Manifesto for a European research network into obsessive-compulsive and related disorders

N.A. Fineberg*, D.S. Baldwin, J.M. Menchon, D. Denys, E. Grünblatt, S. Pallanti, D.J. Stein, J. Zohar, The Obsessive Compulsive and Related Disorders Research Network[1]

Queen Elizabeth II Hospital Mental Health Unit, Howlands, Welwyn Garden City, Hertfordshire AL7 4HQ, UK

Abstract

Obsessive-compulsive and related disorders (O-CRDs) are highly disabling psychiatric illnesses of early-onset. They are responsible for considerable morbidity and socioeconomic burden. Existing treatments are usually only partially successful and there is an urgent need to understand the aetiological factors and neurobiological bases of the disorders in order to develop new and more effective strategies for prevention, early detection and effective treatment.

Emerging data from the neurosciences supports the reconceptualisation of obsessive-compulsive disorder as a spectrum disorder, related to but different from the anxiety disorders and closely aligned with other less well understood psychiatric disorders characterised by compulsive acts such as body dysmorphic disorder, trichotillomania, skin-picking disorder, hoarding disorder; and possibly extending to tic disorders and other neurodevelopmental disorders such as autism.

A new, O-CRDs research network, supported by the Networks Initiative of the European College of Neuropsychopharmacology and comprising leading figures in preclinical and clinical research, has been established. It aims to provide a European perspective on the current debate around internationally-accepted diagnostic criteria and treatment strategies for O-CRDs. Its objectives include; (1) identifying the key outstanding research questions that depend upon cross-centre collaborative investigation, (2) setting a research agenda that is likely to produce an impact on health-outcomes, and (3) strengthening existing projects and collaborative enterprises with these objectives in mind. This paper reviews some of these critical research priorities. By establishing shared multinational databases, collaborative research networks, multicentre studies and joint publications, it is hoped that progress will be achieved.

© 2012 Elsevier B.V. and ECNP. All rights reserved.

*Corresponding author. Tel.: +44 1707 365 085.
E-mail address: kim.fox@hertspartsft.nhs.uk (N.A. Fineberg).

0. Introduction

Emerging clinical and neuroscience data supports the reconceptualization of obsessive-compulsive disorder (OCD) as a spectrum disorder, related to but different from the anxiety disorders and closely aligned with other less well understood psychiatric disorders characterised by compulsive acts such as body dysmorphic disorder, trichotillomania, skin-picking disorder and hoarding disorder; and possibly extending to tic-disorders and other neurodevelopmental disorders such as autism. Obsessive-compulsive and related disorders (O-CRDs) are highly disabling psychiatric illnesses of early-onset and are responsible for considerable morbidity and socio-economic burden. Existing treatments are usually only partially successful and there is an urgent need to understand the aetiological factors and neurobiological bases of the disorders in order to develop new and more effective strategies for prevention, early detection and treatment.

To date, O-CRDs research has tended to be undertaken 'piecemeal', with small single-centre studies using differing methodologies and patient groups, performed according to local expertise and referral-patterns. Some disorders (e.g. skin-picking disorder and hoarding disorder) rarely come to clinical attention and there is a scarcity of specialist centres with the capacity to recruit participants for research. As a result, it has been hard to confirm or refute new findings in this field. There is hence considerable scope for development of multicentre collaborative joint projects that harmonise research methodologies and recruit sufficiently large samples to allow definitive conclusions to be drawn.

To this end, a new O-CRDs research network has been established, supported by the Networks Initiative of the European College of Neuropsychopharmacology and comprising leading figures in preclinical and clinical research. It aims to provide a European perspective on current debates around internationally accepted diagnostic criteria and treatment strategies for O-CRDs Fig. 1. Its objectives include, to (1) identify the key outstanding research questions that depend upon cross-centre collaborative investigation, (2) set a research agenda likely to produce an impact on health-outcomes, and (3) strengthen existing projects and collaborative enterprises. Table 1 summarises ten potentially achievable research priorities that we believe
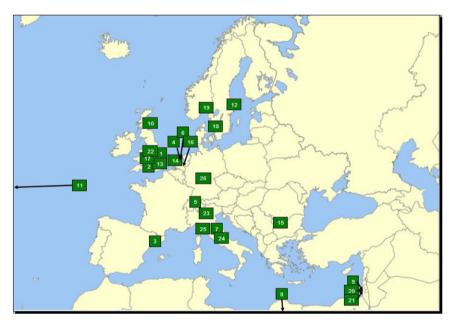

