

# Medically Unexplained Symptoms Evidence Update



August 2017 (Quarterly)

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# Training Sessions 2017

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## August (12.00-13.00)

15th (Tues)	Interpreting Statistics
24th (Thurs)	Critical Appraisal

## September (13.00-14.00)

Fri 1st	Literature Searching
Mon 4th	Critical Appraisal
Tue 12th	Interpreting Statistics
Wed 20th	Literature Searching
Thu 28th	Critical Appraisal

## October (12.00-13.00)

Fri 6th	Interpreting Statistics
Mon 9th	Literature Searching
Tue 17th	Critical Appraisal
Wed 25th	Interpreting Statistics

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# Updates

**NICE** National Institute for  
Health and Care Excellence

## [Epidemiology of functional gastrointestinal disorders in children and adolescents: A systematic review](#)

Source: [PubMed](#) - 07 June 2017 - Publisher: World Journal Of Gastroenterology [Read Summary](#)

## [Sertraline 50mg film-coated Tablets - Summary of Product Characteristics \(SPC\) - \(eMC\)](#)

Source: [electronic Medicines Compendium - eMC](#) - 10 August 2017

This is just the first eMC Summary of Product Characteristics from your search. [See all](#)



No Relevant Evidence

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## [Factitious disorder imposed on self \(Munchausen syndrome\)](#)

- [INTRODUCTION](#)
- [EPIDEMIOLOGY](#)
- [PATHOGENESIS](#)
- [CLINICAL FEATURES](#)
- [ASSESSMENT](#)
- [DIAGNOSIS](#)
- [DIFFERENTIAL DIAGNOSIS](#)
- [MANAGEMENT](#)
- [PROGNOSIS](#)
- [FACTITIOUS DISORDER IMPOSED ON ANOTHER](#)
- [SUMMARY AND RECOMMENDATIONS](#)

Literature review current through: Jul 2017. | This topic last updated: Jan 15, 2016.

## [Medical child abuse \(Munchausen syndrome by proxy\)](#)

- [INTRODUCTION](#)
- [TERMINOLOGY](#)
- [EPIDEMIOLOGY](#)
- [CLINICAL MANIFESTATIONS](#)

- [DIAGNOSTIC EVALUATION](#)
- [DIFFERENTIAL DIAGNOSIS](#)
- [INDICATIONS FOR CONSULTATION WITH A MULTIDISCIPLINARY CHILD ABUSE TEAM](#)
- [MANAGEMENT](#)
- [PROGNOSIS](#)
- [SUMMARY](#)

Literature review current through: Jul 2017. | This topic last updated: Aug 11, 2016.

### **Psychogenic purpura (Gardner-Diamond syndrome)**

- [INTRODUCTION](#)
  - [Psychiatric conditions and malingering](#)
    - [- Munchausen syndrome](#)

Literature review current through: Jul 2017. | This topic last updated: Feb 10, 2017.

### **Factitious diarrhea: Clinical manifestations, diagnosis, and management**

- [INTRODUCTION](#)
- [EPIDEMIOLOGY](#)
- [CLINICAL MANIFESTATIONS](#)
- [DIAGNOSIS](#)
- [DIFFERENTIAL DIAGNOSIS](#)
- [MANAGEMENT](#)
- [SOCIETY GUIDELINE LINKS](#)
- [SUMMARY AND RECOMMENDATIONS](#)

Literature review current through: Jul 2017. | This topic last updated: Aug 14, 2017.

### **Conversion disorder in adults: Terminology, diagnosis, and differential diagnosis**

- [INTRODUCTION](#)
- [TERMINOLOGY](#)
- [DIAGNOSIS](#)
- [DIFFERENTIAL DIAGNOSIS](#)
- [SUMMARY](#)

Literature review current through: Jul 2017. | This topic last updated: Jun 11, 2017.

### **Factitious hypoglycemia**

- [INTRODUCTION](#)
- [ETIOLOGY OF FACTITIOUS HYPOGLYCEMIA](#)
- [CLINICAL CHARACTERISTICS](#)
- [DIAGNOSIS](#)
- [TREATMENT](#)
- [SOCIETY GUIDELINE LINKS](#)
- [INFORMATION FOR PATIENTS](#)
- [SUMMARY AND RECOMMENDATIONS](#)

Literature review current through: Jul 2017. | This topic last updated: Oct 20, 2016.



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## Database Articles

Below is a selection of articles related to medically unexplained symptoms that were recently added to the healthcare databases.

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### **Achieving a balance between the physical and the psychological in headache**

**Author(s):** Underwood R.; Kennis K.; Ridsdale L.

**Source:** British Journal of General Practice; Aug 2017; vol. 67 (no. 661); p. 374-375

**Publication Type(s):** Note

Available in full text at [British journal of general practice: the journal of the Royal College of General Practitioners \[Br J Gen Pract\]](#) NLMUID: 9005323, The - from EBSCOhost

### **Helpful strategies for GPS seeing patients with medically unexplained physical symptoms: A focus group study**

**Author(s):** Aamland A.; Fosse A.; Malterud K.; Ree E.; Abildsnes E.

**Source:** British Journal of General Practice; Aug 2017; vol. 67 (no. 661)

**Publication Type(s):** Article

Available in full text at [British journal of general practice: the journal of the Royal College of General Practitioners \[Br J Gen Pract\]](#) NLMUID: 9005323, The - from EBSCOhost

**Abstract:**Background Patients with long-lasting and disabling medically unexplained physical symptoms (MUPS) are common in general practice. GPS have previously described the challenges regarding management and treatment of patients with MUPS. Aim To explore GPS' experiences of the strategies perceived as helpful when seeing patients with MUPS. Design and setting Three focus group interviews with a purposive sample of 24 experienced GPS were held in southern Norway. Method Discussions were audiotaped and transcribed. Systematic text condensation was used for analysis. Results Several strategies were considered helpful during consultations with patients with MUPS. A comprehensive outline of the patient's medical past and present could serve as the foundation of the dialogue. Reviewing the patient's records and sharing relevant information with them or conducting a thorough clinical examination could offer 'golden moments' of trust and common understanding. A very concrete exchange of symptoms and diagnosis interpretation sometimes created a space for explanations and action, and confrontations could even strengthen the alliance between the GP and the patient. Bypassing conventional answers and transcending tensions by negotiating innovative explanations could help patients resolve symptoms and establish innovative understanding. Conclusion GPS use tangible, down-To-earth strategies in consultations with patients with MUPS. Important strategies were: Thorough investigation of the patient's symptoms and story; sharing of interpretations; and negotiation of different explanations. Sharing helpful strategies with colleagues in a field in which frustration and dissatisfaction are not uncommon can encourage GPS to develop sustainable responsibility and innovative solutions. Copyright © British Journal of General Practice.

### **The role of incongruence between the perceived functioning by patients and clinicians in the detection of psychological distress among functional and motor digestive disorders**

**Author(s):** Rodriguez-Urrutia A.; Eiroa-Orosa F.J.; Accarino A.; Malagelada C.; Azpiroz F.

**Source:** Journal of Psychosomatic Research; Aug 2017; vol. 99 ; p. 112-119

**Publication Type(s):** Article

**Abstract:** Objectives Previous research on gastrointestinal and other medical conditions has shown the presence of incongruence between self- and clinician-reported functioning and its relation with psychopathology. The main objective of this study was to test whether inconsistencies between clinician- and self-assessed functionality can be used to detect psychopathology among patients diagnosed of motor or functional gastrointestinal disorders. Methods One hundred and three patients from a gastroenterology inpatient unit were included in this study. All patients underwent clinical assessment, including intestinal manometry, Rome III criteria for functional gastrointestinal disorders, and psychological and psychiatric evaluation. Patients with suspected gastroparesis underwent a scintigraphic gastric emptying test. Definitive diagnoses were made at discharge. Results Patients with higher levels of incongruence differed in various sociodemographic (age, educational level, work activity and having children) and psychopathological (all SCL-90-R subscales except anxiety and hostility) characteristics. Using general lineal models, incongruence was found to be the variable with stronger relations with psychopathology even when controlling for diagnosis. Interactions were found between incongruence and diagnosis reflecting a pattern in which patients with functional disorders whose subjective evaluation of functioning is not congruent with that of the clinician, have higher levels of psychopathology than patients with motor disorders. Conclusions Incongruence between clinician and self-reported functionality seems to be related to higher levels of psychopathology in patients with functional disorders. These findings underscore the need for routine psychosocial assessment among these patients. Gastroenterologists could use the concept of incongruence and its clinical implications, as a screening tool for psychopathology, facilitating consultation-liaison processes. Copyright © 2017

### **The cross-sectional relation between medically unexplained physical symptoms (MUPS) and the Cortisol Awakening Response**

**Author(s):** Claassen-van Dessel N.; van der Wouden J.C.; van der Horst H.E.; Dekker J.

**Source:** Journal of Psychosomatic Research; Aug 2017; vol. 99 ; p. 130-136

**Publication Type(s):** Article

**Abstract:** Objectives We aimed to assess the cross-sectional relation between levels of cortisol and specific symptom clusters, symptom severity and duration of symptoms in patients with medically unexplained physical symptoms (MUPS). Methods Baseline data of a cohort of MUPS patients were used. We chose the Cortisol Awakening Response (CAR) as a cortisol parameter, using saliva samples. We used confirmatory factor analysis for the identification of 4 specific symptom clusters: (1) gastro-intestinal symptoms; (2) pain; (3) cardio-pulmonary symptoms; and (4) fatigue. For this factor analysis we used the Physical Symptom Questionnaire (PSQ), which assesses the occurrence and frequency of 51 physical symptoms. Symptom severity was measured with the Patient Health Questionnaire-15 (PHQ-15). Duration of symptoms was based on self-reported duration of top 3 symptoms. We performed multiple linear regression to assess relations between CAR and individual factor scores on symptom clusters, symptom severity and duration of symptoms. Results Data from 296 patients (76% female) were included in the analyses. The majority of patients suffered from symptoms in multiple organ systems. Factor analysis confirmed that the model with 4 symptom clusters fitted our data. For the total study population, we found no significant relation between CAR and participants' factor scores on any of the symptom clusters. We also found no significant relations between CAR and severity or duration of symptoms. Conclusion Our results suggest that

within a heterogeneous MUPS population there is no relation between CAR and symptom severity and duration. However, more studies are needed to confirm our findings. Copyright © 2017 Elsevier Inc.

