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Dissociation of decision making under ambiguity and decision making under risk: A neurocognitive endophenotype candidate for obsessive–compulsive disorder

Long Zhang [a,b], Yi Dong [c], Yifu Ji [c], Chunyan Zhu [b], Fengqiong Yu [b], Huijuan Ma [a,b], Xingui Chen [a,b], Kai Wang [a,b,*]

[a] Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Hefei, China
[b] Laboratory of Neuropsychology, Anhui Medical University, Hefei, China
[c] Mental Health Center of Anhui Province, Hefei, China

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ABSTRACT

Evidence in the literature suggests that executive dysfunction is regarded as an endophenotype candidate for obsessive–compulsive disorder (OCD). Decision making is an important domain of executive function. However, few studies that have investigated whether decision making is a potential endophenotype for OCD have produced inconsistent results. Differences in the findings across these studies may be attributed to several factors: different study materials, comorbidity, medication, etc. There are at least two types of decision making that differ mainly in the degree of uncertainty and how much useful information about consequences and their probabilities are provided to the decision maker: decision making under ambiguity and decision making under risk. The aim of the present study was to simultaneously examine decision making under ambiguity as assessed by the Iowa Gambling Task (IGT) and decision making under risk as measured by the Game of Dice Task (GDT) in OCD patients and their unaffected first-degree relative (UFDR) for the first time. The study analyzed 55 medication-naïve, non-depressed OCD patient probands, 55 UFDRs of the OCD patients and 55 healthy matched comparison subjects (CS) without a family history of OCD with the IGT, the GDT and a neuropsychological test battery. While the OCD patients and the UFDRs performed worse than the CS on the IGT, they were unimpaired on the GDT. Our study supports the claim that decision making under ambiguity differs from decision making under risk and suggests that dissociation of decision making under ambiguity and decision making under risk may qualify to be a neurocognitive endophenotypes for OCD.

1. Introduction

Obsessive–compulsive disorder (OCD) is a phenotypically heterogeneous neuropsychiatric disorder, and there is strong evidence that genetic factors play an important role in the development of OCD. The level of monozygotic twin concordance is reported to be 63–87% (Hanna et al., 2005), and family studies show that the risk to first-degree relatives of OCD patients is approximately five times that of the normal population (Nestadt et al., 2000). However, classical genetic linkage and association studies have not yet provided consistent results to identify the contributory genes involved in OCD (Nestadt et al., 2010), which leads to the exploration of other approaches to investigate the genetic basis of OCD, including searching for endophenotype. Endophenotypes are intermediate phenotypes that are not obvious or external but, rather, are microscopic and internal (Gottesman and Gould, 2003). To be more specific, endophenotypes are defined as heritable quantitative traits that are believed to be intermediate between disease phenotypes and the biological processes that underlie them (Reus and Freimer, 1997) and to be correlated with increased genetic risk for a disease, which could exist in both patients and clinically unaffected first-degree relative (UFDR) of patients (Kéri and Janka, 2004). The commonly used assessment measures available for endophenotype analysis include biochemical, neuroimaging, neuroanatomical, endocrinological, and neuropsychological methods. Putative endophenotypes must fulfill the following criteria: be associated with the disease in the population, be heritable, be state-independent, be co-segregated with the disease, and be found among the UFDR of patients at a higher rate than in the general population (Gottesman and Gould, 2003). From this perspective, neurocognitive impairments are

Abbreviations: ANOVA, analysis of variance; CS, comparison subjects; dlPFC, dorsolateral prefrontal cortex; DS, Digit Span; GDT, Game of Dice Task; HARS, Hamilton Anxiety Rating Scale; HDRS, Hamilton Depression Rating Scale; IGT, Iowa Gambling Task; OCD, obsessive–compulsive disorder; OFC, orbitofrontal prefrontal cortex; SCWT, Stroop Color Word Test; TMT, Trail Making Test; ToL, Tower of London; UFDR, unaffected first-degree relative; VF, Verbal Fluency; vmPFC, ventromedial prefrontal cortex; WCST, Wisconsin Card Sorting Test; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.

