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Impaired cognitive flexibility across psychiatric disorders

Jon E. Grant[1] and Samuel R. Chamberlain[2,3]

[1]Department of Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL, USA, [2]Department of Psychiatry, Faculty of Medicine, University of Southampton, Southampton, UK and [3]Southern Health NHS Foundation Trust, Southampton, UK

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Corresponding author:
Jon E. Grant;
Email: jongrant@uchicago.edu

Abstract

Objective: Problems with cognitive flexibility have been associated with multiple psychiatric disorders, but there has been little understanding of how cognitive flexibility compares across these disorders. This study examined problems of cognitive flexibility in young adults across a range of psychiatric disorders using a validated computerized *trans*-diagnostic flexibility paradigm. We hypothesized that obsessive-compulsive spectrum disorders (eg, obsessive-compulsive disorder, trichotillomania, and skin-picking disorder) would be associated with pronounced flexibility problems as they are most often associated with irrational or purposeless repetitive behaviors.

Methods: A total of 576 nontreatment seeking participants (aged 18-29 years) were enrolled from general community settings, provided demographic information, and underwent structured clinical assessments. Each participant undertook the intra-extra-dimensional task, a validated computerized test measuring set-shifting ability. The specific measures of interest were total errors on the task and performance on the extra-dimensional (ED) shift, which reflects the ability to inhibit and shift attention away from one stimulus dimension to another.

Results: Participants with depression and PTSD had elevated total errors on the task with moderate effect sizes; and those with the following had deficits of small effect size: generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), antisocial personality disorder, and binge-eating disorder. For ED errors, participants with PTSD, GAD, and binge-eating disorder exhibited deficits with medium effect sizes; those with the following had small effect size deficits: depression, social anxiety disorder, OCD, substance dependence, antisocial personality disorder, and gambling disorder.

Conclusions: These data indicate cognitive flexibility deficits occur across a range of mental disorders. Future work should explore whether these deficits can be ameliorated with novel treatment interventions.

Introduction

Many psychiatric disorders are characterized by repetitive compulsive behaviors (including, for example, alcohol and substance use disorders, schizophrenia, autism spectrum disorders, eating disorders, gambling disorder, trichotillomania, and skin-picking disorder).[1-7] Obsessive-compulsive disorder (OCD) may reflect the most extreme version of repetitive behavior problems, but the complaint of having to do the same thing over and over again despite negative consequences (ie, being cognitively inflexible, which can be considered an important facet of compulsivity) is also commonly reported in other disorders too.[8-10] OCD is currently regarded, in the Diagnostic and Statistical Manual Version 5 (DSM-5), as part of a spectrum of OC-related conditions, which also includes hair-pulling disorder, skin-picking disorder, hoarding disorder, and body dysmorphic disorder. Whereas in the International Classification of Diseases Version 11 (ICD-11), OC-related disorders are OCD, body dysmorphic disorder, olfactory reference disorder, hypochondriasis, hoarding disorder, and body-focused repetitive disorders (ie, hair-pulling disorder and skin-picking disorder). Of course, diagnostic systems evolve over time and there continues to be extensive debate and research as to which conditions should and should not sit in such a category. The hallmark of these conditions, irrespective of nosological system, is the repetitive "habitual" symptoms and these arguably are suggestive of being "stuck" in a rigid or inflexible behavioral repertoire; that is, the symptoms of these disorders are suggestive of cognitive inflexibility. Because previous studies have largely focused on particular disorders, however, there has been little understanding of how and to what degree cognitive flexibility compares across these disorders using the same sample. The issue may be important because therapies and pharmacotherapy that target impaired cognitive flexibility may be needed as part of the management of other disorders, when this is a prominent feature.

Problems with cognitive flexibility can be measured using computer-based instruments such as the intra-extra-dimensional (IED) set shift task.[11] The IED is adapted from the classic

Wisconsin Card Sorting Test and examines the ability of participants to learn and flexibly adapt a learnt "rule" in order to select correct images presented by the computer. The extra-dimensional (ED) shift, a subtest of the IED, reflects the ability to inhibit and shift attention away from one stimulus dimension to another. Literature has indicated that ED shifting is contingent on the integrity and function of the dorsolateral prefrontal cortices.[12-14] Although the IED is not diagnostic for a particular disorder, the task has shown that people with OCD, body dysmorphic disorder, and anorexia nervosa have all demonstrated ED-shifting deficits.[15-17] It is hard to know if deficits are of similar or different magnitude across disorders since studies typically examine single mental health disorders in isolation, rather than a range of mental disorders within a single study setting (using the same recruitment techniques and methodology).