### **Evaluating challenges for improving medically unexplained symptoms in US military veterans via provider communication**

**Author(s):** Phillips L.A.; McAndrew L.; Laman-Maharg B.; Bloeser K.

**Source:** Patient Education and Counseling; Aug 2017; vol. 100 (no. 8); p. 1580-1587

**Publication Type(s):** Article

**Abstract:** Objectives Medically unexplained symptoms (MUS) are common, with particularly high rates observed in military veterans. Effective patient-provider-communication is thought to be a key aspect of care; however there have been few empirical studies on the association between communication and outcomes for patients with MUS. We evaluate whether discussing veterans' MUS-illness representations and good interpersonal skills have the potential to promote MUS-treatment adherence and improvement. Methods Veterans experiencing MUS (n = 204) reported on their primary care providers' communication about illness representations and interpersonal skills; correlation, regression, and bootstrap-mediation analyses were conducted to test hypotheses regarding veteran-reported outcomes. Main outcomes included satisfaction with the provider, MUS-treatment adherence, intentions to adhere, and expectations for MUS improvement. Results Veterans reported infrequent discussion of MUS illness representations but high degrees of provider interpersonal skills. Communication regarding patients' illness representations and treatment expectations was significantly related to treatment adherence and adherence intentions; provider interpersonal skills were not. Both were related to veteran satisfaction. Conclusions and practice implications Providers' interpersonal skills may be important in chronic illness contexts, such as MUS, by contributing to satisfaction with the provider. The current study suggests that providers may better promote MUS-treatment adherence through discussing MUS illness representations and treatment expectations. Copyright © 2017 Elsevier B.V.

### **Conversion disorder or multiple sclerosis?**

**Author(s):** Frazzetto A.; Tibrewal P.; Dhillon R.; Bastiampillai T.; Harris J.

**Source:** Asian Journal of Psychiatry; Aug 2017; vol. 28 ; p. 177-178

**Publication Type(s):** Letter

### **Contemporary Reviews in Critical Care Medicine: Anaphylaxis.**

**Author(s):** LoVerde, Daniel; Iweala, Onyinye I; Eginli, Ariana; Krishnaswamy, Guha

**Source:** Chest; Aug 2017

**Publication Type(s):** Journal Article Review

**Abstract:** Anaphylaxis is a systemic, life threatening disorder triggered by mediators released by mast cells and basophils activated via allergic (IgE-mediated) or non-allergic (non-IgE-mediated) mechanisms. It is a rapidly evolving, multisystem process involving the integumentary, pulmonary, gastrointestinal and cardiovascular systems. Anaphylaxis and angioedema are serious disorders that can lead to fatal airway obstruction and culminate in cardiorespiratory arrest resulting in hypoxemia and/or shock. Often, these disorders can be appropriately managed in an outpatient setting. However, these conditions can be severe enough to warrant evaluation of the patient in the emergency department and in some cases, hospitalization and management in an intensive care unit (ICU). Recent reports suggest that underdiagnosis and undertreatment of anaphylaxis are common.

Several new syndromes have been described recently including bird-egg, pork-cat, delayed allergy to mammalian meat and a diverse group of mast cell activation disorders. Conditions such as postural orthostatic tachycardia syndrome (POTS), Carcinoid syndrome, Munchausen's stridor and factitious anaphylaxis can present similarly and need to be included in the differential diagnosis. Anaphylaxis is a clinical diagnosis but plasma tryptase and urinary histamine levels are often elevated, allowing diagnostic confirmation. However, diagnostic testing should not delay treatment as results may not be immediately available. The sine qua non of treatment is avoidance of any known triggers and epinephrine, which should never be delayed if this disorder is suspected. Secondary treatments include fluids, bronchodilators, antihistamines and glucocorticoids. Patients with cardiopulmonary arrest, airway or vascular compromise require mechanical ventilation, vasopressors and other advanced life support in the ICU.

### **Munchausen by Proxy: A Qualitative Investigation into Online Perceptions of Medical Child Abuse.**

**Author(s):** Anderson, Anoushka P A; Feldman, Marc D; Bryce, Joanne

**Source:** Journal of forensic sciences; Aug 2017

**Publication Type(s):** Journal Article

**Abstract:**In Munchausen by proxy (MBP) maltreatment, increasingly termed "medical child abuse" (MCA), a caregiver fabricates or induces illness in another. The perpetrator's goal for the behavior is to meet personal emotional needs by forcing unnecessary or misguided medical or psychological treatment. Generally, a mother is the perpetrator and her child is the victim. There is a serious lack of research into most aspects of MCA, and this study is the first to utilize the anonymity of an Internet forum to investigate victims' first-hand experiences of, and the public's opinions about, suspected and confirmed MCA. Three-hundred and fifty-six posts by 348 members were explored and coded using formal qualitative content analysis. By accessing an open-thought online forum, this paper acquired information regarding social perceptions about the nonperpetrating partners who are unaware of the maltreatment; the disturbing and counterintuitive phenomenon of MCA itself; and the resistance often faced by those who attempt to report it.

### **Functional Somatic Syndrome: Assessment and Management.**

**Author(s):** Graver, Christopher J

**Source:** The Journal of the American Osteopathic Association; Aug 2017; vol. 117 (no. 8); p. 511-519

**Publication Type(s):** Journal Article

**Abstract:**Functional somatic syndrome (FSS) occurs in as many as 30% of patients in general medical practice, but it is infrequently a topic of formal instruction. Many physicians feel uncomfortable with medically unexplained symptoms and are unfamiliar with how to assess or manage them. Traditional medical approaches can be ineffective and can contribute to iatrogenic or adverse physiologic effects in patients. Physicians treating patients with FSS should not only consider standard medical tests, but they should also try to gain a deeper behavioral understanding of the mind-body connections that underlie the presenting symptoms. Osteopathic physicians, with their emphasis on holistic patient care, are in a key position to treat patients with FSS. This review provides a brief recapitulation of the literature and illustrates key factors in the assessment and management of FSS.

### **Identifying a borderline personality disorder prodrome: Implications for community screening.**

**Author(s):** Stepp, Stephanie D; Lazarus, Sophie A

**Source:** Personality and mental health; Aug 2017; vol. 11 (no. 3); p. 195-205

**Publication Type(s):** Journal Article

**Abstract:** Elucidating early signs and symptoms of borderline personality disorder (BPD) has important implications for screening and identifying youth appropriate for early intervention. The purpose of this study was to identify dimensions of child temperament and psychopathology symptom severity that predict conversion to a positive screen for BPD over a 14-year follow-up period in a large, urban community sample of girls ( $n = 2\,450$ ). Parent and teacher reports of child temperament and psychopathology symptom severity assessed when girls were ages 5-8 years were examined as predictors of new-onset BPD cases when girls were ages 14-22 years. In the final model, parent and teacher ratings of emotionality remained significant predictors of new-onset BPD. Additionally, parent ratings of hyperactivity/impulsivity and depression severity, as well as teacher ratings of inattention severity, were also predictive. Results also revealed that elevations in these dimensions pose a notable increase in risk for conversion to BPD over the follow-up period. Supplementary analyses revealed that with the exception of parent-reported depression severity, these same predictors were associated with increases in BPD symptom severity over the follow-up period. These findings suggest BPD onset in adolescence and early adulthood can be detected from parent and teacher reports of temperament and symptom severity dimensions assessed in childhood. The identification of this prodrome holds promise for advancing early detection of children at risk prior to the development of the full-blown disorder. Copyright © 2017 John Wiley & Sons, Ltd.