Fig. 1   The Obsessive-Compulsive and Related Disorders Research Network (O-CRN) distribution map. (1) University of Hertfordshire, Queen Elizabeth II Hospital, Welwyn Garden City, Hertfordshire, UK; (2) University of Southampton School of Medicine, Southampton, Hampshire, UK; (3) Department of Psychiatry, Bellvitge University Hospital, Barcelona, Spain; (4) Department of Psychiatry, AMC, University of Amsterdam, Amsterdam, Netherlands; (5) Hospital of Child and Adolescent Psychiatry, University of Zurich, Zurich, Switzerland; (6) VU University Medical Center, Amsterdam, Netherlands; (7) University of Florence, Florence, Italy; (8) Department of Psychiatry, University of Cape Town, South Africa; (9) Chaim Sheba Medical Center, Tel Hashomer, Israel; (10) Advanced Interventions Service Ninewells Hospital, Dundee, UK; (11) Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY; (12) Department of Clinical Neuroscience, Division of Psychiatry, Karolinska Institutet, Stockholm, Sweden; (13) King's College London, Institute of Psychiatry, London, UK; (14) Department of Psychiatry, Leiden University, Medical Center, Leiden, Netherlands; (15) University Hospital for Active Treatment in Neurology and Psychiatry, Sofia, Bulgaria; (16) Noldus Information Technology BV, Wageningen, Netherlands; (17) P1vital Ltd., Oxford, UK; (18) Queen Silvia Children's Hospital, Göteborgs University, Göteborgs, Sweden; (19) Utrecht University, Utrecht, Netherlands; (20) Tel Aviv University, Tel Aviv, Israel; (21) Utrecht Medical Centre, Rudolph Magnus Institute, Utrecht, Netherlands; (22) The Chancellor, Masters & Scholars of the University of Cambridge (UCAM), Cambridge, UK; (23) Department of Psychiatry, University of Milan, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano, Italy; (24) Department of Psychiatric Sciences and Psychological Medicine, Sapienza University of Rome, Rome, Italy; (25) Department of Psychiatry, University of Pisa, Pisa, Italy; (26) Child and Adolescent Psychiatry, University Clinic of Würzburg, Würzburg, Germany; (27) Vita-Salute San Raffaele University, Milano, Italy; (28) Covance, Maidenhead, UK.

Table 1 Top-ten crosscutting issues for translational research into O-CRDs.

Research priorities	Unmet need	Objectives
Refining the nosology.	Biologically and clinically relevant nosological classification of a broad range of disorders characterised by compulsive, habitual and addictive acts.	Translational (human and animal) studies examining psychobiological endophenotypes and treatment-response across a range of compulsive, habitual and addictive behaviours and disorders. Field studies testing reliability of new diagnostic models.
Calculating the burden and cost of O-CRDs to society across Europe.	Primary data relating to direct and indirect costs of OCRDs and their treatment across the lifespan.	Cross-sectional and longitudinal surveys of HRQOL in clinical and population-based OCRDs. Cost-effectiveness analysis of existing treatment modalities.
Defining the natural course of OCD and related disorders using longitudinal studies.	Knowledge of the natural course of O-CRDs and sub-syndromal obsessive-compulsive syndromes, and the key factors that affect long-term outcome.	Longitudinal epidemiological studies investigating incidence, comorbidity, remission, relapse and the associated clinical and demographic factors, across the lifespan.
Reducing the obstacles to timely recognition and treatment.	Accurate recognition and diagnosis of O-CRDs. Strategies to reduce the obstacles to timely treatment.	Strategies for improving recognition and diagnosis of O-CRDs (e.g. clinical screening) and reducing stigma (e.g. public health education). Cost-effectiveness analysis of early intervention with targeted treatments including new delivery methods (e.g. internet CBT).
Clarifying the genetic contribution to O-CRDs.	Candidate genes of relevance for the aetiology, neurobiology and treatment of OCRDs.	Genome-wide linkage and association studies to identify new candidate genes for O-CRDs. Translational studies investigating the behavioural neurobiology (neurochemistry, brain morphology, single unit electrophysiology, functional imaging) of new animal models, e.g. genetically modified mouse lines of relevance.
Identifying environmental risk and maintenance factors.	Environmental risk factors associated with developing illness and maintaining factors common to all O-CRDs and specific to each.	Gene by environmental interaction studies. Family-focused interventions teaching disengagement strategies.
Identifying biomarkers of illness to improve early illness-detection and intervention and biomarkers of treatment-response to plan personalised care.	Biomarkers with a high level of specificity and sensitivity, to provide an innovative platform of diagnostic tools as a basis for early illness-detection and novel treatment-development. Prediction models to inform 'personalised' treatment, allow limited resources (e.g. CBT) to be targeted to those most likely to benefit and optimise clinical outcomes on an individualised basis.	Collaborative studies of gene and endophenotype markers of OCRDs using novel preclinical and clinical approaches, including animal models. Extending 'biomarkers' research to young individuals at high risk of O-CRDs or with prodromal illness, to advance therapeutic intervention and alter the trajectory of the disorder toward a better long-term outcome. Sufficiently powered randomised controlled trials to identify biomarkers and to predict which treatments are more effective for individuals or groups individuals or groups.
Preventing relapse.	Established risk factors for relapse. Improved long-term outcomes following the termination of treatment or relapse.	Longitudinal naturalistic studies exploring relapse and its concomitants in the clinical population to provide a platform for targeted relapse-prevention strategies. RCTs of 'relapsed' cases.