Therefore, the aim of this study was to examine impairments in cognitive flexibility across a range of psychiatric disorders using the IED task, within a single study setting. We hypothesized that multiple psychiatric disorders, particularly OCD, would be associated with pronounced problems in cognitive flexibility in young adults (we chose a limited age range to reduce the confounding effect of age on cognition).

Methods

Participants

A total of 576 participants (aged 18-29 years) were enrolled from general community settings. Study inclusion criteria were: participants had gambled at least 5 times in the past year (since this was part of a wider longitudinal study enriched for gambling behavior); and they were able to be interviewed in person. As impulsivity and other cognitive elements may differ based on age, we chose a narrow age range to reduce the confounding factor of age. Exclusion criteria for this study: hearing or vision problems that made performing cognitive tasks difficult and an inability to understand and consent to the study. Participants were recruited in the Minneapolis and Chicago metropolitan areas using media advertisements. Each participant was compensated with a $50 gift card. The Institutional Review Board of the University of Chicago approved the study and the consent statement. After complete description of the study and an opportunity to ask questions, participants provided written informed consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Assessments

Demographic variables (age, biological sex at birth, gender, and highest completed level of education) were recorded. Participants were evaluated for psychiatric disorders using the Mini International Neuropsychiatric Inventory (MINI),[18] the Minnesota Impulsive Disorders Interview (MIDI) (which screens for compulsive buying, kleptomania, trichotillomania, skin-picking disorder, pyromania, intermittent explosive disorder, compulsive sexual behavior, and binge-eating disorder),[19,20] the ADHD World Health Organization Screening Tool Part A (ASRS v1.1),[21] and the Structured Clinical Interview for Gambling Disorder.[22] All diagnostic assessments were performed by the first author.

In addition to diagnostic measures, participants underwent computerized testing using the IED. The IED is adapted from the classic Wisconsin Card Sorting Test and examines the ability of participants to learn and flexibly adapt a learnt "rule" in order to select correct images presented by the computer.[11] Participants are presented with 4 boxes: 2 contain shapes and 2 are blank. On each trial, participants select the picture they believe to be correct. The computer then provides feedback about whether the choice was correct or incorrect, based on a "rule" that it follows. Therefore, individuals must learn this rule through feedback and then select the correct shape in as many trials as possible. Once the participant chooses a number of correct shapes, the computer switches the rule to introduce a new "correct" shape. The task has 9 task stages examining different aspects of learning and flexibility. The crucial stage is the ED shift stage, where participants must inhibit and shift their attention away from a previously relevant dimension of the pictures, onto a different stimulus dimension that was previously irrelevant. As such, ED-shifting examines this crucial component of cognitive flexibility, which is implicated as a feature of compulsivity. The number of total errors throughout the task (adjusted for stages not completed) and the number of errors specifically pertaining to the ED set shift were the measures of interest.

Data analysis

Only psychiatric disorders endorsed by at least 1% of the participants (ie, at least 5 people per diagnosis) were included for analysis. The profile of poor cognitive flexibility for disorders was quantified by calculating *z*-scores relative to normative data from those participants in the study who did not have mental disorders (hereafter referred to as controls). *z*-scores in this context are equivalent to Cohen's *d* and so reflect effect sizes. By convention, 0.3 would be small, 0.5 medium, and 0.8 large effect sizes.

Results

A total of 576 young adults (mean (standard deviation) age = 22.2 (3.6) years; n = 377 (65.5%) female) were enrolled. Of the 576 participants, 424 (73.6%) had completed college education or higher. The numbers [%] of participants with each disorder of interest were as follows: major depressive disorder 13 [2.3%], panic disorder 7 [1.2%], agoraphobia 25 [4.3%], social anxiety disorder 24 [4.2%], OCD 12 [2.1%], PTSD 6 [1.0%], alcohol dependence 81 [14.1%], alcohol abuse 74 [12.9%], substance dependence 47 [8.2%], substance abuse 43 [7.5%], bulimia 10 [1.7%], generalized anxiety disorder (GAD) 25 [4.3%], antisocial personality disorder 32 [5.6%], ADHD 30 [7.0%], intermittent explosive disorder 11 [2.2%], gambling disorder 94 [19.0%], compulsive sexual disorder 14 [2.8%], compulsive buying disorder 23 [4.7%], and binge-eating disorder 7 [1.4%]. Note that percentages do not always reflect a denominator of 576 cases as this refers to percentage of those who completed that module (ie, for whom data were available).

