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Beyond Cognition: Understanding Affective Impairments in Korsakoff Syndrome

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Abstract

As earlier research on Korsakoff syndrome (KS), a frequent neurological complication of alcohol-dependence (AD), mainly focused on cognition, affective impairments have been little investigated despite their crucial impact in AD. This article proposes new research avenues on this topic by combining two theoretical frameworks: (a) dual-process models, positing that addictions are due to an imbalance between underactivated reflective system and overactivated affective-automatic one; (b) continuity theory, postulating a gradual worsening of cognitive impairments from AD to KS. We suggest that this joint perspective may renew the current knowledge by clarifying the affective-automatic deficits in KS and their interactions with reflective impairments, but also by offering a direct exploration of the continuity between AD and KS regarding reflective and affective-automatic abilities.

Keywords

cognition, dual-process models, emotion, Korsakoff syndrome

Introduction

Korsakoff syndrome (KS) is a neurological condition characterized by severe retrograde and anterograde memory deficits (Butters & Brandt, 1985) and most frequently resulting from a combination of chronic alcohol dependence (AD) and thiamine deficiency (Oscar-Berman, 2012). Brain damages and cognitive impairments related to KS appear far more intense and permanent than those usually reported in AD patients (e.g., Sullivan & Pfefferbaum, 2009). Thus, this observation led to the continuity theory (Ryback, 1971) proposing a linear worsening of cognitive and cerebral deficits between uncomplicated AD and KS, the latter presenting much more serious behavioral and organic impairments. In this view, KS presents an increase of the brain and cognitive damages induced by alcohol neurotoxicity (Oscar-Berman, 2012; Sullivan & Pfefferbaum, 2009) and

already observed in AD (Bühler & Mann, 2011). While the continuity theory has received empirical support from studies showing a continuum between AD and KS for memory abilities (Pitel et al., 2008), this proposal has not been experimentally tested for the other abilities in which impairments are frequently observed in alcohol-related disorders.

In this perspective, dual-process models (Bechara & Damasio, 2005; Mukherjee, 2010) offer an innovative theoretical background to renew the exploration of the continuity theory by exploring its generalization towards other cognitive abilities. Indeed, these models centrally postulate that adapted human behaviors are based on the efficient interaction between two cerebral systems: (a) the "reflective system," a controlled and inhibitory system involved in the cognitive processing of stimuli,

relying on memory and executive functions and initiating controlled-deliberate responses (response–consequences link), and (b) the "affective-automatic system," an appetitive system involved in the impulsive processing of a stimulus and triggering automatic responses based on associative learning (stimulus–response link). More specifically, affective-automatic system is considered as comprising an affective subcomponent associated with the core affect decoding (e.g., facial expression or prosody) and an automatic subcomponent associated with the attribution of a pleasant or aversive value to environmental stimuli through conditioning (Bechara, 2005; Bechara & Damasio, 2005). Neuroscience studies (Daw, Niv, & Dayan, 2005; Hampton & O'Doherty, 2007) have reinforced the dual-process models by showing distinct cerebral networks underlying the two systems: a prefrontal network (mostly orbitofrontal-dorsolateral prefrontal cortices) for the reflective system, and a limbic network (mostly striatum and amygdala) for the affective-automatic one. Importantly, a crucial assumption of the dual-process models is that, in everyday life, reflective and affective-automatic systems constantly interact in order to ensure accurate decision-making, and therefore that their balance is the crucial factor leading to adapted behaviors. With this in mind, these models have been applied to addictions and particularly to AD (Wiers & Stacy, 2006), proposing that AD is characterized by an imbalance between an overactivated affective-automatic system (leading to overreaction to affective stimulations and to automatic approach towards substance-related stimuli) and an underactivated reflective system (leading to a reduced ability to inhibit and regulate these automatic behaviors). Again, the validity of these models in AD has been reinforced by neuroimaging studies showing that frontal (i.e., reflective system) and limbic (i.e., affective-automatic system) networks are particularly vulnerable towards AD-related damages (Oscar-Berman & Marinković, 2007).