#### **Assessment of a Person-Level Risk Calculator to Predict New-Onset Bipolar Spectrum Disorder in Youth at Familial Risk.**

**Author(s):** Hafeman, Danella M; Merranko, John; Goldstein, Tina R; Axelson, David;

**Source:** JAMA psychiatry; Aug 2017; vol. 74 (no. 8); p. 841-847

**Publication Type(s):** Journal Article

**Abstract:** Importance Early identification of individuals at high risk for the onset of bipolar spectrum disorder (BPSD) is key from both a clinical and research perspective. While previous work has identified the presence of a bipolar prodrome, the predictive implications for the individual have not been assessed, to date. Objective To build a risk calculator to predict the 5-year onset of BPSD in youth at familial risk for BPSD. Design, Setting, and Participants The Pittsburgh Bipolar Offspring Study is an ongoing community-based longitudinal cohort investigation of offspring of parents with bipolar I or II (and community controls), recruited between November 2001 and July 2007, with a median follow-up period of more than 9 years. Recruitment has ended, but follow-up is ongoing. The present analysis included offspring of parents with bipolar I or II (aged 6-17 years) who had not yet developed BPSD at baseline. Main Outcomes and Measures This study tested the degree to which a time-to-event model, including measures of mood and anxiety, general psychosocial functioning, age at mood disorder onset in the bipolar parent, and age at each visit, predicted new-onset BPSD. To fully use longitudinal data, the study assessed each visit separately, clustering within individuals. Discrimination was measured using the time-dependent area under the curve (AUC), predicting 5-year risk; internal validation was performed using 1000 bootstrapped resamples. Calibration was assessed by comparing observed vs predicted probability of new-onset BPSD. Results There were 412 at-risk offspring (202 [49.0%] female), with a mean (SD) visit age of 12.0 (3.5) years and a mean (SD) age at new-onset BPSD of 14.2 (4.5) years. Among them, 54 (13.1%) developed BPSD during follow-up (18 with BD I or II); these participants contributed a total of 1058 visits, 67 (6.3%) of which preceded new-onset BPSD within the next 5 years. Using internal validation to account for overfitting, the model provided good discrimination between converting vs nonconverting visits (AUC, 0.76; bootstrapped 95% CI, 0.71-0.82). Important univariate predictors of outcome (AUC range, 0.66-0.70) were dimensional measures of mania, depression, anxiety, and mood lability; psychosocial functioning; and parental age at mood disorder. Conclusions and Relevance This risk calculator provides a practical tool for assessing the probability that a youth at familial risk for BPSD will develop new-onset BPSD within the next 5 years. Such a tool may be used by clinicians to inform

frequency of monitoring and treatment options and for research studies to better identify potential participants at ultra high risk of conversion.

### **Somatization disorder and somatoform symptoms in systematically studied survivors of 10 disasters.**

**Author(s):** Zhang, Gus; North, Carol S

**Source:** Annals of clinical psychiatry : official journal of the American Academy of Clinical Psychiatrists; Aug 2017; vol. 29 (no. 3); p. 182-190

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUND There is little agreement about the association of somatization with exposure to disaster trauma in the existing literature. METHODS Pre-disaster and post-disaster psychiatric disorders, somatization disorder, and individual somatoform (medically unexplained) symptoms were assessed with structured diagnostic interviews in 811 directly exposed survivors of 10 disasters. RESULTS Only 1 individual met criteria for post-disaster somatization disorder; there were no incident cases. Only 21% of all somatic symptoms reported were somatoform symptoms. Although 29% of the sample had  $\geq 1$  post-disaster somatoform symptoms, only 13% of the sample had any incident somatoform symptoms, and only 1.5% of the sample had  $> 1$ . CONCLUSION Somatization disorder is not an observed outcome of disaster. Incidence of individual somatoform symptoms is relatively uncommon and represents a construct that is distinct from somatization disorder. Such symptoms appear to represent nonspecific distress or endemic symptoms in the population and are not necessarily causally related to the disaster. The only studies that have identified somatization symptoms in relation to disaster have used nondiagnostic symptom checklists. As illustrated by the findings from this study, nondiagnostic symptom checklists do not adequately substitute for structured diagnostic instruments in assessment of somatoform psychopathology.

### **'Medically Unexplained Symptoms' - Diverting 5-Year Funding from Mental Health.**

**Author(s):** Blake, Nancy

**Source:** Positive Health; Aug 2017 (no. 240); p. 2-2

**Publication Type(s):** Periodical

Available in full text at [Positive Health](#) - from EBSCOhost

**Abstract:**The article focuses on the "Guidance for Commissioners of Services for People With Medically Unexplained Symptoms (MUS)," produced by the Joint Commissioning Panel for Mental Health. Topics covered include the belief that MUS is a widespread mental health problem, the definition of MUS as persistent bodily complaints for which examination does not reveal sufficient pathology and the conflict between the psychiatric and medical models of myalgic encephalomyelitis (ME).

### **Mind-body interactions: Autonomic and mitochondrial dysregulation play key roles in PBS/IC**

**Author(s):** Kullmann F.A.; Wolf-Johnston A.; Kanai A.; Shiva S.; Birder L.; Chelimsky T.; Rodriguez L.

**Source:** Neurourology and Urodynamics; Jul 2017; vol. 36

**Publication Type(s):** Conference Abstract

**Abstract:**Hypothesis/aims of study There is substantive evidence supporting a role for chronic stress in the development, maintenance and even enhancement of functional bladder disorders such as painful bladder syndrome/interstitial cystitis (PBS/IC). More than half of patients with PBS/IC report daily or constant pain and urinary frequency, which are exacerbated by stressful circumstances.

Stress can alter the sympathetic nervous system, whose activity is augmented in PBS/IC patients. While the etiology of functional disorders such as PBS/IC are not known, alterations in the bladder urothelium have been detected in both patients and animals diagnosed with PBS/IC. The urothelium not only forms a high-resistance barrier but also functions as an integral part of a 'sensory web' that can sense changes in their environment including those produced by chronic stress and via release of transmitters, can activate sensory nerves. There is exciting new evidence that mitochondrial dysfunction and oxidative stress have been implicated in chronic pain as well as autonomic dysregulation. In fact, mitochondrial dysfunction may also be a final common pathway in the pathophysiology of many diseases and disorders that are impacted by chronic stress. Recent evidence shows that individuals with chronic conditions have impairment in mitochondrial pathways. Our novel concept is that abnormal processing of chronic stress involving autonomic and mitochondrial dysregulation can negatively impact urothelial signalling, leading to altered sensations and pain in patients with PBS/IC. The aim of this study was to examine the influence of chronic stress and autonomic signalling on mitochondrial dysfunction in bladder urothelium. Study design, materials and methods This aim was investigated in an animal model consisting of a rat genetically predisposed to stress (Wistar Kyoto), exposed to psychological stress (chronic water avoidance or WAS). \* Female Wistar Kyoto rats (~200g; 3-4 month old) were exposed to WAS for 1h per day for 10 days and sacrificed on day 11 (versus handled groups as controls). \* To assess the impact of sympathetic signalling some rats were treated with guanethidine which depletes catecholamines (50 mg/kg, i.p.; every other day starting 2 days prior to WAS and throughout the WAS protocol) or the adrenergic (alpha1/alpha2) antagonist, phenoxybenzamine (2 mg/kg i.p. every day starting the day WAS protocol was initiated and throughout the WAS protocol). \* Bladders were collected from deeply anesthetized rats and utilized for cell culture and western blot per previously published methods. \* Cultured urothelial cells (UTC) from control and WAS rats were loaded with various intracellular dyes to examine functional (intracellular calcium or mitochondrial) responses. These included: fura-2AM (to measure intracellular calcium concentration,  $[Ca^{2+}]_i$ ), Dihydrorhodamine 123-DHR123 (to measure reactive oxygen species-ROS) and Tetramethylrhodamine methyl ester-TMRM (to measure mitochondria membrane potential,  $\Delta\psi$ ; Figure 1). Results Our findings reveal that WAS UTC exhibit a more depolarized  $\Delta\psi$  (~30%; decreased staining of the fluorescent indicator TMRM indicating a loss of viability; Figure 1) compared to control UTC. We also have evidence for higher baseline  $[Ca^{2+}]_i$  and inability to buffer  $[Ca^{2+}]_i$  after a stimulus (i.e., mitochondria uncoupler carbonyl cyanide-4-(trifluoromethoxy)phenylhydrazone or FCCP 5-10  $\mu$ M). Both guanethidine and phenoxybenzamine treatment of WAS animals normalized these alterations, supporting sympathetic nervous system involvement. There was no difference in basal ROS production in between WAS or control UTC. In contrast, ROS generation in response to stressors ( $H_2O_2$ ; 100  $\mu$ M) was significantly higher in WAS UTC. ROS were also generated in both control and WAS UTC by stimulation of alpha-ARs with phenylephrine (10  $\mu$ M) but not of beta-ARs with isoproterenol (1  $\mu$ M). We also find that chronic stress correlates with increased mucosal protein carbonylation as well as an increase in pAMPK often termed the metabolic gate keeper of the cell. In addition, we find an increase in mitofusin 2, which is thought to suppress cell proliferation and exert apoptotic effects. In all cases, we see a normalization in these targets in WAS animals treated with guanethidine or phenoxybenzamine. Interpretation of results While a number of factors are likely to contribute to chronic pain disorders, accumulating evidence suggests that altered cellular metabolism (i.e. mitochondrial functions) plays a key role. Mitochondrial uptake of calcium is important for cell survival and regulating release of mediators (such as ATP and ROS). The mitochondrial membrane potential  $\Delta\psi$  is an important parameter to assess the functional state of these organelles. Disturbances in  $\Delta\psi$  could result in alterations of cell metabolism, increased ROS production and altered calcium homeostasis; all of which were observed in WAS UTC. Mitochondria are responsible for the majority of oxygen consumption and represent the major source of reactive oxygen species in all cells including urothelium. Chronic stress (with augmented levels of stress mediators such as norepinephrine) can lead to a prolonged change in mitochondrial

properties. For example, the increase in ROS can result in protein carbonylation which is used as a biomarker for oxidative stress. In turn, WAS UTC may increase AMPK, which can activate anti-oxidant defenses. Many of these changes are prevented by treatment with agents that either deplete catecholamines (guanethidine) or block alphaadrenergic receptors (phenoxybenzamine) supporting a role for the sympathetic nervous system. Taken together, chronic stress results in persistent sympathetic-mediated effects that alter cellular (mitochondrial) memory, and this may result in changes to the urothelial barrier and signalling functions. Concluding message Chronic stress triggers a number of changes that ultimately can exacerbate or predispose to disease such as PBS/IC. These novel findings support the concept that abnormal processing of psychological stress involves a complex urothelial-cell signalling network which can be influenced by sympathetic and mitochondrial dysregulation. Mitochondria play an important role in controlling the life and death of a cell. Thus, our results have broad implications for functional pain syndromes and provide new information regarding how changes in mitochondrial functions in chronic stress may influence sensory signalling. Mitochondria targeted therapies may hold future promise to restore abnormal signalling in functional pain disorders such as PBS/IC and may contribute to improvement of symptoms in these patients.

