

Institution: University of Edinburgh		
Unit of Assessment: 4		
Title of case study: D: Adding Functional Neurological Disorders to the global neurology agenda: transforming information, attitudes, diagnosis and patient experience		
Period when the underpinning research was undertaken: 2010 – 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Jon Stone	Consultant Neurologist and Honorary Professor in Neurology	2005 – present
Alan Carson	Consultant Neuropsychiatrist and Honorary Professor	2001 – present
Period when the claimed impact occurred: August 2013 – December 2020		
Is this case study continued from a case study submitted in 2014? N		
1. Summary of the impact		
<p>Underpinning Research: Through studies on epidemiology, diagnosis, treatment and outcome, Edinburgh Neuroscience researchers were the first to systematically recognise, quantify and classify Functional Neurological Disorder (FND); a major but previously poorly understood cause of disability, and the second commonest reason to see a neurologist.</p> <p>Significance and Reach of Impact: The descriptions of FND in key international diagnostic manuals Fifth Edition of the Diagnostic and Statistical Manual (DSM-5; May 2013; revision in 2019) and Eleventh Revision of the International Classification of Disease (ICD-11; June 2018) have been updated to reflect Edinburgh Neuroscience findings. FND are included in the new UK Internal Medicine (2019) and Neurology (approved; will apply from 2022) curricula. 4 national and international professional networks have been set up, giving rise to 2 multicentre clinical trials. This increased understanding and awareness of FND leads to patients being more likely to receive a definitive and accurate diagnosis, relieving them from uncertainty and opening pathways to evidence-based treatment. Edinburgh Neuroscience researchers host an educational website that receives more than 50,000 hits per month. Major charities FND Hope and FND Action were set up inspired by Edinburgh Neuroscience work.</p>		
2. Underpinning research		
<p>The Challenge: FND was seen as rare or a misdiagnosis FND describes patients who exhibit genuine neurological symptoms reflecting a problem with the functioning of the nervous system, rather than structural or organic neurological injury or disease that can be detected with current imaging, electrophysiological or other methods. Symptoms of FND vary widely but include limb weakness, non-epileptic seizures, sensory disturbances, problems with speech, dizziness and blackouts. Other names for the condition include Conversion Disorder, Dissociative Disorder, psychogenic or 'non-organic' disorders, as well as stigmatising terms such as 'hysteria'. Prior to Edinburgh Neuroscience research, FND was widely considered to be relatively rare, transient, or a misdiagnosis, with patients often dismissed as having 'nothing wrong'.</p> <p>Functional symptoms are common and an alternative cause is rarely found In the early 2000s, Stone and Carson (together with Sharpe, at UoE until 2011) began to systematically research FND. A study of 3,781 neurology outpatients across Scotland over 18 months showed that functional disorders were the second most common category of diagnosis (16%) after headache (19%). Moreover, at follow-up, only 0.4% of these patients had received an alternative diagnosis that explained the original symptoms [3.1].</p> <p>Edinburgh Neuroscience researchers also completed the largest and longest follow-up study of patients with functional limb weakness, one of the commonest subtypes of FND. This demonstrated symptoms persist for more than 14 years in 80% of patients and, crucially, misdiagnosis, and the emergence of an alternative explanation for the symptom, are rare (1%)</p>		

[3.2]. These studies continue to be cited as pivotal in the field and were hugely influential in the subsequent recognition that FND is a common and long-term neurological condition associated with significant disability.

FND as a positive diagnosis in which psychological stress is not always present

An important aspect of Edinburgh Neuroscience research has been the focus on diagnosis of FND based on the *presence* of specific positive clinical signs, as opposed to exclusion of other possible diagnoses based on *absence* of signs of other disease, such as imaging abnormalities indicative of stroke or multiple sclerosis. An example of an FND-positive clinical finding is Hoover's sign: weakness of hip extension that normalises when the patient is focusing on flexion of the contralateral hip; Edinburgh Neuroscience researchers have found this, and a range of other signs, to be sensitive and specific indicators of FND. For example, Hoover's sign was present in 60/107 (56%) of people with FND but only in 1/45 (2%) of matched controls [3.3].

A long-held view of FND was that a recent or childhood adverse event, such as abuse or emotional neglect, was a necessary cause of the disorder; it was a diagnostic criterion within the DSM-IV. In 2010, during the preparation of DSM-5, Edinburgh Neuroscience researchers published an editorial in the *American Journal of Psychiatry*, using their body of research to argue that 1) a psychological stressor was a contributory risk factor rather than an essential diagnostic requirement and 2) diagnosis should be made on the basis of presence of positive symptoms rather than absence of signs of other disease [3.4]. These changes were accepted and published in DSM-5 in May 2013 (see below). The dropping of the stressor was in 2018 further supported by an exhaustive systematic review and meta-analysis by Edinburgh Neuroscience researchers, which found that 20-70% of patients with FND do not have this risk factor [3.5].