As underlined before, beyond the empirical support received from episodic memory impairments (Pitel et al., 2008), the continuity theory has received very little confirmation from other abilities, and has centrally not been tested for the processes related to affective-automatic system and its interactions with reflective processes. Since affective and interpersonal deficits have been shown to play a crucial role in the development and persistence of alcohol-related problems (Thoma, Winter, Juckel, & Roser, 2013), a specific exploration of these processes in KS appears important to test the generalizability of the continuity theory, beyond the usual cognitive abilities, but also to (a) enrich the current experimental and theoretical knowledge regarding the impairments associated with alcohol-related disorders; and (b) propose new therapeutic models focusing on affective and social variables. On this basis, exploring the continuity theory in the framework offered by dual-process models appears particularly adapted to assess the reliability of the continuity theory towards affective processing as well as to explore affective–cognitive interactions in KS.

This article will first provide a brief statement on the findings suggesting an overactivation of the affective-automatic system in AD. Then, while highlighting the critical need to explore affective processes and affective–cognitive interactions in KS, a hypothesis will be presented (on the basis of preliminary results presented in Figure 1) suggesting abnormalities of the affective-automatic system and systems' imbalance in KS. Finally, some crucial directions for future research will be proposed (Figure 2), aiming to test the continuity theory in this perspective by following three main research axes: (a) exploring the deficits of the affective subsystem in KS; (b) exploring the deficits of the automatic subsystem in KS, and (c) direct testing of the interactions between the affective-automatic and reflective systems.

Abnormalities of the Affective-Automatic System in AD

While no systematic exploration of the affective-automatic system in a dual-process model framework has yet been proposed, several experimental results suggest that this system is abnormally activated in AD. Concerning the affective subsystem, affective state can be globally defined as a multimodal experience (combining physiological, cognitive, and behavioral components) elicited by internal (e.g., memories, goals) or external (e.g., perceptual stimuli) signals and which modulates future actions and mental states (Bechara & Damasio, 2005; Johnson, Kim, & Risse, 1985). In view of the central role played by affective states in everyday life, the effective perception and processing of affective stimuli coming from our internal or social environment is a crucial ability to develop and maintain adapted social interactions or, more generally, to ensure a global well-being. It has been shown during the last decade that AD is characterized by disturbances in a wide-range of affective functions, and that these deficits are not only highly involved in the development of AD but also in relapse after detoxification (Thoma, Friedmann, & Suchan, 2013). Initial affective processing studies (Kornreich et al., 2002) in AD have focused on facial expression recognition (i.e., the ability to determine which affective state is expressed by a human face) and have revealed that AD is associated with a global impairment in the identification of facial expressions, and particularly with an overestimation of the intensity of negative affects. More recent studies (Maurage, Campanella, Philippot, Martin, & De Timary, 2008) suggested that this deficit is specific for affective features of the face (as AD patients are not impaired in the identification of other complex facial features such as gender or age) and is generalized to other affective stimuli (i.e., body postures) and other sensorial modalities (i.e., prosody; Maurage et al., 2009). It is now well established that AD is linked with a massive modification of affect decoding, centrally characterized by oversensitivity to negative affective states.