Table 1 (*continued*)

Research priorities	Unmet need	Objectives
Tackling treatment-resistant illness.	Standards for effective/optimum treatment including clear, evidence-based protocols. Core competencies (knowledge abilities, attitudes and values). Guidance on the 'next steps' after first-line interventions have failed. Established determinants of treatment non-response.	Development and dissemination of evidence-based protocols and core competency standards. Systematic research into the long-term cost-effectiveness and mechanism of effect of pharmacological, psychological and surgical treatment for 'treatment-resistant' disease.
Discovering new treatment targets.	New pharmacological compounds, psychological and somatic strategies for OCRDs.	Developing reliable animal and human models (genetic, neuropsychological, neuroanatomical) to improve understanding of the mediating mechanisms underpinning compulsive and impulsive behaviour, as a heuristic for new treatment targets and as a means of testing them out in advance of clinical trials.

will drive the field forward over the next ten years. The complete review is available online.

1. Refining the nosology

Although not yet finalised, the DSM-5 work group is recommending that in the forthcoming classification, OCD will be included under a broader grouping of O-CRDs that includes disorders currently classified elsewhere, including trichotillomania, body dysmorphic disorder, compulsive skin picking and a new category entitled 'hoarding disorder' (www.dsm5.org). These disorders share with OCD a fundamental inability to modify repetitive, unwanted, maladaptive acts. Other disorders considered to share a nosological relationship with OCD, but for which the evidence supporting overlap may be less well defined, include Tourette's syndrome, hypochondriasis, obsessive-compulsive personality disorder, pathological gambling and autistic spectrum disorder. The American Psychiatric Association DSM-5 Committee has called for translational research to improve the diagnostic classification of disorders such as OCD. Therefore, new studies investigating endophenotype-determinants of OCD in relation to a broad spectrum of putatively related disorders, both within and outside the new DSM-5 category, are required.

   Accumulating evidence from preclinical studies suggests that related neurobiological and neurocognitive processes that mediate behavioural-inhibition, habit-learning and reward-processing, i.e. those domains associated with a range of other disorders including impulse-control and addictive disorders, may each contribute toward vulnerability to compulsive activity. A growing literature recognises that the neurobiology underpinning OCD and at least some of these disorders may share special characteristics including impairment in structural and functional aspects of cortico-striatal neurocircuitry (Fineberg et al., 2010). Better understanding of the similarities and differences among the genetic, neurobiological and socio-demographic

determinants of OCD and related disorders and the characteristics of their treatment-response would clarify the nosological relationship between disorders characterised primarily by compulsive, impulsive and addictive behaviours. However, understanding the determinants of disease and basing a new classification on these, may not necessarily improve clinical utility; field-testing of the proposed diagnostic criteria across an integrated network of clinical research centres is also required. Taken together, such improvements would be expected to have a positive impact upon the accuracy of prognostication and lead to better health services informatics, planning and delivery.