Development and testing of new treatments for FND

Prior to Edinburgh Neuroscience research, there was little understanding or acceptance of FND as a common or 'real' condition in neurological practice, and no evidence base for treatment. As a direct result of their systematic evaluation, quantification and classification, FND is now recognised by research funders as a common and serious condition that justifies further research into its cause, diagnosis and treatment. For example, the Edinburgh Neuroscience team helped to design CODES, a GBP2,100,000 multicentre National Institute of Health Research (NIHR)-funded clinical trial testing a specific form of cognitive behavioural therapy (CBT) on patients with FND (also known as dissociative) seizures. This trial found the CBT group to have significant improvements in duration of freedom from seizures, health-related quality of life, and psychological distress, among other outcomes [3.6]. The Edinburgh Neuroscience researchers are also co-investigators in an ongoing NIHR-funded trial (Physio4FMD; GBP1,100,000) testing specifically designed physiotherapy treatments on patients with FND causing motor symptoms (functional motor disorder, FMD).

3. References to the research

[3.1] Stone J, Carson a, Duncan R, et al. Symptoms 'unexplained by organic disease' in 1144 new neurology out-patients: how often does the diagnosis change at follow-up? *Brain* 2009; 132: 2878–88. [doi: 10.1093/brain/awp220](https://doi.org/10.1093/brain/awp220)

[3.2] Gelauff JM, Carson A, Ludwig L, Tijssen MAJ & Stone J. 'The prognosis of functional limb weakness, a 14-year case-control study' *Brain* 2019 142(7): 2137-2148. [doi: 10.1093/brain/awz138](https://doi.org/10.1093/brain/awz138)

[3.3] Stone J, Warlow C, Sharpe M. The symptom of functional weakness: a controlled study of 107 patients. *Brain* 2010 133:1537–1551. [doi: 10.1093/brain/awq068](https://doi.org/10.1093/brain/awq068)

[3.4] Stone J, Lafrance WC, Levenson JL and Sharpe M. Issues for DSM-5: Conversion Disorder. *Am J Psychiatry* 2010 167:6, 626-627 [doi: 10.1176/appi.ajp.2010.09101440](https://doi.org/10.1176/appi.ajp.2010.09101440)

[3.5] Ludwig L, Pasman JA, Nicholson T, Aybek S, David AS, Tuck S, Kanaan RA, Roelofs K, Carson A, Stone J. Stressful life events and maltreatment in conversion (functional neurological) disorder: systematic review and meta-analysis of case-control studies. *Lancet Psychiatry* 2018; 5:307-320 [doi: 10.1016/S2215-0366\(18\)30051-8/](https://doi.org/10.1016/S2215-0366(18)30051-8/)

[3.6] Goldstein LH, Robinson EJ, Mellers JC, Stone J, Carson A [...] Chalder T. Cognitive behavioural therapy for adults with dissociative seizures (CODES): a pragmatic, multicentre, randomised controlled trial. *Lancet Psychiatry* 2020, 7(6), p 491-505. [doi: 10.1016/S2215-0366\(20\)30128-0](https://doi.org/10.1016/S2215-0366(20)30128-0)

4. Details of the impact

In 2015, the President of the Royal College of Psychiatrists summarised the overall impact of Edinburgh Neuroscience research in this area as follows: “*Over the last 15 years, [it] has made a unique contribution to functional disorders at the interface between neurology and psychiatry. [...] If we wind back to 2000, these disorders were invisible in training curricula, there was very little research and there was no information for patients. None of that is true now.*” [5.1].

Impact on practitioners

Diagnostic manuals

Edinburgh Neuroscience research has driven changes in the diagnostic criteria for FND in the 2 main diagnostic manuals used by healthcare professionals worldwide: the DSM-5 (May 2013) [5.2a], and the ICD-11 (2018) [5.2b].

In the DSM-IV, a diagnosis of FND required a psychological stressor and exclusion of other possible diagnoses. By contrast, the DSM-5 dropped the need for a psychological stressor and required the presence of positive clinical signs [5.2a]. The text editor of the DSM-5 Somatic Symptoms Disorder chapter confirmed that the DSM-5 work group: “*asked Professor Jon Stone (University of Edinburgh) to write the first draft of the section on Conversion (Functional Neurological Symptom) Disorder for the 2013 manual. His seminal studies, and that of his group, provided the evidence on which transformative changes to the diagnostic criteria were based. [...] He had articulated these in an earlier joint position paper [3.5] which was adopted by DSM-5.*” [5.2c].