Beyond this specific deficit in affect decoding, impairments in more complex affective and social abilities have also been recently described. Affective states decoding deficits are strongly associated with interpersonal problems (Kornreich et al., 2002). Similarly, it has recently been shown that AD is linked with altered functioning in abilities combining affective and social aspects, such as empathy (Thoma et al., 2013), and with biased internal representations of social interactions. It
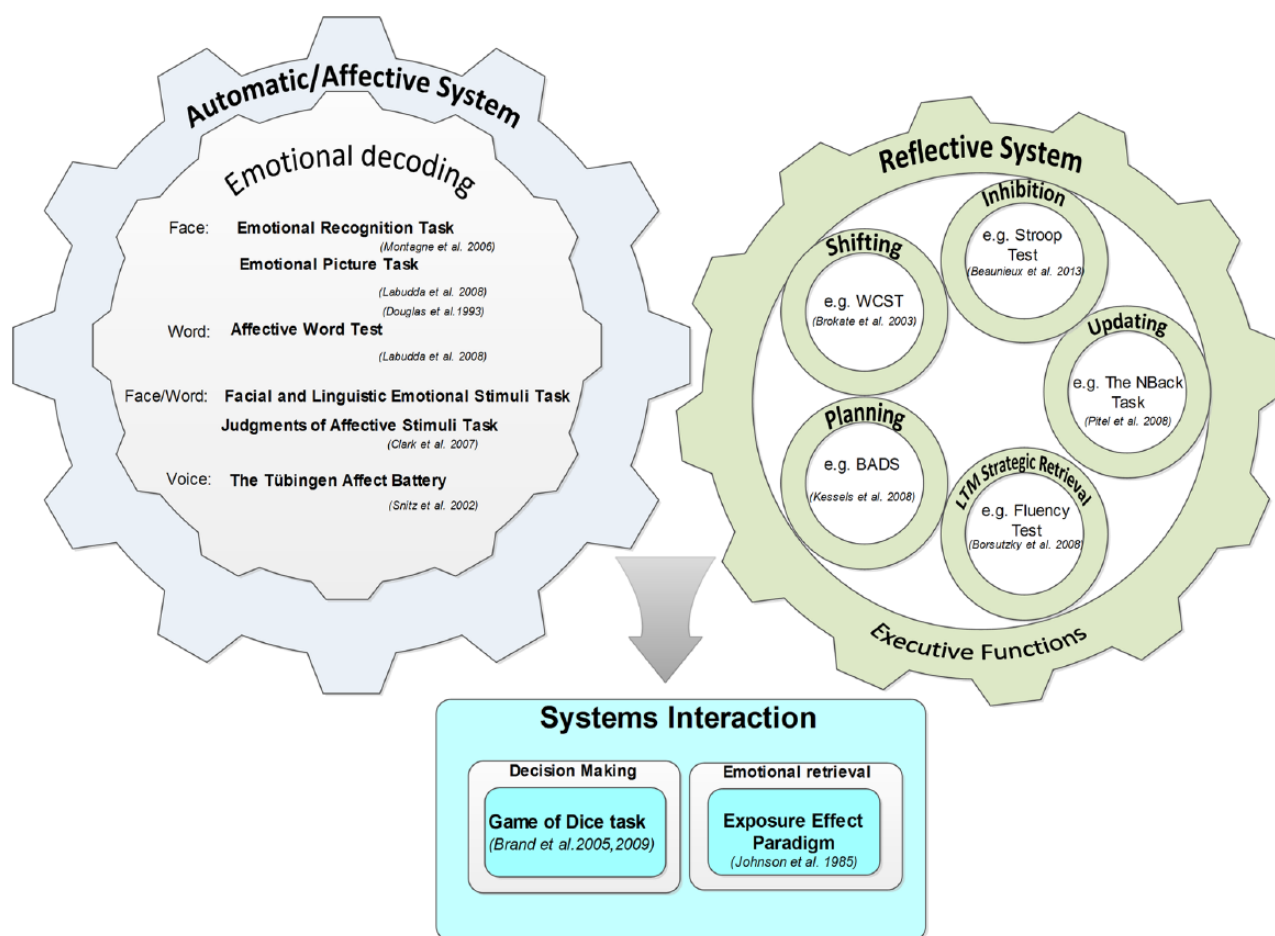
Figure 1. Schematic illustration of previous KS assessment organized according to the dual-process models perspective.

thus appears that affective and interpersonal abilities are strongly altered in AD, and that these impairments rely on alteration of the affective subsystem. In line with this proposal, an fMRI study (Maurage et al., 2012) has recently shown that AD is associated with increased activation of the limbic system (i.e., insula, anterior cingular cortex) in a social exclusion paradigm, indexing excessive frustration and negative feelings of the alcohol-dependent individuals when rejected by others. These data further reinforce the hypothesis of hyper-activation of the affective subsystem when triggered by affective or social stimuli.