2. Calculating the burden and cost of O-CRDs to society across Europe

OCD is associated with impairment across a broad range of functional and health-related quality of life (HRQoL) domains. Greater impairment in family life and activities of daily living has been reported in patients with OCD, compared to those with other anxiety disorders or depression; in addition their families and caregivers are more burdened as they must accommodate to the challenges of living with someone with a highly-pervasive mental disorder. In its most severe and chronic form, OCD is associated with high levels of long-term hospitalisation or residential care and requires specialist mental health services, but the illness is often less overtly incapacitating and frequently gets overlooked by health-professionals. In addition, people with non-comorbid OCD are less likely than those with a comorbid disorder to be treated and few receive appropriate treatment (Torres et al., 2007).

   Only a few studies have examined the epidemiology of O-CRDs) and there is little data describing their functional impact. Whereas only a small proportion of community respondents meet full DSM-IV criteria for lifetime (2.3%) or 12-month (1.2%) prevalence of OCD, up to one quarter of

the population are thought to experience sub-syndromal obsessions or compulsions at some time (Ruscio et al., 2010). Obsessive-compulsive syndromes are associated with significant psychiatric comorbidity (e.g. with anxiety, depressive and substance-use disorders) at both an individual and familial level (Bienvenu et al., 2012). The public health burden associated with OCD is likely to be greater than its modest prevalence suggests and the costs extend beyond the direct costs of treatment for the disorder to include the considerable burden of the associated comorbidities, together with the indirect costs associated with lost occupational income for the patient and their family. There is a scarcity of primary data on which to base such analyses and the existing estimates depend on numerous assumptions, to the extent that the full impact of OCD-related disorders in Europe is poorly understood. Indeed, a recent comprehensive cost-data review was unable to identify any relevant European cost-studies of OCD published within the last 10 years (Wittchen et al., 2011).

There is thus a clear need for community-based studies to explore the direct and indirect costs of O-CRDs across the lifespan. Specifically, we need to obtain reliable estimates of incidence, of cumulative prevalence across the age-range and of remission rates along with associated clinical and demographic determinants that may alter the trajectory of disease. Such primary data are required to calculate the relative cost and outcome of 'evidence-based' treatments for patients at various levels of illness-severity and comorbidity. With this data we may refine health-economic models and direct resources toward greatest need. For example, the possibility of stratifying CBT-intensity according to OCD-severity (e.g. shorter treatment-courses), or implementing novel and potentially less costly methods of delivery (e.g. primary versus secondary care; face-to-face versus telephone versus internet), introduces an important extra dimension to any such analysis.

3.   Defining the natural course of O-CRDs using longitudinal studies

Remarkably little prospective research has been conducted on the course of O-CRDs and we remain relatively ignorant of the key factors affecting the long-term outcome for most disorders. Such data is of crucial importance in understanding aetiology, planning treatment and improving prognostication. Traditionally, OCD is considered to be a relatively unremitting disorder, with the greatest prevalence occurring in early-middle adult life. However, some studies indicate a continuous and chronic course of illness, while others report a more favourable outcome that may reflect differences in the clinical, demographic or treatment characteristics of the study-population or in the methodology, e.g. length of follow-up. As a result, considerable uncertainty remains as to the natural course and outcome of O-CRDs.

As treatments for OCD, such as SSRIs and CBT, have become available in primary care, patients entering secondary care represent an increasingly treatment-refractory group. Prospective studies, tracing the course of OCD in a non-clinical adult population, would be less prone to ascertainment-bias toward resistant and poor-outcome cases. Consequently, there is a pressing need for longitudinal community-based analysis of incidence, comorbidity and remission that includes evaluation of a broad spectrum of O-CRDs, including those characterised by 'behavioural addiction', such as compulsive internet-use and compulsive sexual behaviour, using age-defined cohorts including young children, adolescents and the elderly. This would provide fresh data on the critical trajectories that occur over the lifespan and may inform new aetiological theories linking these disorders. Such data would also provide an essential basis for designing preventative trials and targeting early interventions. There is an additional unmet need to investigate the impact of O-CRDs in the elderly population, where data is almost non-existent. The study of OCD symptoms from adulthood into the elderly could help us understand how brain development (or neurodegeneration) might result in the reduction of symptoms. Conversely, if there is no reduction in severity with age, it would be important to understand why elderly OCD patients seem to 'disappear' from psychiatric services.