### **A cohort study of caesarean section and interstitial cystitis/bladder pain syndrome**

**Author(s):** Chang K.M.; Lee M.H.; Wu H.; Lin H.; Wu S.

**Source:** Neurourology and Urodynamics; Jul 2017; vol. 36

**Publication Type(s):** Conference Abstract

**Abstract:** Hypothesis/aims of study Interstitial cystitis/bladder pain syndrome (IC/BPS) is a clinical syndrome of the bladder that is characterized by pelvic pain and urinary urgency and frequency in the absence of identifiable causes. Clinicians have noted that large proportions of patients with IC/BPS had a history of pelvic surgery. Delivery itself is a trauma to pelvic area that was one of the hypothetic causes of IC/BPS. We tried to investigate the causal effect of cesarean section on IC/BPS after controlling confounding factors in a large nationwide cohort study. Study design, materials and methods From the Longitudinal Health Insurance Database 2010 (LHID2010) which including 1 million insured patients, women received caesarean section or vaginal delivery between 2002 and 2013 were included. Women younger than 18 years or those with both methods of delivering were excluded. IC/BPS diagnosed before delivery or occurred within 1 year after delivery were also excluded. All included women were followed until the end of 2013 to detect the event of IC/BPS. The risk of IC/BPS during the study period in the caesarean section cohort was compared with the vaginal delivery cohort after controlling the confounding factors. Results The caesarean section rate in our database was 35.7%. Mean age of women was 30.60 $\pm$ 4.86 years, and 28.88 $\pm$ 4.67 years, in caesarean section cohort (n=20391) and the vaginal delivery cohort (n=36748), respectively. The comorbidities of pelvic inflammation disease, leiomyomata, adhesion fibromyalgia, depression, anxiety and systemic lupus erythematosus in the cesarean section cohort were significantly higher than in the vaginal delivery cohort (p<0.05). However, comorbidities of pelvic organ prolapse and stress incontinence in the vaginal delivery cohort were significantly higher than in the cesarean section cohort (p<0.05). After controlling age and the comorbidities, the risk of IC/BPS revealed no different between these two cohorts (HR 1.464, 95%CI 0.956-2.241). The interval between delivery and diagnosis of IC/BPS was also not significantly different between two cohorts (5.281  $\pm$  3.022 vs. 5.124  $\pm$  2.600 years, p=0.789). The incidence densities of IC/BPS were similar among two cohorts and the general population. Interpretation of results The Caesarean rate in our data was higher than the developed countries. The mean age of caesarean delivery was higher than vaginal delivery statistically. Caesarean section most likely related to pathological or functional disorders (such as inflammation, neoplasm or systemic diseases). In contrast, vaginal delivery most likely related to mechanical pelvic disorders (such as prolapse or incontinence). However, after controlling the comorbidities, the risk of IC/BPS revealed no different between these two cohorts. The developed

interval time of IC/BPS after delivery was not different between caesarean and vaginal delivery cohorts. There is no causal effect of IC/BPS by delivery due to the similar incidence densities with the general population in our database. Limitation: The effect of delivery frequency could not be accurately analyzed in LHID 2010. Concluding message The risk of IC/BPS was not affected by different birth delivery methods (caesarean section or vaginal delivery). Similar incidence densities with the general population revealed no causal effect by delivery. The developed interval time of IC/BPS after delivery also showed no different between caesarean and vaginal delivery cohorts. Other pelvic surgery should be further evaluated in the future.

### **Induced vomiting for attention seeking and secondary gain: An unusual cause of pseudo-resistant hypertension**

**Author(s):** Zakka K.; Bitar M.; Lakkis B.; Koubar S.H.

**Source:** JRSM Open; Jul 2017; vol. 8 (no. 8)

**Publication Type(s):** Article

Available in full text at [JRSM Open](#) - from Highwire Press

**Abstract:**In patients with complex psychosocial history presenting with resistant hypertension, observed therapy should be implemented early on to avoid unnecessary investigations and delayed diagnosis. Copyright © 2017, © The Author(s) 2017.

### **Determining the relationship of kinesiophobia with respiratory functions and functional capacity in ankylosing spondylitis**

**Author(s):** Er G.; Angin E.

**Source:** Medicine (United States); Jul 2017; vol. 96 (no. 29)

**Publication Type(s):** Article

**Abstract:**Ankylosing spondylitis (AS) is a common inflammatory rheumatic disease that affects the axial skeleton, causes inflammatory lower back pain, and structural and functional disorders, which affect quality of life negatively. The purpose of this study is to investigate the effects of kinesiophobia in AS on pulmonary function tests (PFTs) and functional performance. Thirty-one individuals with AS (n=19 male, n=12 female) who were suitable on the basis of the Modified New York (MNY) criteria were included in the study. The participants were given the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Bath Ankylosing Spondylitis Metrology Index (BASMI), in addition to the Tampa Scale for Kinesiophobia (TKS), PFTs, respiratory muscle strength, pain evaluation, and 6-minute walking test (6MWT). The mean values were found as the following: TKS, 41.65+/-7.59; pain visual analog scale (VAS) score, 6.23+/-2.86; forced vital capacity (%) (FVC), 75.35+/-17.92%; forced expiratory volume in first second (%) (FEV1), 73.45+/-17.20%; FEV1/FVC (%), 75.58+/-15.99%; peak expiratory flow (%) (PEF), 54,90+/-20.21%; forced expiratory flow at 25% to 75% (FEF25-75), 77.71+/-27.05%; maximal inspiratory pressure (MIP), 62.06+/-31.68; maximal expiratory pressure (MEP), 95.94+/-36.60; 6MWT, 445.88+/-99.48. The scores obtained in TKS were found related to the values of FVC (%), FEV1 (%), chest expansion, BASFI, modified Schober test, lumbar lateral flexion, cervical rotation, and total BASMI score (r=-0.43, -0.36, -0.41, 0.42, -0.49, -0.56, -0.52, 0.56, respectively; PCopyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc.

### **Prise en charge des symptomes medicaleme nt inexpliques en medecine interne : un paradigme de la relation medecin-malade en situation d'incertitude**

**Medically unexplained symptoms' care in internal medicine: A paradigm of doctor-patient relationship in situation of uncertainty**

**Author(s):** Ranque B.; Nardon O.

**Source:** Revue de Medecine Interne; Jul 2017; vol. 38 (no. 7); p. 458-466

**Publication Type(s):** Short Survey

**Abstract:** Medically unexplained symptoms (MUS) are extremely common in general practice as in all medical specialties, but their designation is not unambiguous and the approaches to take care of the patients differ from conventional therapeutic approaches. The difficulty is not to confirm the diagnosis, which is rapidly obvious with some experience, but to establish a genuinely human therapeutic relationship, without any technical help, which pushes the doctor to the edge of his empathy and communication skills. The discomfort or even distress regularly encountered by physicians in front of a patient with MUS shows that the foundations of the doctor-patient relationship under uncertainty are poorly mastered. Patients with MUS are regularly abused by the doctors, who unwittingly participate in the maintenance of their symptoms and even freeze them, leading to disastrous psychosocial and economic consequences. Yet the doctor-patient relationship is the key to their recovery or, at least, their improvement. The means of a successful patient-centered relationship are not always intuitive but can be learned. It is therefore essential to include SMI in medical school curricula and post-graduate medical education. Finally, if the management of early MUS mainly concerns the family medicine, that of severe MUS, including some fibromyalgia and chronic fatigue syndromes, falls within the scope of the internist doctor, who should be able to deliver a comprehensive care in partnership with the general practitioner and possibly a psychiatrist. Copyright © 2016 Societe Nationale Francaise de Medecine Interne (SNFMI)

### **Non-organic Vision Loss in the Afghanistan and Iraq Conflicts**

**Author(s):** Broderick K.M.; Ableman T.B.; Wroblewski K.J.; Weber E.D.; Enzenauer R.W.; Wain H.J.

**Source:** Neuro-Ophthalmology; Jul 2017; vol. 41 (no. 4); p. 175-181

**Publication Type(s):** Article

**Abstract:** Non-organic visual loss (NOVL), defined as a decrease in visual acuity or field without an identifiable organic cause, can be challenging to diagnose, especially in patients whose NOVL is superimposed on some component of true organic pathology. Exposure to combat puts soldiers at risk of emotional distress and physical trauma, which can contribute to the development of NOVL with conversion disorder or malingering. This case series describes six patients with NOVL who sustained ocular or non-ocular injuries while serving in combat operations in Iraq and Afghanistan, and highlights diagnostic pearls and components of inter-disciplinary management in the unique military context. Copyright © This article is not subject to U.S. copyright law.