AD is also associated with abnormal activation of the automatic subsystem, and particularly with an excessive sensitivity towards alcohol-related stimuli (e.g., pictures of alcoholic beverages, alcohol odors). This has been experimentally established in a large range of paradigms, notably using attentional bias procedures. It has been shown that AD is linked with massive automatic capture of the attentional resources by alcohol-related stimuli compared to non-alcohol-related ones (Field, Munafò, & Franken, 2009), which, in turn, is linked with increased physiological arousal and craving. Neuroimaging findings also reported higher activation of limbic (i.e., insula, accumbens, cingulate) and cortical (i.e., cortex orbitofrontal and superior fontal) brain regions for AD compared to healthy subjects during a

comparison between alcohol-related and non-alcohol-related cues (Myrick et al., 2004). Moreover, as the intensity of this attentional bias is correlated with increased future substance-seeking and consumption behaviors as well as with the probability of relapse after detoxification treatment, therapeutic programs have been proposed in AD to reduce this sensitivity and thus to potentially reduce consumption or relapse risk (Fadardi & Cox, 2009; Schoenmakers et al., 2010). These studies reinforce the proposal made by dual-process models that alcohol acquires powerful appetitive properties through the affective-automatic system (Bechara & Damasio, 2005), leading to automatic approach behaviors when confronted with alcohol-related cues. Other tasks notably based on implicit association or memory association (Field & Cox, 2008; Peeters et al., 2013) have largely confirmed this overactivation of the automatic subsystem in AD and its implication in the emergence and maintenance of drinking habits. To sum up, it clearly appears that AD is associated with a massive overactivation of the affective-automatic system, which plays a crucial role in the persistence of alcohol consumption. However, the functioning of this system has not been experimentally tested in KS, which makes it difficult to draw any conclusions concerning the modifications of this system's functioning during the disease evolution.
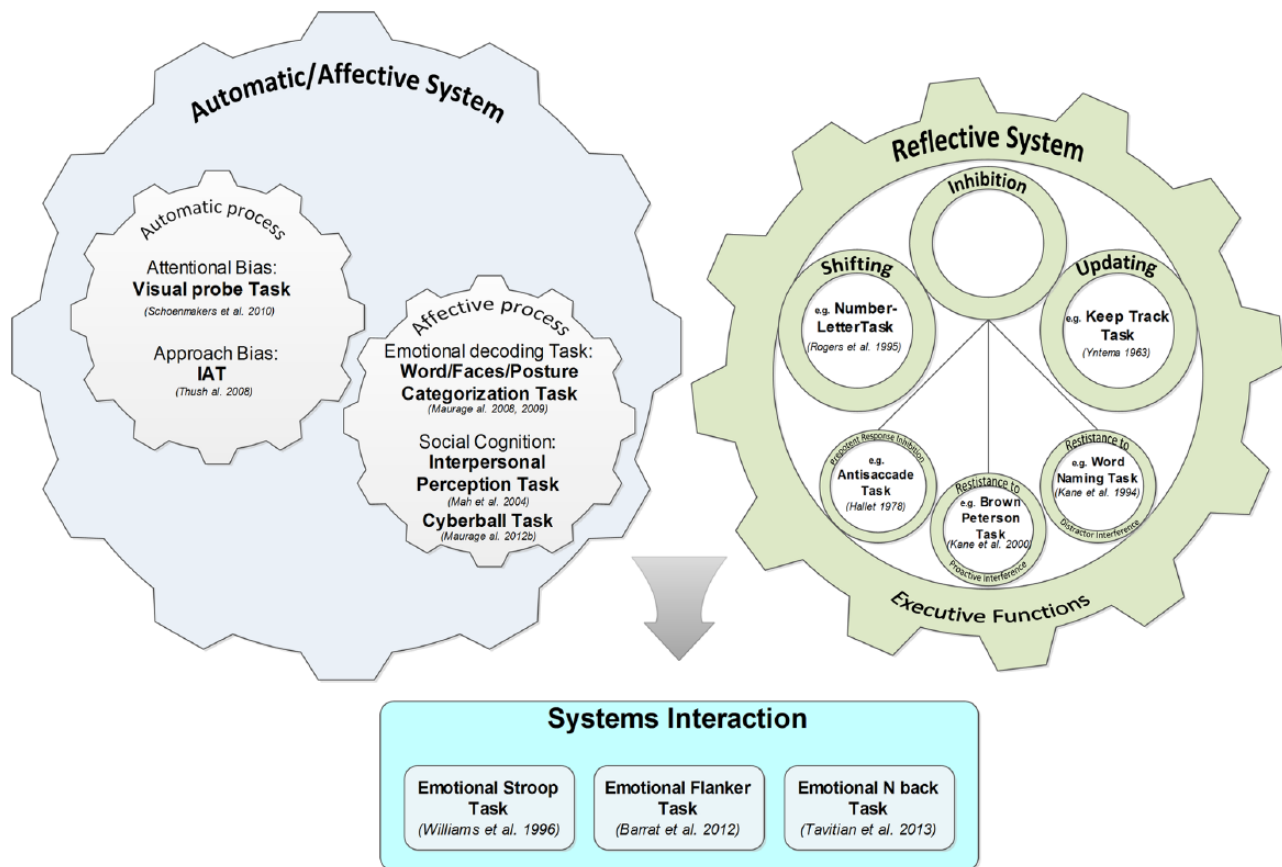
Figure 2. Schematic illustration of future KS and AD assessment related to the suggested research plan following a dual-process perspective and focusing on the affective-automatic system, the reflective system, and both systems interactions.

