly, and in line with the role of self-focused attention in CD, attentional distraction can reduce motor conversion symptoms (e.g., Monday and Jankovic, 1993; Lang et al., 1995; McAuley and Rothwell, 2004; Kumru et al., 2007; Wolfsegger et al., 2013; Stins et al., 2015). A next question to address is whether and how stress and neurobiologic stress reactions can alter cognitive processes in patients with CD.

Stress and cognitive function in CD

There is increasing evidence that patients with CD show increased attentional and memory processing of emotional stimuli. In a study assessing attention to subliminally presented negative, positive, and neutral face stimuli, patients with PNES displayed a clear attentional bias specific for negative (angry-looking) faces. In addition, the magnitude of this bias was positively correlated to trauma rates (Bakvis et al., 2009a). There are also indications for increased startle responses (Seignourel et al., 2007) and increased amygdalar activity in reaction to emotional faces in CD (Voon et al., 2010). Moreover, processing threat stimuli was associated with altered connectivity between the amygdala and motor areas in the brain (Voon et al., 2010; Aybek et al., 2014). Aybek et al. tested CD patients during reactivation of adverse memories, from which patients were or were not able to escape through developing physical symptoms (as judged by independent raters). During reactivation of escape memories versus nonescape memories, CD patients showed increased activity in the left dorsolateral prefrontal cortex and decreased activity in the left hippocampus, accompanied by increased activity in right supplementary motor area and temporoparietal junction. These findings were taken to suggest that abnormal emotion and memory control are associated with alterations in symptom-related motor planning in CD.

Another line of evidence suggests altered stress sensitivity in major neuroendocrine and arousal systems in CD. For example, PNES patients were found to have lower heart rate variability, which is taken as an indication of hyperarousal (Bakvis et al., 2009b). In addition, PNES patients were found to show higher baseline cortisol levels (Mehta et al., 1994; Tunca et al., 2000; Bakvis et al., 2010a), which may be related to the experience of trauma (Bakvis et al., 2009b, 2010a). Based on these and other findings, several literature reviews have suggested that CD is associated with a general state of hyperarousal (Lang and Voon, 2011; Van der Kruijs et al., 2011; Reuber and Mayor, 2012; Kozlowska, 2013). The question arises whether these stress mechanisms function independently of cognitive mechanisms in the production of CD, or whether a more integrative account should be proposed.

TOWARDS AN INTEGRATION

To our knowledge, only few studies have actually tested the premise that alterations in cognitive functions relate to heightened stress sensitivity in the case of CD.

Bendefeldt et al. (1976) were among the first to explore whether neuropsychologic functioning of CD patients altered after stress induction. In both stress and nonstress conditions, CD patients (compared to clinical controls) scored worse on measures of controlled attention, but performance was even worse in the stress condition. This first finding thus suggested that there may be an amplifying effect of stress on attentional processes relevant for CD. Recent findings confirmed this hypothesis. Bakvis et al. (2010b) found that PNES patients, compared to healthy controls, showed more working-memory interference when exposed to emotional stimuli and this working-memory deficit was stronger after stress induction. Also, heightened cortisol stress reactivity predicted the magnitude of this deficit in CD patients. Another study on attentional function showed that basal cortisol levels predict attentional bias to angry-face cues in CD patients, type PNES (Bakvis et al., 2009a). Thus, there is emerging evidence for a link between neurobiologic stress sensitivity and altered attentional function in CD.

How can we integrate those findings? Based on our earlier model of medically unexplained somatic symptoms (Roelofs and Spinhoven, 2007), as well as the current review, we suggest that life adversities may affect medically unexplained somatic symptoms via at least two routes: via associative learning and via their effect on relevant neurobiologic stress systems. Below we detail these routes.

Associative learning leads to altered mental representations

As for the first, somatosensory experiences during traumatic events may directly be linked to affective states and later activation of those affective states may reactivate the somatosensory experience (or "body maps": Kozlowska, 2005, or mental symptom representations: Brown, 2004) that in turn leads to symptom expectations (or priors, Edwards et al., 2012; see Fig. 13.1, route a).

Life events lead to alterations in neurobiologic stress systems

As for the second, life adversities may lead to alterations in the responsiveness of major stress system like the HPA axis (e.g., Sapolsky, 1996; Anisman et al., 1998; McEwen, 1998; Elzinga et al., 2003). Scarce studies in CD show a similar relation between early trauma and HPA axis hyperresponsiveness (Bakvis et al., 2010a, b; Fig. 13.1, route b). Note that HPA axis hyperresponding may also arise from different factors, such as temperament or genetic predisposition.