* Corresponding author at: Department of Neurology, The First Affiliated Hospital of Anhui Medical University, Jixi Road, Hefei, Anhui Province, China. Tel./fax: +86 551 62923704.
E-mail address: wangkai1964@126.com (K. Wang).

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regarded to be the most promising candidate endophenotypes for many psychiatric disorders (Delorme et al., 2007). Moreover, measures of neurocognitive function are widely considered to be valuable endophenotypes in large part because of their demonstrated reliability and stability over time (Rund, 1998).

Searching for candidate endophenotypes has been extensively applied to some psychiatric disorders, for instance, schizophrenia (Leppänen et al., 2008), mood disorders (Ancín et al., 2010), autism (Delorme et al., 2007), and attention deficit hyperactivity disorder (Albrecht et al., 2008). To date, few studies that have searched for endophenotypes of OCD mainly focused on neurocognitive functions. The first research that adopted this approach showed that OCD patients and their UFDR had deficits in motor inhibition (Chamberlain et al., 2007). Similar studies also found impairments in planning and working memory processes (Delorme et al., 2007), cognitive flexibility (Cavedini et al., 2010), volitional action generation (Kloft et al., 2013), performance monitoring (Riesel et al., 2011) and behavioral reversal (Viswanath et al., 2009) presented in both OCD probands and their UFDR. Moreover, to remove the effect of the drug treatment, a study by Rajender et al. (2011) reported impaired set-shifting and inhibitory control in patients with drug-naïve OCD and their UFDR. In light of the abovementioned results, we propose that certain domains of cognitive functions including cognitive flexibility, response inhibition and planning could be potential neurocognitive endophenotypes for OCD.

Decision making is another important domain of cognitive functions. However, individuals with OCD frequently experience serious impairments in everyday decision making. That is, making decision appears to be dysfunctional in the clinical OCD setting in the context of obsessive doubting and uncertainty (Dittrich and Johansen, 2013). Some authors even regard decision making impairments to be the underlying cause of obsessive and compulsive symptoms and suggest that conceptualizing OCD as a disorder of decision making allows the application of novel approaches to measure symptom provocation and their elimination to further determine the neural mechanisms of OCD (Dittrich and Johansen, 2013; Sachdev and Malhi, 2005). Moreover, the conceptualization of OCD as a decision making disorder may lead to new approaches for the cognitive behavioral therapy of this disorder (Sachdev and Malhi, 2005). Therefore, neuropsychological studies on the decision making for OCD patients have received much attention (Boisseau et al., 2013; Starcke et al., 2009, 2010). Many studies in OCD patients have highlighted impaired decision making as potential vulnerability marker of the disorder, and researchers have suggested that the ritualistic behaviors related with OCD result from a detrimental sensitivity to immediate gains without proper judgments about long-term consequences of such behaviors (Cavedini et al., 2002). Such impairments in decision making may provide an endophenotype or an intermediate marker of brain dysfunction (Boisseau et al., 2013).