What is Known About the Affective-Automatic System in KS?

The original description of KS (Korsakoff, 1889) did not report impaired affective and interpersonal abilities, but later studies have repeatedly identified disturbances for these processes in KS. These patients are indeed often described as affectively detached, apathetic, irritable, or euphoric (Douglas & Wilkinson, 1993; Labudda, Todorovski, Markowitsch, & Brand, 2008). These clinical observations draw attention to KS ability to process affective responses, and early findings focused on the role played by frontal lobes in these affective changes. Indeed, frontal lobe dysfunctions have long been identified as being involved in KS memory deficits (Janowsky, Shimamura, Kritchevsky, & Squire, 1989; Kopelman, 1991) as well as in executive functioning (Scott & Schoenberg, 2011). As frontal system dysfunctions and the subsequent deterioration in executive functioning is an important contributor to KS (van Oort & Kessels, 2009), affective changes have initially been understood as a secondary consequence of the reflective system disruption rather than as an altered production or processing of affective stimulations per se (Douglas & Wilkinson, 1993; Johnson et al., 1985; Snitz, Hellinger, & Daum, 2002). For example, an exposure effect study (Johnson et al., 1985) aiming at manipulating preferences

for a neutral melody by a mere repeated exposure suggested a preserved ability to acquire affective response for KS as they showed similar preferences than healthy controls. However, a more subtle exploration of affective abilities suggested that these functions are impaired in KS. First, the same study also showed that, in a task involving the development of preferences towards other individuals, KS patients were more imprecise than controls at making a preference based on the description of the character. Moreover, while the basic discrimination of linguistic and affective prosody appears preserved, KS is associated with serious impairment of affective prosody perception when semantic content is neutral or incongruent (Snitz et al., 2002). This leads to the proposal that affective abilities might be disrupted in KS when subtle affective processing is required. One potential explanation of these findings is that whereas basic discrimination of affective content may be specifically associated with the affective-automatic system, complex affective processing may involve both reflective and affective systems, leading to an altered affective judgment due to the interaction between altered affective decoding and poor executive control (Brand & Fujiwara, 2003; Labudda et al., 2008). This proposal is further reinforced by neuroimaging studies showing limbic and prefrontal impairments, these areas both being involved in affective states processing (Oscar-Berman & Marinković, 2007).

Affective recognition impairment has been extensively explored in AD and it has been shown to strongly contribute to nonadaptive behavior and poor social integration, which in turn constitute major relapse factors (D'Hondt, Campanella, Kornreich, Philippot, & Maurage, 2014; Maurage et al., 2012; Snitz et al., 2002). Unfortunately, compared to the number of studies of AD, there are currently very few studies assessing affective recognition in KS, hampering the empirical testing of the clinical proposal that KS might be associated with affective impairments. It has nevertheless been shown that KS patients have a facial expression recognition impairment, with stronger difficulties for specific categories, particularly fear, anger, and surprise (Montagne, Kessels, Wester, & de Haan, 2006). Also, when KS patients have to categorize stimuli (e.g., words and pictures) according to their affective valence (i.e., positive, negative, neutral), they present impaired affective judgments that are mainly characterized by a tendency to overestimate the affective content of neutral stimuli (Clark, Shagrin, Pencina, & Oscar-Berman, 2007; Labudda et al., 2008). Other findings (Davidoff et al., 1983) pointed out that KS patients had a better memorization of short stories with sexual content rather than neutral or aggressive ones, whereas no differences were found among AD and healthy subjects. These findings might suggest that motivational-affective factors (i.e., sexual content) influence KS selective attention and immediate recall in a similar way that alcohol-related cues lead to automatic approach behaviors in AD studies (Field & Cox, 2008; Peeters et al., 2013). In other words, this affective-motivational factor described by Davidoff et al. (1983) which facilitates KS capacity to recall affectively valenced stories might have been a first hint of current conceptions proposed by the dual-process models and would correspond to the automatic subsystem.