While the first publication of the DSM-5 occurred before the REF2021 census period, the transformed criteria have been in place, guiding the decision-making of healthcare professionals, ever since. Furthermore, the new criteria were retained and strengthened in the DSM-5-Text Revision (initiated in 2019). The text editor confirmed he invited Stone to carry out this revision, “*on the basis of his status as the leading researcher in the field. Of particular note, his group's paper in Lancet Psychiatry in 2018 is now the key work that strengthens the earlier decision to drop stressful events as an essential diagnostic criterion.*” [5.2c]

In the ICD-11, for the first time, a description of “dissociative neurological symptom disorder”, appears under the menu for both “diseases of the nervous system” and “mental and behavioural disorders” [5.2b]. Stone was an advisor to the World Health Organization Topic Advisory Group for Neurology and authored an article in *Neurology* in 2014, which strongly recommended this joint ownership [5.2d].

UK clinical curricula in Internal Medicine and Neurology

As a direct result of Edinburgh Neuroscience research, FND has been incorporated into standard training for specialising clinicians in the UK [5.3a]; the Internal Medicine curriculum (from August 19), includes Functional Disorder in the main table of conditions [5.3b] and the UK Neurology specialist training curriculum (from August 22) will include it as 1 of 10 core capabilities [5.3c]. The Chair of Neurology of the Joint Royal College of Physicians Training

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Board attested to the influence of Edinburgh research in these inclusions: *“Although there are other professionals involved in Functional Neurological Disorders in the UK, [...] it has been Professor Stone and Professor Carson who have articulated most clearly, and with the most credibility, the need to embed an appreciation of FND in the curricula of trainees in Internal Medicine and in Neurology”* [5.3a]

Professional structures and training

Edinburgh Neuroscience research findings have led to 3 UK and 1 international professional networks, which foster research collaborations and enable practitioners to learn and share best practice:

- UK Functional Neurological Society has since 2011 led to a range of collaborative research projects culminating in the first international consensus statements on 1) physiotherapy for FND ([5.4a]; downloaded 40,000 times since publication in 2014) and 2) occupational therapy for FND [5.4b]. The Society’s collaborations also underpinned the CODES and Physio4FMD trials.
- The Association of British Neurologists special interest group in FND (2016; [5.4c])
- UK Functional Neurological Forum (2015 [5.4d])
- FND Society, an international multidisciplinary society dedicated to advancing research and improving the diagnosis and treatment of patients with FND. This was formed by Stone and Carson together with Mark Hallett (USA) in 2017, following the first-ever FND conference attended by over 550 experts from neurology, psychiatry, psychology and allied health. By October 2020, FND Society had 488 members from 19 countries [5.4e].
- Carson has led a training course at the annual international congress of the Royal College of Psychiatrists every year for 23 years, using Edinburgh Neuroscience research to train psychiatrists to recognise and manage patients with FND [5.4f].

Impact on clinical practice*New dedicated FND services*

Edinburgh Neuroscience research is also impacting clinical practice in the UK through the emergence of new neurology services, established with the explicit purpose of receiving patients with FND. Examples include new services in Cambridge (established in 2013 [5.5a]) and Bristol (2017 [5.5b]). Both founders credit their exposure to Edinburgh Neuroscience research as transformative to their attitude and practice, with the founder of the Bristol service stating: *“Being able to quote the scientifically rigorous work of Profs Stone and Carson helped me defend my interest and successfully make the case for a better service in Bristol”* [5.5a]. Together, these services have received over 1,000 patients since their launch. Notably, these dedicated FND services can lead to NHS resource savings: the founder of the Cambridge service notes: *“In association with the finance department, it was estimated that attendance at the FND clinic, thereby receiving a clear diagnosis and management plan, could save over GBP2,000 per patient, by reducing future hospital ‘encounters’. From data collected in 2014-2016, two thirds of patients improved (over a variable follow up period).”* [5.5b]

Patient experience

Previously, patients typically attended multiple primary and secondary care visits without gaining any diagnosis or appropriate treatment [5.6a]. With healthcare professionals now better aware of FND through updated diagnostic manuals, inclusion of FND in the medical curriculum and professional structures, patients are more likely to receive an earlier and definitive diagnosis of FND. This has been shown to significantly reduce patient distress [5.6b]. Importantly, there is evidence from randomised clinical trials that targeted interventions for FND can improve symptoms. For example, a randomised feasibility trial, based on treatments first co-authored by Edinburgh Neuroscience, demonstrated symptom improvement (72% good outcome in intervention vs 18% in controls) in 60 patients with FMD following targeted physiotherapy [5.7]. The CODES trial serves as further evidence that interventions specifically targeted for FND can significantly improve patient experience and wellbeing. Thus, the fundamental impact of Edinburgh’s body of research on FND has been to transform FND from a vague entity that was widely considered rare, transient or a misdiagnosis, to a common,

long-lasting and debilitating condition for which specific treatments are now being sought and tested.