However, the few studies that have investigated decision making in OCD patients and their UFDR have produced inconsistent results. The various study tasks used by researchers may account for this inconsistency. Two studies that used the Iowa Gambling Task suggested that deficits in decision making could qualify as a suitable endophenotype candidate for OCD (Cavedini et al., 2010; Viswanath et al., 2009), but another study that used the Cambridge Gamble task found that OCD patients and their UFDR showed intact decision making compared to normal controls (Chamberlain et al., 2007). To date, from a neuroscientific perspective, there are at least two types of decision making that differ in mainly the degree of uncertainty and how much useful information about consequences and their probabilities is provided to decision maker (Brand et al., 2006). In some situations, outcomes and probabilities are implicit, and the decision makers have to initially find some effective information and figure out the options' qualities by themselves by means of processing feedback of previous choices. This type of decision making is often termed decision making under ambiguity, which is usually measured with the Iowa Gambling Task (IGT; Bechara et al., 1994). In the IGT, participants have to maximize a fictitious amount of money by successively choosing cards from four different card decks. Participants do not know the amount of cards they need to choose or which card decks are disadvantageous (i.e., coupling large gains with even larger losses and leading to a negative overall balance in the long term) or advantageous (i.e., coupling small gains with even smaller losses and leading to a positive overall balance in the long term). Therefore, the possible choices are full of ambiguity and participants must learn to avoid the disadvantageous card decks using feedback from previous trials. In contrast to decision making under ambiguity, explicit information about the potential consequences of various choices and their probabilities are provided in some decision situations. This type of decision making is referred to as decision making under risk, which is usually measured with the Game of Dice Task (GDT; Brand et al., 2005). The GDT requires subjects to decide between different options that are explicitly related to a specific amount of gain/loss. Furthermore, winning probabilities are obvious and stable from the beginning of the task. Some options, which are related with high potential gains/losses, but low winning probabilities are risky; and other options, which are related with lower potential gains/losses, but higher winning probabilities are non-risky. Thus, subjects can estimate the risk related with each option and may apply strategies to maximize profit. So far, however, only one study has investigated decision making under ambiguity as measured by the IGT and decision making under risk as measured by the GDT in patients with OCD (Starcke et al., 2010). The study found that while OCD patients performed worse than comparison subjects on the IGT, they were unimpaired on the GDT. Meanwhile the study further emphasized dysfunctions of the orbitofrontal cortex (OFC), but suggested intact functioning of the dorsolateral prefrontal cortex (dlPFC) in patients with OCD (Starcke et al., 2010). The study also provided support for the notion that there is a fundamental distinction between decision making under ambiguity and decision making under risk (Clark et al., 2008).

Previous studies have suggested that unimpaired IGT performance, in the sense of preferentially selecting the advantageous options, depends on intact functioning of the ventromedial prefrontal cortex (vmPFC)/OFC. Patients with vmPFC/OFC lesions (Bechara et al., 2000; Manes et al., 2002) showed deficits on the IGT. Even in a rat analogue of the IGT, rats with OFC lesions preferred to choose larger but more unpredictable rewards over smaller but more reliable rewards under conditions of uncertainty and ambiguity (Pais-Vieira et al., 2007). However, the dlPFC plays a major role in the GDT. Neuropsychological studies have found that subjects with compromised dlPFC function show impaired performance on the GDT (Brand et al., 2007; Delazer et al., 2007). Neuroimaging studies have demonstrated that decision making under risk as assessed by the GDT depends on the activation of the dlPFC (Labudda et al., 2008). Many functional imaging and morphometric magnetic resonance imaging studies of OCD have supported the notion that abnormalities in key gray matter regions, such as the OFC, thalamus, anterior cingulate cortex, and striatum play important roles in its pathophysiology (Alvarenga et al., 2012; Piras et al., 2013). In particular, the OFC plays a central role in most neurobiological models of OCD. These findings suggest that a dysfunctional cortico-striato-thalamo-cortical circuitry contributes to the pathophysiology of OCD (Friedlander and Desrocher, 2006; Menzies et al., 2008). Furthermore, neuroimaging studies have identified abnormally reduced activation of the lateral OFC in OCD patients and their UFDR during reversal learning (Chamberlain et al., 2008). As for the dlPFC, studies on the potential involvement of the region in the pathophysiology of OCD are inconsistent. Although some research has shown abnormalities in the dlPFC activity of OCD patients (van den Heuvel et al., 2005), other studies have not yielded similar results (Abbruzzese et al., 1995; Whiteside et al., 2004). One important reason that the findings of dlPFC functioning in OCD patients are inconsistent is because the abnormal activation of the dlPFC, in many cases, is often related to special symptom dimensions. For example, there is a correlation between the “aggressive/harm” dimension and a structural substrate encompassing the dlPFC,