These preliminary results offer initial indications as to how KS patients decode affective stimuli. Nevertheless, there is no precise detail about the nature of these impairments, especially compared to AD patients, which reinforces the need for a thorough continuity theory investigation. Therefore, two possible hypotheses could explain these preliminary findings: (a) in agreement with the continuity theory, KS patients might present an overactivation of the affective-automatic system leading to an exaggerated perception of affective content; or (b) in case of discrepancy in the continuity theory, KS patients would present reduced activation of the affective-automatic system leading to lowered arousal levels. A step beyond would be to postulate differential deficits across the subcomponents of this system (i.e., automatic and affective subsystems), as it might indeed be postulated that the validity of this continuity theory varies across the automatic-affective system, a continuum being found for the affective subcomponent but not for automatic subcomponent, or conversely. However, the lack of data concerning the automatic subsystem is patent, as, to the best of our knowledge, no study has explored the deficits directly related to this subsystem in KS and nothing is known concerning the alcohol-related attentional and approach biases in these patients, or their implications on craving and relapse. To sum up, whereas the cognitive alterations provoked by frontal dysfunction have been extensively

described (Oscar-Berman, 2012), the behavioral consequences of limbic structure dysfunctions (i.e., amygdala and mammillary bodies) are far less understood. A better understanding of these affective deficits is thus needed to determine the involvement of the automatic-affective system in KS.

What is Known About Affective–Cognitive Interactions in AD and KS?

While the dual-process models have identified two separate systems, their main assumption is that correct decision-making (which can be defined as the mechanism of making a choice after analyzing possible consequences on the basis of reward and punishment in previous experiences) relies on a constant interaction between affective-automatic and reflective systems. The balance between these systems is thus essential to produce appropriate behaviors depending on the environment. Neurocognitive studies (Mitchell, 2011) demonstrated that decision-making processes implicate constant interactions between limbic and prefrontal networks. Interactions between affective-automatic and reflective systems also highly influence risky behavior in alcoholism (Camchong, Endres, & Fein, 2014; Le Berre et al., 2014). At first, when alcohol use is voluntary, the reflective system (i.e., prefrontal network with orbitofrontal cortex [OFC], dorsolateral prefrontal cortex [DLPFC], ventromedial prefrontal cortex [vmPFC]) initiates intentional and controlled behavior that is accompanied with reward effects mediated by affective-automatic system (i.e., amygdala, striatum, and insula; Everitt & Robbins, 2005). Later, a transition to compulsory consumption with less behavioral control is mediated by less activation of reflective system and more activation of affective-automatic system (Camchong et al., 2014; Everitt & Robbins, 2005). The imbalance between systems is thus at the heart of addictive behaviors (Makris et al., 2008), as these pathologies can be understood as decision-making impairments: AD patients make choices that bring immediate reward without considering the delayed inherent punishment (Noel et al., 2011). Hence, they usually exhibit risky decision-making characterized by an insensitivity to future consequences, which, in turn, contributes to dysfunctional behavior in daily life (Bechara, 2005). Even though decision-making deficits in AD are thought to result from the interaction between impaired executive functioning and dysfunctional affective processing (Noel et al., 2011), the direct interactions between systems have been only minimally explored in experimental paradigms.