Figure 1 shows the magnitude of deficits in cognitive flexibility in different disorders compared to controls. Participants with depression and PTSD had elevated total errors on the task with moderate effect sizes; and those with the following disorders had deficits of small effect size: GAD, OCD, antisocial personality disorder, and binge-eating disorder. When we examined the ED shifting errors, participants with PTSD, GAD, and binge-eating disorder exhibited deficits with medium effect sizes; and those with

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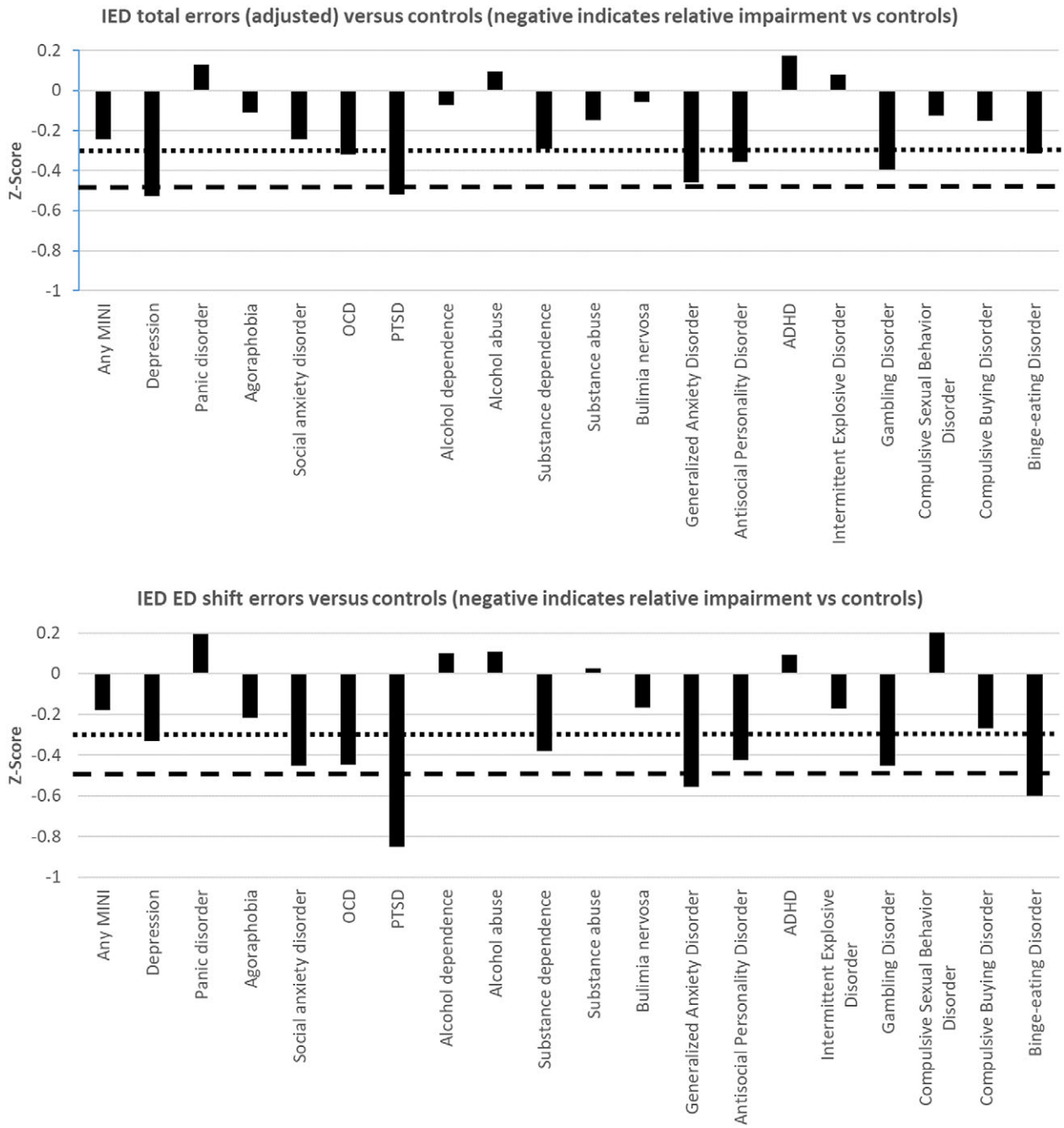

Figure 1. Profile of cognitive flexibility problems across the range of mental health conditions. Top panel shows *z*-scores for total errors (adjusted) on the IED task in patient groups vs controls. Lower panel shows *z*-scores for extra-dimensional (ED) set shifting errors for patient groups vs controls. The dotted lines indicate threshold for at least small effect size deficit (*z*-score ≥ −0.3), and the dashed lines show threshold for at least medium effect size deficit (*z*-score ≥ −0.5), vs controls.

the following disorders had small effect size deficits: depression, social anxiety disorder, OCD, substance dependence, antisocial personality disorder, and gambling disorder.