### **Somatoform disorders in neurology**

**Author(s):** Benabdeljlil M.; El Fakir W.; Faris M.E.A.; Barra A.; Belghiti I.E.A.; Harbouz S.; Joulaibi S.; Neqrouz M.; Rahmani M.; Aidi S.

**Source:** European Journal of Neurology; Jul 2017; vol. 24 ; p. 142

**Publication Type(s):** Conference Abstract

**Abstract:** Background and aims: Functional or medically unexplained symptoms are very common in neurological consultation. In the DSM-IV, these disorders are classified as somatoform disorders. They represent about 30% of the activity of liberal neurologists. Methods: We report 35 cases of somatoform disorders hospitalized in our general neurology unit over a period of 6 years between 2011 and 2016. The ages ranged from 15 to 80 years. They were 29 women (87.8% of cases). Results: Psychogenic headaches were the most frequent presenting conditions (42.4%), followed by motor deficits (39.3%), lethargic states (12.1%), ocular symptoms (12.1%), pain (9%), movement disorders (9%), sensory disturbances (6%) and psychogenic nonepileptic seizures (6%). Ten patients

exhibited 2 symptoms or more. Anxiodepressive comorbidity was noted in 15% of cases. Eighteen percent of cases had similar episodes in the past. Most of the patients were treated by antidepressants, mainly Amitriptyline, even in the absence of depression. Physiotherapy was used whenever necessary. The evolution was favorable in 57.5% with full recovery before discharge in 42.4%. Conclusion: 50% of the patients with somatoform disorders are identified by neurologists. The neurologist is faced with the challenge of asserting the diagnosis and making the decision to stop investigations. He should implement an empathetic relation with the patient to announce the diagnosis and during all the follow-up. Some patients should be examined by a psychiatrist because up to two thirds have psychiatric comorbidity. Our series underline the importance for the neurologist to know these disorders in order to establish a comprehensive diagnostic approach and an appropriate medical care.

**Author response: Munchausen syndrome by genetics: Next-generation challenges for clinicians**

**Author(s):** Zittel S.; Alvarez-Fischer D.; Schweiger U.; Klein C.; Munchau A.

**Source:** Neurology; Jul 2017; vol. 89 (no. 3); p. 307

**Publication Type(s):** Letter

Available in full text at [Neurology](#) - from Ovid

**Letter re: Munchausen syndrome by genetics: Next-generation challenges for clinicians**

**Author(s):** Oliveira J.R.M.

**Source:** Neurology; Jul 2017; vol. 89 (no. 3); p. 307

**Publication Type(s):** Letter

Available in full text at [Neurology](#) - from Ovid

**Medically unexplained visual loss in children and young people: An observational single site study of incidence and outcomes**

**Author(s):** Daniel M.C.; Dahlmann-Noor A.H.; Coughtrey A.; Heyman I.

**Source:** Eye (Basingstoke); Jul 2017; vol. 31 (no. 7); p. 1068-1073

**Publication Type(s):** Article

**Abstract:** Purpose To determine the incidence of medically unexplained visual loss (MUVL) in children in an open access children's eye casualty. Patients and methods We collated demographic and clinical data of consecutive patients younger than 16 years who presented to the children's eye casualty at Moorfields Eye Hospital over a 12-month period and were diagnosed with MUVL or suspected MUVL. We reviewed the clinical records at least 3 months after initial presentation. We calculated the incidence using the number of new patient attendances over the same period as denominator (n=2397). We used descriptive analysis. Main outcome measures: number of patients diagnosed with MUVL, proportion of patients with a history of or present psychological problems, recovery rate, and improvement in visual acuity. Results We identified 85 cases of MUVL (54 females; median age: 9 years (IQR 7-12)). The median duration of follow-up was 1.2 months (IQR 0-4.3). The estimated annual incidence was 3.5% (95% confidence interval 2.9-4.4%). Thirty-three per cent of children had a history of psychiatric disorders, reported a stressful life event, or showed signs of psychiatric disorder at the time of first presentation. The recovery rate was 25%. Median improvement in best-corrected visual acuity from presentation to last appointment was 0.22 (IQR 0.06-0.43) logMAR. Conclusion The incidence of MUVL is higher and the rate of resolution lower than previously reported. MUVL may be associated with mental health problems. We recommend

screening for psychological problems to facilitate access to psychological treatment. Copyright © 2017 Macmillan Publishers Limited, part of Springer Nature.

### **Association of Gastrointestinal Functional Disorders and Migraine Headache: a Population Base Study**

**Author(s):** Lankarani K.B.; Akbari M.; Tabrizi R.

**Source:** Middle East Journal of Digestive Diseases; Jul 2017; vol. 9 (no. 3); p. 139-146

**Publication Type(s):** Article

Available in full text at [Middle East Journal of Digestive Diseases](#) - from ProQuest

**Abstract:**BACKGROUND Migraine is one of the prevalent headaches. Many of patients with migraine, complain of gastrointestinal symptoms. There is limited studies on relation of gastrointestinal symptoms and migraine headache at population level. METHODS In this population-based study, 1038 subjects older than 15 year from a rural area in Fars province, south of Iran. were investigated for functional gastrointestinal disorders. By cluster random sampling, 160 of these persons invited to receive endoscopy along with histopathology samples of upper gastrointestinal tract. Data were analyzed using Pearson chi-square and Fisher exact. RESULTS Mean age of participations were 34.3 years with female to male of 3:1. The prevalence of migraine, irritable bowel syndrome (IBS), reflux, and dyspepsia were 24.6%, 17.7%, 17.4%, and 32.1%, respectively. There were significant relationship between migraine and functional gastrointestinal diseases (odds ratio of association for migraine with IBS, reflux, and dyspepsia were 3.43, 1.68, and 1.68 with p-value Copyright © 2017, Shiraz University of Medical Sciences. All rights reserved.

### **Pharmacotherapy for Pediatric Neurogenic Bladder**

**Author(s):** Kroll P.

**Source:** Pediatric Drugs; Jul 2017 ; p. 1-16

**Publication Type(s):** Article In Press

**Abstract:**Neurogenic bladder (NB) is a nonspecific term that may describe conditions ranging from areflectic noncontractile bladder to detrusor overactivity. The most common cause of NB in children is the presence of dysraphic malformations. Urodynamic evaluations make it possible to describe bladder dysfunctions and to plan a therapeutic strategy for each patient. In a child with NB there are two major dangerous functional problems seen in urodynamic investigations: high intravesical pressure in the storage phase and high pressure during urination. The basic goals of urologic treatment for a child with NB are the protection of the urinary tract from complications and improvement of continence. Treatment for a child with NB is usually conservative, and focuses on achieving safe bladder pressures during storage with reliable emptying, via voiding or catheterization. The two most important forms of conservative treatment are clean intermittent catheterization and pharmacological treatment of functional disorders. Some drugs are used in the treatment of functional disorders in children with NB, but none of the drugs are officially approved for small children and babies. Copyright © 2017 The Author(s)

### **Possible adverse effects of the quadrivalent human papillomavirus vaccine in the region of southern Denmark: A retrospective, descriptive cohort study**

**Author(s):** Cramon C.; Poulsen C.L.; Holden I.K.; Johansen I.S.; Hartling U.B.

**Source:** Danish Medical Journal; Jul 2017; vol. 64 (no. 7)

**Publication Type(s):** Article

**Abstract:**Introduction: Since the introduction of the quadrivalent human papillomavirus vaccine, young girls and women have reported a broad range of symptoms. These have been described as possible adverse effects of the vaccine. In this study, we describe demographic characteristics, symptomatology, clinical and laboratory test results in patients referred with suspected adverse effects in the Region of Southern Denmark. Methods: We conducted a retrospective, descriptive study. The patients filled out a questionnaire, were interviewed by a doctor and received a standard physical examination and laboratory tests. Results: The study comprised 200 patients. The median age at referral was 22 (interquartile range (IQR): 19.5-26) years, and age at first vaccination was 14 (IQR: 12-21) years. The most common symptoms were headache (93%), fatigue/ tiredness (93%) and dizziness when standing up (90%). The median number of symptoms in each patient was 15. Five patients (2.5%) were diagnosed with postural orthostatic tachycardia syndrome (POTS). Of all patients, 183 (91.5%) were terminated without a somatic diagnosis, one patient (0.5%) was terminated with a functional disorder and 11 patients (5.5%) were still in diagnostic workup when the present study concluded. Conclusions: The patients reported a wide range of symptoms. We found an overall low prevalence of POTS. It should be further investigated whether these patients might suffer from a functional disorder rather than from adverse effects associated with the vaccine. Copyright © 2017, Danish Medical Association. All rights reserved.