As the dual-process theory constitutes the dominant model explaining AD, past studies mostly explored separately the reflective and affective-automatic systems, leaving aside the systems' interaction (i.e., using a specific experimental task that jointly examines both systems). This is even more obvious in KS, where almost no study specifically explored these interactions. However, it has been shown that KS patients have deficits in decision-making as conceptualized by gambling tasks such as the Game of Dice Task (GDT; Brand, 2005). The computerized GDT was designed to assess the impact of executive functions on decision-making in a gambling situation in which subjects

have to increase their gain by throwing dice and betting on various number combinations. In this study, KS patients were highly impaired on GDT and these deficits were correlated with executive function impairments (i.e., categorization, monitoring, using feedback). Interestingly though, in addition to its reliance on the reflective system, this task is also correlated with affective processing impairments, as an efficient affective processing of feedback from previous decisions is needed to guide later choices (Brand et al., 2009; Oscar-Berman, 2012). In order to disentangle the respective involvement of executive functions and feedback-processing deficits in decision-making impairments, a modified GDT version was proposed (Brand et al., 2009). Findings pointed out that KS patients present executive dysfunctions, and also demonstrated that they do not take advantage from feedback, confirming the involvement of altered affective processing. Furthermore, in a similar gambling paradigm, the Iowa Gambling Task (IGT), a recent fMRI study (Le Berre et al., 2014) underlined relationship between decision-making impairment and gray matter shrinkage in AD in cerebral regions such as vmPFC, anterior cingulate cortex and hippocampal formation. Although not yet replicated with KS, associations between these brain regions and poor decision-making performances in AD are another hint to better understand why amnesic KS patients are impaired at decision-making tasks. These initial results thus highlight the involvement of an imbalance of these systems in KS, but they have up to now not been verified and extended using other paradigms.

Future Directions: Understanding Affective Impairments in KS

Dual-process theories of AD have emerged during the last decade (Houben, Nederkoorn, Wiers, & Jansen, 2011; Wiers & Stacy, 2006) and gained a dominant position in this field. However, they have mostly been tested on recently detoxified AD individuals, and the evolution of the deficits across the different stages of the pathology (and singularly in the transition between AD and KS) remains largely unexplored. Centrally, the continuity theory still has to be confirmed beyond executive processing, through the direct comparison of the impairments observed between AD and KS patients with respect to the affective-automatic system and its interaction with the reflective one. The current understanding of the systems' impairments is presented in Figure 1. While offering a valuable exploration of the deficits related to KS, these previous studies have left many areas unexplored, and a systematic evaluation of these dual-process models by comparing AD and KS is needed. Given this perspective, main avenues for future research (summarized in Figure 2) can be proposed, relying on three research axes:

1. *Exploration of the affective subsystem*: Future studies should focus on the development of a thorough exploration of this subsystem in AD and KS, first by determining the extent of this affective states decoding deficit across complex facial features (Maurage et al., 2008) and also examining deficits with regard to other

affective stimuli (i.e., body postures) and sensorial modalities (i.e., prosody; Maurage et al., 2009). Besides, visual deficits might also be regarded as a determining factor in affective alteration, as recent findings suggest, by mean of electrophysiological data, that a mutual effect between affect and vision is already seen in early stages of information processing (D'Hondt, Lepore, & Maurage, 2014). It will also be important to precisely identify the evolution of these deficits during the transition from AD to KS. On this basis, more complex affective abilities and social cognition should be explored. For instance, social interactions and the regulation of social exclusion should be assessed by reliable tasks, for example the Cyberball Task that elicits social exclusion feelings (Maurage et al., 2012). More ecological tasks (e.g., Interpersonal Perception Task; Mah, Arnold, & Grafman, 2004) might also be used to evaluate fine social abilities that are essential to independently managing everyday life.