4.   Reducing the obstacles to timely recognition and treatment

Shame and secrecy surround OCD and many of the related disorders and constitute an important obstacle to diagnosis and treatment. Consequently, these illnesses are poorly recognised and only a minority of cases receives timely treatment. Comorbidity may increase the likelihood that the individual will present to a doctor, but usually fails to improve the accuracy of diagnosis. Preliminary data indicate that an early onset of illness increases the need for combined treatments and hospitalisation, while delayed treatment is associated with poorer treatment-response and clinical outcome (Dell'Osso et al., 2010). If replicated, these findings would provide a strong case for targeted early-intervention for OCD. Early intervention may be particularly relevant for disorders that are associated with considerable psychiatric comorbidity, since the early detection and treatment of the primary disorder could also prevent the onset of the secondary comorbidity.

The long-term, societal costs of early-onset OCD highlight the importance of delivering interventions at the earliest signs of illness and at the greatest level of efficacy and tolerability. A number of prototypical screening instruments for OCD have been piloted, e.g. Z-FOCS (Fineberg et al., 2008) and SOC-S (Uher et al., 2007), and there is a growing case for investigating the impact of targeted screening and other early-intervention strategies. Mechanisms for improving treatment-access for remote populations (e.g. internet-based treatment) and for socially disadvantaged groups also merit further study.

5.   Clarifying the genetic contribution to O-CRDs

OCD is a complex disorder and its pathogenesis is likely to be influenced by genetic and environmental factors. First-degree relatives of patients are exposed to a four-fold greater risk of developing OCD symptoms, relative to family

members of comparison subjects (Pauls, 2008). Early access to new candidate genes for O-CRDs (e.g. glutamate-transporter SLC1A1, glutamate-receptor GRIK2, and tryptophan-hydroxylase 2) through collaboration in genome-wide association studies; coupled with investigation of behavioural neurobiology (neurochemistry, brain morphology, single unit electrophysiology and functional imaging) of new animal models including neuropsychological models and genetically-modified mouse lines of relevance to O-CRDs (such as CDH-13 and SAPAP-3), using interdisciplinary translational strategies, may advance the discovery and development of genetic biomarkers of O-CRDs diagnostics and treatment-response. In addition, such data is likely to provide entirely new insights into the role of the various monoamines in brain development and function in relation to neuropsychiatric disorders and pinpoint new targets for treatment-development.

6.   Identifying environmental risk and maintenance factors

Twin studies suggest that at least 50% of the aetiology of OCD and related disorders is environmental (Iervolino et al., 2011). A broad range of childhood neurodevelopmental, behavioural, personality and environmental risk factors, associated with a diagnosis of OCD and with O-C symptoms in adulthood, has been identified. Effort needs to be put into the identification of environmental risk factors common to all O-CRDs and also those which are specific to each. For this, gene-by-environment interaction studies are likely to represent the best way forward.

Paediatric OCD is associated with high levels of family accommodation (i.e., participation in behaviours), which is associated with higher levels of childhood OCD severity, persistence of illness and enduring treatment-resistance. Therefore, research into family-focused interventions that teach disengagement strategies may improve treatment-response in OCD.

7.   Identifying biomarkers of illness to improve early detection and intervention and biomarkers of treatment-response to plan personalised care

Despite dedicated research and some breakthroughs in the scientific understanding of relevant neurobiological and psychosocial factors, the causes of O-CRDs remain largely unknown. This lack of certainty hinders the accurate diagnosis, prediction of prognosis, and development of advanced treatment-approaches. Translational studies targeting pathogenic mechanisms at the genetic and endophenotypic (functional and structural) neuroanatomical level, complemented by animal modelling, may clarify crucial neurobiological mechanisms and form the basis for early illness-detection and novel treatment-development.

The discovery of a set of markers from psychopathology, genetics, neuropsychology and neuroimaging domains may provide an innovative platform of diagnostic tools with a high level of specificity and sensitivity to understand and detect early-onset compulsive behaviours. Equipped with such a platform, the clinician would have new tools for diagnosis and targeted therapy that could be expected to accelerate recovery with fewer treatment failures, rebounds or dropouts. Extending 'biomarkers' research to young individuals at high risk of developing O-CRDs (such as the unaffected offspring of O-CRD parents) or in a prodromal phase, may bring forward early interventions that might alter the trajectory of the disorder toward a better long-term outcome.