Impact on awareness and understanding of FND

Prior to Edinburgh Neuroscience research, there was little information or support available to patients with FND, and they were widely stigmatised. In 2009, Edinburgh Neuroscience researchers addressed this by creating an online portal neurosymptoms.org. Updated in 2018, neurosymptoms.org is now (in 2020) available in 13 languages, of which the English version alone receives 50,000-60,000 hits per month [5.8a]. This website is widely recognised as the worldwide go-to portal that neurologists recommend to their patients [5.8b].

Edinburgh Neuroscience research and neurosymptoms.org have led to the formation of 2 new charities that work to raise awareness, provide peer support and campaign for better treatment and care of patients with FND. FND Hope was registered in 2012, with a UK branch opened in 2017, and by 2019 had 18,000 members in 100 countries [5.9a]. FND Action was registered in 2016, and by 2019 had 7,000 members and 100,000 Facebook followers [5.9c]).

Both charities credit their existence in part to the pioneering research of Edinburgh Neuroscience: the founder of FND Hope attests to the “*profound impact that the research of Professors Stone and Carson had on first [her] desire to start the charity and second, [her] ongoing motivation to grow it*”, while the co-founder of FND Action stated that the research had been “*invaluable in helping gain a better understanding of FNDs, which in turn helps towards our plight of advocating for better care for those diagnosed. [...] They have helped break down the barriers of stigma attached to these diagnoses*” [5.9c].

5. Sources to corroborate the impact

[5.1] Quote from President of the Royal Society of Psychiatrists, 2015

[5.2] Changed diagnostic criteria in international diagnostic manuals

a. DSM-5 chapter on Somatic Symptom Disorders (May 2013)

b. ICD-11 section on dissociative neurological symptom disorder (June 2018)

c. Testimonial from the text editor of the DSM-5 Somatic Symptom Disorders chapter

d. Stone et al. 2014 *Neurology* doi: [10.1212/WNL.0000000000001063](https://doi.org/10.1212/WNL.0000000000001063)

[5.3] Inclusion of FND in the UK medical curriculum.

a. Testimonial from Chair of Neurology Specialist Advisory Committee (Joint Royal College of Physicians Training Board)

b. Internal Medicine curriculum (implemented since August 2019)

c. Approved proposal for Neurology curriculum (will apply from August 2022)

[5.4] New professional structures

a. Consensus recommendation on physiotherapy for FMD; Nielsen et al. 2014 *J Neurol Neurosurg Psychiatry* doi: [10.1136/jnnp-2014-309255](https://doi.org/10.1136/jnnp-2014-309255)

b. Occupational therapy consensus statement; Nicholson et al. 2020 *J Neurol Neurosurg Psychiatry* doi: [10.1136/jnnp-2019-322281](https://doi.org/10.1136/jnnp-2019-322281)

c. [ABN special interests group](#)

d. [FNForum website](#)

e. [FND Society website](#)

f. Letter of Support from Royal College of Psychiatrists Congress Manager

[5.5] Testimonials re: FND-specific services from a. Bristol b. Cambridge

[5.6] Published articles describing patient experience

a. Burke M. (2019) *JAMA Neurology* doi:[10.1001/jamaneurol.2019.3043](https://doi.org/10.1001/jamaneurol.2019.3043)

b. Stone J (2016) *Practical Neurology* doi: [10.1136/practneurol-2015-001241](https://doi.org/10.1136/practneurol-2015-001241)

[5.7] Feasibility trial: Jordbru et al. 2014 *J Rehab Med* doi: [10.2340/16501977-1246](https://doi.org/10.2340/16501977-1246)

[5.8] a. Letter from Director of University of Cincinnati Department of Neurology, citing Neurosymptoms.org as the go-to portal for neurologists to recommend to patients

b. Google Analytics for neurosymptoms.org 1st June – 31st December 2020

[5.9] New charities dedicated to FND a. Testimonial from FND Hope International

b. Testimonial from FND Hope UK c. Testimonial from FND Action