Stress and stress-induced cortisol increases may in turn affect attentional processes in CD (Fig. 13.1, route b), in particular by increasing attention to emotional stimuli (Bakvis et al., 2009a, b, 2010a; Grisham et al., 2014). These findings can be combined with findings on higher arousal, as described above; it was found that individuals who frequently report physical symptoms experience more symptoms in reaction to negative stimuli only when their arousal is high (Constantinou et al., 2013). Stress has also been shown to increase action monitoring and self-focused attention, while impairing voluntary attention (Wegner and Giuliano, 1980; Vedhara et al., 2000; Braunstein-Bercovitz, 2003; Hsu et al., 2003; Liston et al., 2006, 2009; Roelofs et al., 2006), which may in turn worsen (motor) performance (Baumeister and Steinhilber, 1984; Schücker et al., 2013). Such mechanisms may be relevant because CD has consistently been associated with increased self-focused attention (Roelofs et al., 2006; De Lange et al., 2007, 2008, 2010; Cojan et al., 2009) and because self-focused attention may lead to increased symptom perception (Brown, 2004). The Bayesian predictive coding model by Edwards et al. (2012) offers a valuable explanatory framework detailing how such an increase in symptom perception occurs through enhancement of the precision of the predicted sensory or motor outcome (Fig. 13.1 route c), that in turn leads to perception of sensory and motor symptoms (Fig. 13.1 route d).

Concluding, we extend cognitive models where life adversities lead to abnormal priors (through representations and beliefs, route a) with the notion that life events may also lead to changes in neurobiologic stress systems, such as the HPA axis, that in turn amplify the attention processes that are at the core of the symptoms (route b). When given too much attention, priors may become

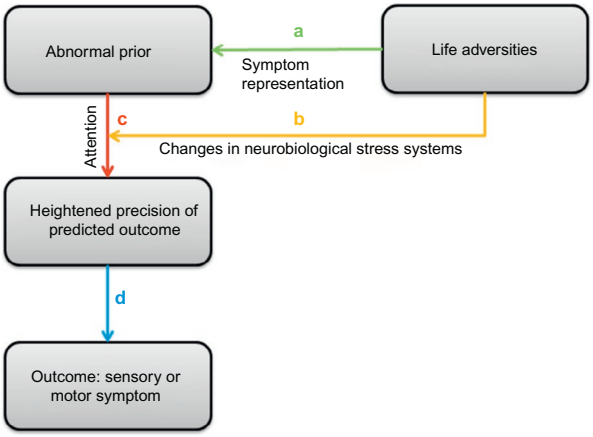

Fig. 13.1. Schematic illustration of the proposed mechanisms by which life adversities may affect conversion disorder symptoms. The tentative model is based on the integration of neurobiological stress models, associative learning models, and predictive coding models of medically unexplained somatic symptoms.

overly precise (route c) and act in a self-fulfilling manner, leading to sensory or motor symptoms (route d).

SUMMARY AND RESEARCH AGENDA

In sum, from the literature review on life adversities in CD, we can conclude that CD is associated with slightly increased trauma reports. A substantial proportion of CD patients (ranging from 0% to 86%) do not report having experienced traumatic events in their history. However, in those studies where trauma reports were linked to symptom severity in CD, it was consistently found that the presence and severity of life adversities were related to greater symptom severity in CD.

Therefore, we propose that explanatory models of CD should account for mechanisms that may explain symptoms without a role of trauma history as well as for mechanisms that may be amplified by trauma and alterations in stress-responsiveness. The present chapter provides such integration, by reviewing current major cognitive models and by integrating the most relevant Bayesian predictive coding model by Edwards et al. (2012) on the role of attention and beliefs in CD with emerging evidence on the relation between stress and attention functioning in CD. We propose that stress and stress-related factors may affect symptom beliefs (via learning mechanisms) and may affect attentional mechanisms (partly via its effect on neurobiologic stress systems).

Future research should directly test premises of Bayesian feedforward and feedback mechanisms proposed for CD and should test whether stress can amplify both these processes. There is a great need for large-cohort longitudinal studies on the development and maintenance of medically unexplained somatic symptoms, including CD. Such studies are needed to determine predisposing, precipitating, and consequential factors that affect the development and maintenance of the disorder. As regards predisposing factors, not only trauma history but also demographic, personality, genetic, neurobiologic, and context variables should be taken into account. As regards precipitating factors, cognitive processes (attention, memory, and belief biases) should be directly tested and monitored over time. The present chapter did not cover consequential factors, such as change of context due to having CD, although it acknowledges that those factors should be monitored as well to get a complete picture.

Finally, in the presented model attention processes are considered to be central to CD. The role of attention in interaction with stress factors may not only be of mechanistic value. The clinical relevance of each of the processes could be investigated in intervention studies where the proposed underlying components of CD are treated in isolation. For example, initial evidence shows that attention distraction can reduce conversion symptoms momentarily. It would be important for future studies to integrate attentional, belief, and stress physiology assessments before and after treatment and to investigate whether these factors should be directly targeted in effective treatments for CD.

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