Discussion

This is the first study that we are aware of that has used a validated, *trans*-diagnostic task of cognitive flexibility across multiple disorders in a diverse, nontreatment seeking sample of young adults, in a single study setting. This study showed that several disorders were associated with greater effect size of impairment in cognitive flexibility than OCD, as indexed by ED-shifting deficits, among these being PTSD, GAD, binge-eating disorder, and gambling disorder. If we think about impaired flexibility as a reflection of compulsivity, then these data may be some of the first to suggest that compulsivity contributes to 2 common anxiety disorders (PTSD and GAD) as well as 2 more traditional impulsivity disorders such as gambling and binge eating, in addition to playing a role in OCD (as would conventionally be a focus of research). It is important to note that we examined participants' task performance as they "presented" that is *in vivo*—we did not control for impact of comorbidities—this would not have been possible with these sample sizes.

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In the case of anxiety disorders, these findings are largely consistent with the available literature. A small study of adolescents with GAD (n = 34) found that youth with GAD demonstrated greater cognitive inflexibility on the IED task compared to youth with OCD.[23] Similarly in a study of 31 adults with GAD using the Wisconsin Card Sorting Test, deficits in cognitive flexibility were reported.[24] Furthermore, the research suggests that binge-eating disorder and gambling disorder seem to have some pronounced impairments in cognitive flexibility.[25-28]

Prior meta-analysis reported medium-large effect size deficits in cognitive flexibility in OCD.[29] The current study found a small effect size deficit in OCD—reasons for this difference in magnitude are unclear but could for example reflect different genetic or familial loading between samples (the current study was a non-treatment seeking sample whereas many studies in the prior meta-analysis involved patients recruited from clinical settings). ED-shifting deficits appear to run in families and to represent a candidate vulnerability marker for OCD.[30,31] It is also possible that specific OCD subtypes may exhibit different levels of cognitive inflexibility.

While this study is one of the first to present the profile of flexibility performance across a range of mental health disorders within a single study setting, several limitations need to be considered. First, this was a nontreatment seeking sample and as such findings may not generalize to clinical cohorts or other settings. Second, the study focused on 1 neurocognitive task rather than also evaluating other aspects of compulsivity (including other cognitive tasks but also *trans*-diagnostic questionnaires). Third, this study was not designed to control for other variables that may be linked to disorders differentially (eg, rates of depressive symptoms) and had relatively small sample sizes for some of the disorders of interest. Relatedly, as noted, we did not control for comorbidities since the sample sizes would have been too small to facilitate this (given that comorbidity is common per disorder). It is arguably more important to consider whether affected individuals experience relative cognitive impairment in vivo, as opposed to "once comorbidities are controlled for"—since the latter then would potentially underrepresent the actual problems experienced by those individuals. Similarly, we could not examine the potential role of other variables such as age, gender distribution, duration of illness, and treatments received, due to the relatively small cell sizes. For the same reason, we did not describe each disorder's characteristics in more detail. Though a nontreatment seeking sample, some individuals would have been receiving previously established treatments and this information (including duration of any such treatments) was not available—nor could it have been analyzed due to the sample sizes. Additionally, although we kept the age range narrow to reduce age effects on cognitive tasks, the age range of participants in this study may influence the generalizability of findings. Furthermore, these results emerged from a sample of young adults with a relatively short duration of illness for most of these disorders and therefore these findings may differ in adults with a long duration of illness (and/or duration of untreated illness). Ideally future work would use a similar "single study" approach but recruit a much larger sample, with a wider age range, in order to validate these findings and ensure they are reproducible.

Conclusion

In conclusion, cognitive flexibility deficits were identified across a range of psychiatric conditions in a single study setting, but the largest magnitude deficits were seen for disorders not conventionally commonly considered within the "compulsivity" framework. Future studies should evaluate a broader range of features characteristic of compulsivity. These findings highlight the need to consider compulsivity across a range of disorders including whether it may be possible to use novel treatment approaches to ameliorate such compulsive tendencies across disorders.

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