2. *Exploration of the automatic subsystem*: This exploration is usually conducted with two classes of tests (Wiers & Stacy, 2006). The first class includes attentional bias measures (ABM), essentially the Visual Probe Task (Schoenmakers et al., 2010), a reaction-time task in which two stimuli (i.e., one alcohol-related and one neutral picture) are presented as cues indicating the following appearance of an arrow that has to be processed. This task is applied to determine the subject's automatic attentional engagement toward alcohol-related stimuli and to measure the ability to disengage attention from it (Schoenmakers et al., 2010). The second class includes approach bias tests such as the Implicit Association Test (IAT; Thush et al., 2008) in which stimuli are classified into categories (e.g., alcohol-related or neutral) and affective attributes (e.g., positive and negative). This test is thought to illustrate the spontaneous association to a cue (alcohol-related or not; Wiers & Stacy, 2006). Although ABM and IAT may partially involve controlled cognitive processes (Wallaert, Ward, & Mann, 2010), these tasks are now widely used to explore attentional bias toward alcohol-related stimuli among AD and appear to be reliable measures of the automatic subsystem. Applying these tests to the KS population and comparing them with AD performances would directly test the continuity theory. Indeed, it might be hypothesized that the automatic subsystem will be even more overactivated in KS, thus confirming the continuity theory and extending it towards the affective-automatic system. But it might alternatively be postulated that the extension of brain impairments related to KS will lead to reduced activity in limbic areas and thus to reduced overactivation of this subsystem.

3. *Interactions between affective-automatic and reflective systems*: Several tasks have been developed to directly evaluate these interactions and can be applied to AD and KS in order to directly test the main proposal of

dual-process models, that is, the hypothesis that addictions are due to an imbalance between these systems. For example, the Emotional Stroop Task (Williams, Mathews, & MacLeod, 1996) involves presentation of neutral and affective stimuli (i.e., word or image) for which the subject has to maintain his/her attention on the stimulus color rather than on the word's meaning. A second paradigm of interest is the Emotional Flanker Task (Barratt & Bundesen, 2012) requiring the categorization of a presented target face (i.e., positive or negative) while ignoring distractor faces presented on the target's right and left flanks. The third task proposed to investigate the interaction between reflective and affective-automatic systems is the Emotional N-Back Task (Tavitian et al., 2014) which consists in presenting a sequence of letters flanked by affectively laden faces (i.e. happy, fearful, neutral) and asking the subject to respond to a letter that matches another one presented N steps earlier.

In conclusion, by means of a solid theoretical background such as the dual-process system model, this article underlines the usefulness of simultaneously exploring affective processing and clarifying the relationship between affect and cognition among AD and KS patients. At the clinical level, adding an examination of KS automatic/affective processes could facilitate KS care in psychiatry and neurology. A clinical perspective could make use of attentional bias modification training (Schoenmakers et al., 2010), which is a modified visual probe task in which a probe replaces neutral stimuli in all trials. Concretely, the subject is trained to disengage attention from alcohol-related cues (Schoenmakers et al., 2010). Moreover, a better understanding of KS affective processing could promote the development of new rehabilitation tools to reduce interpersonal difficulties encountered by KS patients. At the fundamental level, comparing AD and KS performances with the aforementioned tasks could help to step forward to the investigation of the classical continuity theory, as there is, to date, no proposal concerning the evolution of affective-automatic disturbances from AD to KS. It might indeed be hypothesized that: (a) as assumed by the continuity theory, KS would show an overactivation of the automatic/affective system or (b) on the contrary, a reduced activation of the automatic/affective system would be observed among KS. Also, this hypothesis may vary across the system itself, a continuum being found for the affective subcomponent but not for automatic subcomponent, or vice versa. It should also be noted that several factors related to demographical (gender, age, family history of alcohol consumption) and psychopathological (personality traits, comorbid depression or anxiety, dual diagnoses) variables should be taken into account and controlled for in future studies, as they might constitute risk factors strongly influencing the results observed (Finn, Sharkansky, Brandt, & Turcotte, 2000; Schuckit, 1994). Moreover, while the present article focused on alcohol-related KS, it should be underlined that KS can have non-alcohol-related etiologies (e.g., be provoked by strictly nutritional deficiencies; Larnaout et al., 2001; Peters,

Parvin, Petersen, Faircloth, & Levine, 2007), the continuity theory of course being inapplicable to such cases.

Besides, future research should likely incorporate neurophysiological correlates involved in reflective–affective processes and their interactions. A fundamental perspective could be the exploration of "*the triadic neurocognitive approach to addiction*" proposed by Noel, Brevers, and Bechara (2013) which includes a third axis (i.e., the insular system) considered as a modulator of the interactions between reflective and affective-automatic systems. To this end, the triadic model (Noel et al., 2013) would be an important consideration if placed in the context of continuity theory (i.e., comparing AD and KS neural correlates of these three systems).

Declaration of Conflicting Interests

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