### **The "rectosigmoid brake": Review of an emerging neuromodulation target for colorectal functional disorders**

**Author(s):** Lin A.Y.; Milne T.; Bissett I.P.; O'Grady G.; Dinning P.G.

**Source:** Clinical and Experimental Pharmacology and Physiology; Jul 2017; vol. 44 (no. 7); p. 719-728

**Publication Type(s):** Review

**Abstract:**The regulation of gastrointestinal motility encompasses several overlapping mechanisms including highly regulated and coordinated neurohormonal circuits. Various feedback mechanisms or "brakes" have been proposed. While duodenal, jejunal, and ileal brakes are well described, a putative distal colonic brake is less well defined. Despite the high prevalence of colonic motility disorders, there is little knowledge of colonic motility owing to difficulties with organ access and technical difficulties in recording detailed motor patterns along its entire length. The motility of the colon is not under voluntary control. A wide range of motor patterns is seen, with long intervals of intestinal quiescence between them. In addition, the use of traditional manometric catheters to record contractile activity of the colon has been limited by the low number of widely spaced sensors, which has resulted in the misinterpretation of colonic motor patterns. The recent advent of high-resolution (HR) manometry is revolutionising the understanding of gastrointestinal motor patterns. It has now been observed that the most common motor patterns in the colon are repetitive two to six cycles per minute (cpm) propagating events in the distal colon. These motor patterns are prominent soon after a meal, originate most frequently in the rectosigmoid region, and travel in the retrograde direction. The distal prominence and the origin of these motor patterns raise the possibility of them serving as a braking mechanism, or the "rectosigmoid brake," to limit rectal filling. This review aims to describe what is known about the "rectosigmoid brake," including its physiological and clinical significance and potential therapeutic applications. Copyright © 2017 John Wiley & Sons Australia, Ltd

### **Identifying feigning in Trauma-Exposed African immigrants**

**Author(s):** Weiss R.A.; Rosenfeld B.

**Source:** Psychological Assessment; Jul 2017; vol. 29 (no. 7); p. 881-889

**Publication Type(s):** Article

Available in full text at [Psychological Assessment](#) - from ProQuest

**Abstract:**As the populations of Western countries become more diverse, the risk of inaccurately generalizing knowledge from majority ethnic groups to minority groups is increasing. However, few of the measures used in forensic assessment are based on normative samples that represent the considerable diversity present in forensic settings. This study examined 4 commonly used measures of feigning: the Dot Counting Test (DCT; Boone, Lu, & Herzberg, 2002); the Miller Forensic Assessment of Symptoms (M-FAST; Miller, 2001); the Test of Memory Malingering (TOMM; Tombaugh, 1996); and a validity scale (atypical responding; ATR) on the Trauma Symptom Inventory-2 (Briere, 2011). The study compared performance on these measures of feigning among 3 groups of African immigrants: honest participants with and without posttraumatic stress disorder, and participants asked to feign distress-related symptoms. The data were used to assess the classification accuracy of each measure and the effect of demographic and cultural variables. Three of the 4 measures (M-FAST, TOMM, and ATR) significantly differentiated between participants asked to respond honestly and those asked to feign, although no measure produced higher than moderate classification accuracy. The M-FAST and DCT produced high false positive rates in the honest groups, ranging from 33% to 63%. Surprisingly, demographic and cultural variables were not significantly associated with test scores. The results emphasize the need for future related research. Copyright © 2016 American Psychological Association.

### **Swallow-induced syncope and carotid sinus hypersensitivity: Coincident or associated conditions?**

**Author(s):** Zaid E.A.; Haim M.; Alnsasra H.; Konstantino Y.

**Source:** Journal of Electrocardiology; Jul 2017; vol. 50 (no. 4); p. 523-525

**Publication Type(s):** Article

**Abstract:**Swallow induced syncope is a rare clinical condition which is thought to result from an abnormal vagal reflex leading to bradycardia and cerebral hypoperfusion. It mostly occurs in patients with organic or functional disorders of the esophagus, and often requires permanent pacemaker implantation, along with treatment of the underlying esophageal pathology. In the following case, we report of a 71-year-old male with achalasia post per oral endoscopic myectomy, who presented with syncope and documented AV-block while eating solid food. In addition, long sinus pauses were noted during carotid sinus massage, suggesting that the two distinct entities may be associated, and further supporting the mechanism of neurally mediated syncope in the pathophysiology of swallow-induced syncope. Copyright © 2017 Elsevier Inc.

### **Complexity Assessed by the INTERMED in Patients With Somatic Symptom Disorder Visiting a Specialized Outpatient Mental Health Care Setting: A Cross-sectional Study**

**Author(s):** van Eck van der Sluijs J.F.; de Vroege L.; van Manen A.S.; van der Feltz-Cornelis C.M.;

**Source:** Psychosomatics; Jul 2017; vol. 58 (no. 4); p. 427-436

**Publication Type(s):** Article

**Abstract:**Background Somatic symptom disorders (SSD), a new classification in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition is associated with problematic diagnostic procedures and treatment that lead to complex care. In somatic health care, the INTERMED has been used to assess levels of complexity; however, in SSD this instrument has not yet been applied. Objective This study aims to explore complexity in patients with SSD using the INTERMED, hereby contributing to an increased comprehension of this new patient group. Method In this cross-sectional study, the INTERMED was used to assess complexity in outpatients with SSD at the Clinical Centre of Excellence for Body, Mind, and Health (The Netherlands), along biologic, psychological, social, and health care domains. This was done retrospectively with patient files from consecutive patients from 2011 until 2015. Results In the total SSD sample (N = 187), 63% was female, the mean age (standard deviation) was 42 (+/-12.4) years, with an average educational level. The mean

INTERMED score was 23.5 indicating high overall complexity in this population. A high proportion of our sample (69%) scored as highly complex (>20). High complexity was associated with higher depression and anxiety scores, but not with a higher number of physical symptoms. Conclusions This study demonstrates that patients with SSD form a high-complex group, with higher scores compared with literature about multiple sclerosis, rheumatoid arthritis, or patient waiting for a liver transplant. INTERMED outcomes indicate a need for extensive diagnostic procedures and integrated multidisciplinary care for patients with SSD. Attention should especially be paid to mental disorders (depression and anxiety), given their association with high complexity. Copyright © 2017 The Academy of Psychosomatic Medicine.

### **Dystonie de type 12 : un diagnostic rare et difficile Dystonia 12: A rare and difficult diagnosis**

**Author(s):** Leroy P.; Meyer F.; Vaessen S.; Misson J.-P.; Doummar D.

**Source:** Archives de Pediatrie; Jul 2017; vol. 24 (no. 7); p. 637-639

**Publication Type(s):** Article

**Abstract:**We report a case of dystonia 12, also called rapid-onset dystonia-parkinsonism, which occurred in a young 12-year-old boy. Type 12 dystonia is a genetic syndrome characterized by a pathogenic mutation on ATP1A3 gene encoding the subunit alpha 3 of Na-K-ATPase protein, resulting in neuronal dysfunctions. It remains a rare syndrome with less than 100 cases described in the literature. Its atypical presentation and its rarity may lead to a wandering diagnosis, even in some cases to a conversion hysteria diagnosis. Today, unfortunately, there is no effective treatment. Copyright © 2017 Elsevier Masson SAS

### **A "Sleeping Beauty" With a "Heart-Hand": Kleine-Levin Syndrome Treated With Bupropion and Carbamazepine in a Patient With Holt-Oram Syndrome**

**Author(s):** Marques J.G.; Peralta A.R.; Faro Viana P.

**Source:** Clinical EEG and Neuroscience; Jul 2017; vol. 48 (no. 4); p. 270-271

**Publication Type(s):** Article

Available in full text at [Clinical EEG and Neuroscience](#) - from ProQuest

### **Prevalence, types and associations of medically unexplained symptoms and signs. A cross-sectional study of 1023 adults with intellectual disabilities**

**Author(s):** Osugo M.; Morrison J.; Allan L.; Kinnear D.; Cooper S.-A.

**Source:** Journal of Intellectual Disability Research; Jul 2017; vol. 61 (no. 7); p. 637-642

**Publication Type(s):** Article

**Abstract:**Background: Medically unexplained symptoms and signs are common in the general population and can respond to appropriate managements. We aimed to quantify the types and prevalence of unexplained symptoms and signs experienced by adults with ID and to determine the associated factors. Method: In a population-based study, 1023 adults with ID aged 16 and over had a detailed health assessment, which systematically considered symptoms and signs. Descriptive data were generated on their symptoms and signs. Backwards stepwise logistic modelling was undertaken to determine the factors independently associated with the unexplained symptoms. Results: Medically unexplained symptoms and signs were present in 664 (64.9%), 3.8 times higher than in the general population, and 470 (45.9%) had multiple unexplained symptoms or signs. Some were similar to those reported in the general population, such as dyspnoea, dyspepsia, headache, nausea and dizziness. However, others are not commonly reported in the general population,

including dysphagia, ataxia, polyuria, oedema and skin rash. Having unexplained symptoms and signs was independently associated with older age, female gender, not having Down syndrome, extent of ID and more GP visits in the last 12 months. It was not associated with living in deprived areas, type of living/support arrangements, number of hospital visit in the last 12 months, smoking, autism, problem behaviours or mental disorders. Conclusions: People with ID have substantial additional unexplained symptoms and signs, some of which are painful or disabling. These findings should inform the content of health checks undertaken for adults with intellectual disabilities, which should not just focus on management of their long-term conditions and health promotion. Copyright © 2017 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd

### **High healthcare utilization near the onset of medically unexplained symptoms**

**Author(s):** McAndrew L.M.; Phillips L.A.; Helmer D.A.; Maestro K.; Greenberg L.M.; Anastasides N.; Engel C.C.; Quigley K.S.