From an EU perspective, treating OCD from the outset using the most effective strategy is likely to represent better value than treating a more severe presentation downstream. Combining SSRI with CBT may improve outcomes, but is more costly and there is little current evidence to identify who might benefit from the combination. There is a need for adequately powered randomised controlled trials with the capacity to identify biomarkers that predict which treatment or combination of treatments will be more efficacious for individuals or groups of patients; and which offer the scope to refine prediction-models and deliver new methods of personalised-treatment to optimise clinical outcomes on an individual basis.

8.   Preventing relapse

Patients with OCD need to remain well to maintain quality of life. Little is known about long-term outcomes following the termination of a course of CBT, but robust data from randomised controlled studies suggests that continuing an SSRI protects against relapse, whereas discontinuation leads to relapse and reduction in life quality. Continuation-treatment with SSRI is therefore an important strategy for long-term wellbeing. There remains a need for studies of CBT booster-regimes, as an alternative method to prevent relapse. Clinical programmes aimed at improving treatment-adherence, including co-operative care planning and risk-assessment, also need to be developed.

Most relapse-prevention studies have investigated highly selected patients lacking major psychiatric comorbidity, which may underestimate relapse rates. We still know very little about risk factors for relapse in OCD, nor do we understand how best to treat relapsed OCD. Longitudinal naturalistic studies exploring treatment-relapse and its concomitants would provide important information for targeted relapse-prevention strategies and a springboard for designing new treatment-trials in relapsed cases.

9.   Tackling treatment-resistant illness

Despite the availability of evidence-based pharmacological and psychological interventions, roughly 40% of patients with OCD do not respond, remain troubled by severe symptoms, and endure continuing disability. Little is known about the determinants of treatment non-response in the O-CRDs, or the next steps after first-line interventions (SSRI or CBT) have failed. The results of childhood OCD CBT-studies performed in specialist centres suggest more encouraging outcomes could be expected and 'technical treatment failure' seems to be a common cause for apparent refractoriness, i.e. patients have not received an adequate dose or type of treatment. There is a clear need

to define what constitutes the minimum effective/optimum treatment and to ensure that clear, evidence-based protocols that include routine outcomes-measurement and the core competencies (knowledge, abilities, attitudes, values) required by clinicians to deliver these treatments to a satisfactory standard, are agreed, disseminated and adopted.

Adjunctive antipsychotics in moderated doses are effective in roughly 40% of adults with SSRI-resistant OCD, though we do not have dose-finding nor comparator studies to determine the relative efficacy and tolerability of different first or second-generation compounds. High doses of SSRI might prove effective in otherwise SSRI-resistant cases, though definitive trials are lacking. CBT-resistant OCD has received even less study. Systematic research into the effectiveness and cost-effectiveness of treatment for the substantial proportion of patients with costly 'treatment-resistant' disease is needed. Such treatment needs additionally to be tested in 'special' populations, for example in people with developmental disorders.

Neurosurgical techniques that interrupt the neural connections between the frontal lobes and subcortical and limbic structures, including cingulotomy and capsulotomy, have shown some evidence of efficacy for the most treatment-refractory cases, but controlled studies have not been performed (Matthews and Eljamel, 2003). Less ablative strategies, such as continuous deep-brain stimulation (DBS) using electrodes implanted in nodes within the cortico-striatal neurocircuitry, including the nucleus accumbens and the sub-thalamic nucleus, are currently under investigation and may present a clinically effective strategy (Denys et al., 2010). Before such treatment can be accepted outside the research setting, important questions regarding the optimal electrode placement, stimulation parameters and adverse effects require confirmation. Specific forms of CBT and intensive hospital-based interventions might be appropriately integrated with neuromodulation in DBS-implanted subjects, to take advantage of enhanced neuroplasticity, but these still require systematic evaluation since there has been a tendency for different groups to pilot different techniques. By harmonising research methodology across multiple treatment centres, the mechanism of effect of DBS, about which very little is as yet understood, may be elucidated using a combination of surgical, electrophysiological, brain-imaging and neuropsychological paradigms. Also, alternative, non-invasive, techniques for neurostimulation, such as repetitive transcranial magnetic stimulation or theta burst stimulation, warrant further investigation and development, both as a research tool and as a clinical adjuvant technique.

10. Discovering new treatment targets

For many O-CRDs, no 'evidence based' treatment exists and clinical research remains in its infancy. The identification of new pharmacological compounds and psychological strategies is hence a key priority. Animal models provide a complementary approach to human preclinical studies. Transgenic and neuropsychological models of compulsivity that offer new insights into the mediating genetic, neuropsychological and neurochemical mechanisms implicated in controlling compulsive and impulsive behaviour could reasonably be expected to lead to novel treatment-targets that may be applicable across a broad range of disorders that share compulsivity in their psychobiology.