**Source:** Journal of Psychosomatic Research; Jul 2017; vol. 98 ; p. 98-105

**Publication Type(s):** Article

**Abstract:** Objective Patients with medically unexplained syndromes (MUS) often do not receive appropriate healthcare. A critical time for effective healthcare is the inception of MUS. The current study examined data from a prospective longitudinal study of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) soldiers to understand the relationship of increasing physical symptom burden to healthcare utilization. Methods Data was examined from a prospective study of OEF/OIF soldiers assessed before and one year after deployment (n = 336). Physical symptom burden was measured with the Patient Health Questionnaire (PHQ-15). Analyses were conducted with polynomial regression and response surface analysis (RSA). Results Increases in physical symptom burden predicted greater healthcare utilization one year after deployment: primary care practitioner (slope = - 0.26, F = 4.07, p = 0.04), specialist (slope = - 0.43, F = 8.67, p = 0.003), allied health therapy (e.g., physical therapy) (slope = - 0.41, F = 5.71, p = 0.02) and mental health (slope = - 0.32, F = 4.04, p = 0.05). There were no significant difference in utilization between those with consistently high levels and those with increases in physical symptom burden. Conclusion This is the first prospective study to examine, and show, a relationship between onset of clinically significant physical symptoms and greater healthcare utilization. Our data suggest that patients with increasing physical symptom burden have the same level of healthcare as patients with chronic physical symptom burden. Needed next steps are to better understand the quality of care at inception and determine how to intervene so that recommended approaches to care are provided from the onset. Copyright © 2017

### **Associations of treatment effects between follow-up times and between outcome domains in interventions for somatoform disorders: Review of three Cochrane reviews**

**Author(s):** Chowdhury S.; Burton C.

**Source:** Journal of Psychosomatic Research; Jul 2017; vol. 98 ; p. 10-18

**Publication Type(s):** Article

**Abstract:** Background Interventions for somatoform disorders typically address a range of outcomes. We aimed to examine treatment effects across outcome domains and specifically assess the association, at study level, between short and long term treatment effects and between treatment effects in different outcome domains. Methods We used data from recent systematic reviews of interventions for somatoform disorders to address three questions: We described outcome domains and measures by compiling forest plots of standardised mean difference. We examined the association of changes in outcome between short and long-term and between different outcome

domains by non-parametric correlation. Results We analysed data from 47 studies across four outcome domains: physical symptoms, health-related quality of life, depression and anxiety. Short-term and long-term treatment effects within each outcome domain were broadly similar and were correlated. Reported reduction in physical symptoms was correlated with reductions in depression ( $\rho = 0.73$ ,  $p = 0.002$ ) and anxiety ( $0.70$ ,  $p < 0.001$ ) and increase in quality of life ( $0.54$ ,  $p = 0.03$ ). Conclusion Short term changes in outcome measures are correlated with longer term changes; outcome changes are correlated across domains independently of the type of treatment. Copyright © 2017 Elsevier Inc.

### **The association of experience of violence and somatization, depression, and alexithymia: a sample of women with medically unexplained symptoms in Turkey.**

**Author(s):** Anuk, Dilek; Bahadır, Güler

**Source:** Archives of women's mental health; Jul 2017

**Publication Type(s):** Journal Article

**Abstract:**The aim of the study was to examine the relationship between the levels of somatization, depression as well as alexithymia, and MUS in women going through violence experience in three contexts (childhood, adulthood, and both childhood and adulthood). The study was performed on 180 patients attending the Internal Medicine Department of Istanbul University Medical Faculty. The data of women with MUS ( $n = 50$ ) were compared those of women with acute physical conditions ( $n = 46$ ) and chronic physical conditions ( $n = 84$ ). Semi-structured Interview Form, Childhood Abuse and Neglect Inventory, Brief Symptom Inventory, Beck Depression Inventory, and the Toronto Alexithymia Scale were administered. The levels of somatization and depression were found to be higher in women who were exposed to emotional abuse (EA) and physical abuse (PA) in adulthood in the MUS group compared with those of the women exposed to EA and PA in adulthood in the other groups. The levels of somatization, depression, and alexithymia in the MUS group exposed to childhood emotional abuse (CEA) were also higher than those in the controls exposed to CEA. The levels of somatization and alexithymia in the MUS group who were exposed to childhood physical abuse (CPA) were higher than those in the controls exposed to CPA. The levels of somatization and depression in the MUS group who were exposed to violence both in childhood and in adulthood were higher than those in the controls who experienced violence both in childhood and in adulthood. Most women exposed to domestic violence present to health care institutions with various physical and psychological symptoms in Turkey. So, it is important that health caregivers also ask questions about experiences of violence and psychological symptoms in women presenting with medically unexplained symptoms.

### **The perpetrators of medical child abuse (Munchausen Syndrome by Proxy) - A systematic review of 796 cases.**

**Author(s):** Yates, Gregory; Bass, Christopher

**Source:** Child abuse & neglect; Jul 2017; vol. 72 ; p. 45-53

**Publication Type(s):** Journal Article Review

**Abstract:**INTRODUCTION Little is known about the perpetrators of medical child abuse (MCA) which is often described as "Munchausen's syndrome by proxy" or "factitious disorder imposed on another". The demographic and clinical characteristics of these abusers have yet to be described in a sufficiently large sample. We aimed to address this issue through a systematic review of case reports and series in the professional literature. METHOD A systematic search for case reports and series published since 1965 was undertaken using MEDLINE, Web of Science and EMBASE. 4100 database records were screened. A supplementary search was then conducted using Google Scholar and reference lists of eligible studies. Our search yielded a total sample of 796 perpetrators: 309 from

case reports and 487 from case series. Information extracted included demographic and clinical characteristics, in addition to methods of abuse and case outcomes. RESULTS Nearly all abusers were female (97.6%) and the victim's mother (95.6%). Most were married (75.8%). Mean caretaker age at the child's presentation was 27.6 years. Perpetrators were frequently reported to be in healthcare-related professions (45.6%), to have had obstetric complications (23.5%), or to have histories of childhood maltreatment (30%). The most common psychiatric diagnoses recorded were factitious disorder imposed on self (30.9%), personality disorder (18.6%), and depression (14.2%). CONCLUSIONS From the largest analysis of MCA perpetrators to date, we provide several clinical recommendations. In particular, we urge clinicians to consider mothers with a personal history of childhood maltreatment, obstetric complications, and/or factitious disorder at heightened risk for MCA. Longitudinal studies are required to establish the true prognostic value of these factors as our method may have been vulnerable to publication bias.

### **Japanese standard for clinical stabilometry assessment: Current status and future directions.**

**Author(s):** Yamamoto, Masahiko; Ishikawa, Kazuo; Aoki, Mitsuhiro; Mizuta, Keisuke; Ito, Yatsuji;

**Source:** Auris, nasus, larynx; Jul 2017

**Publication Type(s):** Journal Article Review

**Abstract:**Stabilometry is a useful tool for examining patients with functional disorders of the vestibular system. However, measurement techniques and devices vary by country. Therefore, international standardization of stabilometry is mandatory to validate the exchange of important findings. This was advocated at the 1983 Posturography Meeting in Kyoto but has not been adopted worldwide, and each country has continued to use unique regional measurement methods. In Japan, stabilometry has widespread application in medical practice in conjunction with research into its applications. With a goal of international standardization, we present details of stabilometry measurement methods and their application in Japan, together with a brief history and potential future directions of stabilometry.

### **Assessment of neuroinflammation in patients with idiopathic rapid-eye-movement sleep behaviour disorder: a case-control study.**

**Author(s):** Stokholm, Morten Gersel; Iranzo, Alex; Østergaard, Karen; Serradell, Mónica; Otto, Marit;

**Source:** The Lancet. Neurology; Jul 2017

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUND Findings from longitudinal follow-up studies in patients with idiopathic rapid-eye-movement sleep behaviour disorder (IRBD) have shown that most patients will eventually develop the synucleinopathies Parkinson's disease, dementia with Lewy bodies, or multiple system atrophy. Neuroinflammation in the form of microglial activation is present in synucleinopathies and is a potential therapeutic target to halt or delay the neurodegenerative process. We aimed to investigate whether neuroinflammation is present in patients with IRBD and its possible relation to nigrostriatal dopamine function. METHODS In this prospective, case-control, PET study, patients with IRBD and no clinical evidence of parkinsonism and cognitive impairment were recruited from tertiary sleep centres in Spain (Barcelona) and Denmark (Aarhus). We included patients with polysomnography-confirmed IRBD according to established criteria. Healthy controls were recruited through newspaper advertisements. Controls had no motor or cognitive complaints, a normal neurological examination, and a mean group age similar to the IRBD group. In patients with IRBD, we assessed microglial activation in the substantia nigra, putamen, and caudate with <sup>11</sup>C-PK11195 PET, and dopaminergic axon terminal function in the putamen and caudate with <sup>18</sup>F-DOPA PET. Controls underwent either <sup>11</sup>C-PK11195 PET or <sup>18</sup>F-DOPA PET. We compared <sup>18</sup>F-DOPA uptake and <sup>11</sup>C-PK11195 binding potential between groups with an unpaired, two-tailed Student's t

test. **FINDINGS** Between March 23, 2015, and Oct 19, 2016, we recruited 20 consecutive patients with IRBD and 19 healthy controls. 11C-PK11195 binding was increased on the left side of the substantia nigra in patients with IRBD compared with controls (Student's t test, mean difference 0.153 [95% CI 0.055 to 0.250],  $p=0.003$ ), but not on the right side (0.121 [-0.007 to 0.250],  $p=0.064$ ). 11C-PK11195 binding was not significantly increased in the putamen and caudate of patients with IRBD. 18F-DOPA uptake was reduced in IRBD in the left putamen (-0.0032 [-0.0044 to -0.0021],  $p<0.0001$ ) and right putamen (-0.0032 [-0.0044 to -0.0020],  $p<0.0001$ ), but not in the caudate. **INTERPRETATION** In patients with IRBD, increased microglial activation was detected by PET in the substantia nigra along with reduced dopaminergic function in the putamen. Further studies, including more participants than were in this study and longitudinal follow-up, are needed to support our findings and evaluate whether the presence of activated microglia in patients with IRBD represents a marker of short-term conversion to a clinically defined synucleinopathy in the near future. **FUNDING** Danish Council for Independent Research, Instituto de Salud Carlos III (Spain).

**Yonder: Loneliness, breast cancer, medically unexplained symptoms, and delivering babies.**

**Author(s):** Rashid, Ahmed

**Source:** The British journal of general practice : the journal of the Royal College of General Practitioners; Jul 2017; vol. 67 (no. 660); p. 315

**Publication Type(s):** Journal Article

**PubMedID:** 28663424

Available in full text at [British journal of general practice: the journal of the Royal College of General Practitioners \[Br J Gen Pract\]](#) NLMUID: 9005323, The - from EBSCOhost

**Impaired awareness of motor intention in functional neurological disorder: implications for voluntary and functional movement.**

**Author(s):** Baek, K; Doñamayor, N; Morris, L S; Strelchuk, D; Mitchell, S; Mikheenko, Y; Yeoh, S Y;

**Source:** Psychological medicine; Jul 2017; vol. 47 (no. 9); p. 1624-1636

**Publication Type(s):** Journal Article

**PubMedID:**

Available in full text at [Psychological Medicine](#) - from ProQuest

**Abstract:** **BACKGROUND** Functional neurological disorders (FNDs), also known as conversion disorder, are unexplained neurological symptoms unrelated to a neurological cause. The disorder is common, yet poorly understood. The symptoms are experienced as involuntary but have similarities to voluntary processes. Here we studied intention awareness in FND. **METHOD** A total of 26 FND patients and 25 healthy volunteers participated in this functional magnetic resonance study using Libet's clock. **RESULTS** FND is characterized by delayed awareness of the intention to move relative to the movement itself. The reporting of intention was more precise, suggesting that these findings are reliable and unrelated to non-specific attentional deficits. That these findings were more prominent with aberrant positive functional movement symptoms rather than negative symptoms may be relevant to impairments in timing for an inhibitory veto process. Attention towards intention relative to movement was associated with lower right inferior parietal cortex activity in FND, a region early in the processing of intention. During rest, aberrant functional connectivity was observed with the right inferior parietal cortex and other motor intention regions. **CONCLUSION** The results converge with observations of low inferior parietal activity comparing involuntary with voluntary movement in FND, emphasizing core deficiencies in intention. Heightened precision of this impaired intention is consistent with Bayesian theories of impaired top-down priors that might influence the sense of involuntariness. A primary impairment in voluntary motor intention at an early processing stage

might explain clinical observations of slowed effortful voluntary movement, heightened self-directed attention and underlie functional movements. These findings further suggest novel therapeutic targets.

**Database:** Medline

**Are media reports able to cause somatic symptoms attributed to WiFi radiation? An experimental test of the negative expectation hypothesis.**

**Author(s):** Bräscher, Anne-Kathrin; Raymaekers, Koen; Van den Bergh, Omer; Witthöft, Michael

**Source:** Environmental research; Jul 2017; vol. 156 ; p. 265-271

**Publication Type(s):** Journal Article

**Abstract:** People suffering from idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) experience numerous non-specific symptoms that they attribute to EMF. The cause of this condition remains vague and evidence shows that psychological rather than bioelectromagnetic mechanisms are at work. We hypothesized a role of media reports in the etiology of IEI-EMF and investigated how somatosensory perception is affected. 65 healthy participants were instructed that EMF exposure can lead to enhanced somatosensory perception. Participants were randomly assigned to watch either a television report on adverse health effects of EMF or a neutral report. During the following experiment, participants rated stimulus intensities of tactile (electric) stimuli while being exposed to a sham WiFi signal in 50% of the trials. Sham WiFi exposure led to increased intensity ratings of tactile stimuli in the WiFi film group, especially in participants with higher levels of somatosensory amplification. Participants of the WiFi group reported more anxiety concerning WiFi exposure than the Control group and tended to perceive themselves as being more sensitive to EMF after the experiment compared to before. Sensational media reports can facilitate enhanced perception of tactile stimuli in healthy participants. People tending to perceive bodily symptoms as intense, disturbing, and noxious seem most vulnerable. Receiving sensational media reports might sensitize people to develop a nocebo effect and thereby contribute to the development of IEI-EMF. By promoting catastrophizing thoughts and increasing symptom-focused attention, perception might more readily be enhanced and misattributed to EMF.

**Assessment of Somatization and Medically Unexplained Symptoms in Later Life.**

**Author(s):** van Driel, T J W; Hilderink, P H; Hanssen, D J C; de Boer, P; Rosmalen, J G M;

**Source:** Assessment; Jul 2017 ; p. 1073191117721740

**Publication Type(s):** Journal Article

**Abstract:** The assessment of medically unexplained symptoms and "somatic symptom disorders" in older adults is challenging due to somatic multimorbidity, which threatens the validity of somatization questionnaires. In a systematic review study, the Patient Health Questionnaire-15 (PHQ-15) and the somatization subscale of the Symptom Checklist 90-item version (SCL-90 SOM) are recommended out of 40 questionnaires for usage in large-scale studies. While both scales measure physical symptoms which in younger persons often refer to unexplained symptoms, in older persons, these symptoms may originate from somatic diseases. Using empirical data, we show that PHQ-15 and SCL-90 SOM among older patients correlate with proxies of somatization as with somatic disease burden. Updating the previous systematic review, revealed six additional questionnaires. Cross-validation studies are needed as none of 46 identified scales met the criteria of suitability for an older population. Nonetheless, specific recommendations can be made for studying older persons, namely the SCL-90 SOM and PHQ-15 for population-based studies, the Freiburg Complaint List and somatization subscale of the Brief Symptom Inventory 53-item version for studies in primary care, and finally the Schedule for Evaluating Persistent Symptoms and Somatic Symptom Experiences Questionnaire for monitoring treatment studies.

**A preliminary investigation of sleep quality in functional neurological disorders: Poor sleep appears common, and is associated with functional impairment**

**Author(s):** Graham, Christopher D.; Kyle, Simon D.

**Source:** Journal of the Neurological Sciences; Jul 2017; vol. 378 ; p. 163-166

**Publication Type(s):** Journal Peer Reviewed Journal Journal Article

**Abstract:** Purpose: Functional neurological disorders (FND) are disabling conditions for which there are few empirically-supported treatments. Disturbed sleep appears to be part of the FND context; however, the clinical importance of sleep disturbance (extent, characteristics and impact) remains largely unknown. We described sleep quality in two samples, and investigated the relationship between sleep and FND-related functional impairment. Methods: We included a sample recruited online via patient charities ( N = 205) and a consecutive clinical sample ( N = 20). Participants completed validated measures of sleep quality and sleep characteristics (e.g. total sleep time, sleep efficiency), mood, and FND-related functional impairment. Results: Poor sleep was common in both samples (89% in the clinical range), which was characterised by low sleep efficiency ( M = 65.40%) and low total sleep time ( M = 6.05 h). In regression analysis, sleep quality was negatively associated with FND-related functional impairment, accounting for 16% of the variance and remaining significant after the introduction of mood variables. Conclusions: These preliminary analyses suggest that subjective sleep disturbance (low efficiency, short sleep) is common in FND. Sleep quality was negatively associated with the functional impairment attributed to FND, independent of depression. Therefore, sleep disturbance may be a clinically important feature of FND. (PsycINFO Database Record (c) 2017 APA, all rights reserved) (Source: journal abstract)

**Dissimulation strategies on standard neuropsychological tests: A qualitative investigation.**

**Author(s):** Jones, Stephanie M.

**Source:** Brain Injury; Jul 2017; vol. 31 (no. 8); p. 1131-1141

**Publication Type(s):** Academic Journal

**Abstract:** Objective: Most previous studies in the area of malingering neuropsychological deficits have focused on the development and validation of measures to detect falsification of symptoms or suboptimal performance. The present study employs qualitative methods to investigate strategies employed by individuals attempting to feign cognitive impairment. This study aims to achieve a richer and more detailed understanding of the phenomenon of feigning. Method: Detailed semi-structured interviews were administered to 15 non-neurological individuals instructed to feign cognitive impairment on a standard neuropsychological test battery. The interviews, which considered the strategies used and the thinking underlying participants' choices, were subjected to Thematic Analysis. Results: Thematic Analysis revealed three main organising themes. Participants described Using Strategies, on specific tests and generally across the battery, Having a Rationale for their decisions and spontaneously commented on their Experience of the Task. Conclusion: The findings of the present study reveal numerous potentially useful identifiers of feigning strategies, including many not previously reported. The resulting themes point to the development of more effective methods for detecting feigned cognitive impairments and could have a significant impact on the way that neuropsychological testing sessions are conducted.

**Database:** CINAHL

## Exercise: Systematic Reviews

There are 7 key steps that need to be taken when carrying out a Systematic Review.

Can you put them in order?

A. Quality assessment

B. Study selection

C. Synthesis

D. Data extraction

E. Define the question

F. Literature search

G. Writing up

*For assistance with carrying out a **systematic review search** or a **literature search**, please email [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk).*

Answers: 1E; 2F; 3B; 4D; 5A; 6C; 7G



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