11. Conclusions

The O-CRN is an initiative to provide a much-needed platform for translational and implementational research into the diagnosis and treatment of a broad range of mental disorders characterised by compulsive behaviour and existing within the dimension of anxiety-affective disorders on the one hand and impulsive-compulsive disorders on the other. Through establishing shared multinational databases and collaborative research networks, it is anticipated that much progress will be made. By advancing knowledge of the underpinning brain-based mechanisms and by identifying reliable biomarkers of disease and treatment-response, such research would be anticipated to advance the early detection of illness and allow the most effective treatments to be targeted to those most likely to respond.

Role of funding source

Contributors

N.A. Fineberg took overall charge in composing, writing the final draft and submitting the manuscript. D.S. Baldwin managed the literature searches related to EU policies. J. Menchon contributed to the manuscript on core competencies and the health economic burden of OCD. D. Denys contributed to the manuscript on novel treatment and deep brain stimulation for OCD. E. Grünblatt wrote the genetics of OCD section. S. Pallanti contributed to the section on new treatments and treatment of resistant illness. D. Stein proof read the manuscript and contributed to the nosogical status section. J. Zohar contributed to the section on early intervention and better recognition of the disorder.

Conflict of interest

Acknowledgements

Appendix A.   Supplementary information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.euroneuro.2012.06.006.

References

Bienvenu, O.J., Samuels, J.F., Wuyek, L.A., Liang, K.Y., Wang, Y., Grados, M.A., et al., 2012. Is obsessive-compulsive disorder an anxiety disorder, and what, if any, are spectrum conditions? A family study perspective. Psychol. Med. 42 (1), 1–13.

Dell'Osso, B., Buoli, M., Hollander, E., Altamura, A.C., 2010. Duration of untreated illness as a predictor of treatment response and remission in obsessive-compulsive disorder. World J. Biol. Psychiatry 11 (1), 59–65.

Denys, D., Mantione, M., Figee, M., van den Munckhof, P., Koerselman, F., Westenberg, H., et al., 2010. Deep brain stimulation of the nucleus accumbens for treatment-refractory obsessive-compulsive disorder. Arch. Gen. Psychiatry 67 (10), 1061–1068.

Fineberg, N.A., Krishnaiah, R.B., Moberg, J., O'Doherty, C., 2008. Clinical screening for obsessive-compulsive and related disorders. Israel J. Psychiatry 45 (3), 151–160.

Fineberg, N.A., Potenza, M.N., Chamberlain, S.R., Berlin, H.A., Menzies, L., Bechara, A., et al., 2010. Probing compulsive and impulsive behaviors, from animal models to endophenotypes: a narrative review. Neuropsychopharmacology 35, 591–604.

Iervolino, A.C., Rijsdijk, F.V., Cherkas, L., Fullana, M.A., Mataix-Cols, D., 2011. A multivariate twin study of obsessive-compulsive symptom dimensions. Arch. Gen. Psychiatry 68 (6), 637–644.

Matthews, K., Eljamel, M.S., 2003. Status of neurosurgery for mental disorder in Scotland. Selective literature review and overview of current clinical activity. Br. J. Psychiatry 182, 404–411.

Pauls, D.L., 2008. The genetics of obsessive compulsive disorder: a review of the evidence. Am. J. Med. Genet. C. Semin. Med. Genet., 133–1392.

Ruscio, A.M., Stein, D.J., Chiu, W.T., Kessler, R.C., 2010. The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. Mol. Psychiatry 15 (1), 53–63.

Torres, A.R., Prince, M.J., Bebbington, P.E., Bhugra, D.K., Brugha, T.S., Farrell, M., et al., 2007. Treatment seeking by individuals with obsessive-compulsive disorder from the British psychiatric morbidity survey of 2000. Psychiatr. Serv. 58 (7), 977–982.

Uher, R., Heyman, I., Mortimore, C., Frampton, I., Goodman, R., 2007. Screening young people for obsessive compulsive disorder. Br. J. Psychiatry 191, 353–354.

Wittchen, H.U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., et al., 2011. The size and burden of mental disorders and other disorders of the brain in Europe. Eur. Neuropsy chopharmacol. 21 (9), 655–679.