CORTEX 49 (2013) 1610–1626

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research report

The neural network sustaining crossmodal integration is impaired in alcohol-dependence: An fMRI study

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ARTICLE INFO

Article history:
Received 7 December 2011
Reviewed 6 March 2012
Revised 22 March 2012
Accepted 27 April 2012
Action editor Pia Rotshtein
Published online 8 May 2012

Keywords:
Crossmodality
Alcohol-dependence
Face
Voice
fMRI
Psychophysiological interactions

ABSTRACT

Introduction: Crossmodality (i.e., the integration of stimulations coming from different sensory modalities) is a crucial ability in everyday life and has been extensively explored in healthy adults. Still, it has not yet received much attention in psychiatry, and particularly in alcohol-dependence. The present study investigates the cerebral correlates of crossmodal integration deficits in alcohol-dependence to assess whether these deficits are due to the mere accumulation of unimodal impairments or rather to specific alterations in crossmodal areas.
Methods: Twenty-eight subjects [14 alcohol-dependent subjects (ADS), 14 paired controls] were scanned using fMRI while performing a categorization task on faces (F), voices (V) and face–voice pairs (FV). A subtraction contrast [FV–(F+V)] and a conjunction analysis [(FV–F) ∩ (FV–V)] isolated the brain areas specifically involved in crossmodal face–voice integration. The functional connectivity between unimodal and crossmodal areas was explored using psycho–physiological interactions (PPI).
Results: ADS presented only moderate alterations during unimodal processing. More centrally, in the subtraction contrast and conjunction analysis, they did not show any specific crossmodal brain activation while controls presented activations in specific crossmodal areas (inferior occipital gyrus, middle frontal gyrus, superior parietal lobule). Moreover, PPI analyses showed reduced connectivity between unimodal and crossmodal areas in alcohol-dependence.
Conclusions: This first fMRI exploration of crossmodal processing in alcohol-dependence showed a specific face–voice integration deficit indexed by reduced activation of crossmodal areas and reduced connectivity in the crossmodal integration network. Using crossmodal paradigms is thus crucial to correctly evaluate the deficits presented by ADS in real-life situations.

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doi:10.1016/j.cortex.2012.04.012

1. Introduction

Crossmodal processing is the ability to construct a unified representation on the basis of stimuli coming from distinct sensorial modalities (Driver and Spence, 2000). As stimulations are most often integrated in a multi-sensorial flow, this ability is ubiquitous and important for human daily adaptive behaviors like social interactions, spatial attention or perceptuo-motor coordination (Campanella and Belin, 2007; Lalanne and Lorenceau, 2004). While only explored recently, crossmodal mechanisms constitute a blooming research field in neuroscience (Amedi et al., 2005; Calvert et al., 2001; De Gelder and Bertelson, 2003), and several brain areas specifically dedicated to multisensory integration (mainly the superior parietal lobule, inferior occipital, middle frontal and superior temporal sulci) have been identified (Joassin et al., 2011a, 2011b; Love et al., 2011).

Nevertheless, while the brain correlates of crossmodal integration among healthy individuals are well established, few data exist on impaired multimodal integration, particularly among psychiatric populations. Recent results in schizophrenia (De Gelder et al., 2005; Ross et al., 2007; de Jong et al., 2009; Pearl et al., 2009; Szycik et al., 2009; Seubert et al., 2010a; Van den Stock et al., 2011), autism (Foss-Feig et al., 2010; Kwakye et al., 2011; Mongillo et al., 2008; van der Smagt et al., 2007) and Alzheimer's disease (Delbeuck et al., 2007) have suggested large-scale crossmodal deficits in these populations. As crossmodal integration is crucial in daily life, these impairments could be partly responsible for cognitive and social alterations observed in psychiatric states. These preliminary data should thus be extended to offer a more ecological and valid evaluation of psychiatric populations' deficits (Campanella and Belin, 2007), and to better understand healthy crossmodal integration, as exploring an impaired processing among clinical populations can shed new light on normal functioning (Laurienti et al., 2005). The urgency to explore crossmodal abilities in psychiatric states is particularly patent for alcohol-dependence, which is the most wide spread psychiatric disorder (Harper and Matsumoto, 2005). Indeed, the consequences of alcohol-dependence have been extensively investigated at the cognitive and cerebral levels (Bechara et al., 2001; Bülher and Mann, 2011; Harper, 2009; Noël et al., 2001), but previous studies were based on unimodal paradigms, thus preventing any conclusion on the deficits presented by alcohol-dependent subjects (ADS) in real-life situations. Using crossmodal paradigms could thus improve the understanding of alcohol-related impairments (Campanella et al., 2010). The usefulness of crossmodal paradigms in addiction has also been recently underlined in the field of cue-reactivity studies, as a recent review (Yalachkov et al., 2012a) showed that using crossmodal cues (instead of the unimodal visual ones classically used) highly improves the ecological validity of these cues and strongly enhances the induced cue-reactivity. This observation thus further stresses the urgency to switch towards crossmodal stimulations in addiction research and to explore the brain correlates of crossmodality in addictive states.

We recently conducted the two first studies exploring crossmodal integration in alcohol-dependence. As alcohol-dependence leads to social disturbances (Uekermann and Daum, 2008; Uekermann et al., 2005) and as social information is multimodal by essence (Ethofer et al., 2006; Kreifelts et al., 2007), complex social stimuli (faces and voices) were used to increase the ecological value of the paradigm. A first behavioral exploration (Maurage et al., 2007a) showed that the crossmodal facilitation effect [i.e., increased performance for congruent bimodal stimulations as compared to unimodal ones (Latinus et al., 2010; Ngo and Spence, 2010)], indexing successful crossmodal integration (Calvert et al., 2001), is impaired in alcohol-dependence. A second event-related potentials study (Maurage et al., 2008) showed massive impairment of the specific electrophysiological components associated with audio–visual integration in alcohol-dependence, confirming this crossmodal deficit. Nevertheless, the low spatial resolution of event-related potentials did not allow localizing the areas involved in this deficit. Centrally, these preliminary studies did not confirm the specificity of this deficit, namely whether the crossmodal impairment in alcohol-dependence is due to real alterations in brain areas dedicated to crossmodal integration or rather to the simple addition of unimodal impairments provoked by global brain alterations.

The present study thus aimed at determining the brain correlates of crossmodal integration in alcohol-dependence. In line with previous findings on alcohol-dependence, we predicted that alcohol-dependence will lead to specific crossmodal impairment. Namely, we thus hypothesized that ADS will present impaired behavioral facilitation effect and specific cerebral alterations during audiovisual integration. If so, the specific crossmodal activations (resulting from the comparison between crossmodal and unimodal conditions) should be markedly altered in alcohol-dependence, particularly in crossmodal areas (inferior occipital gyrus, middle frontal gyrus, superior parietal lobule). Alternatively, if the crossmodal deficit is just the consequence of more global brain alterations and corresponds to the accumulation of unimodal deficits (i.e., the addition of the brain alterations for faces and voices), the specific crossmodal activations should be globally preserved in alcohol-dependence. Finally, as alcohol-dependence leads to white matter impairments (Pfefferbaum et al., 2005; Yeh et al., 2009) and as crossmodal processing relies on efficient connections between unimodal and crossmodal areas, reduced crossmodal areas activations could be due to impaired connectivity with unimodal ones. Psychophysiological interactions (PPI) exploring functional connectivity between unimodal and crossmodal areas were used to test this hypothesis.

2. Methods and materials

2.1. Participants

Fourteen alcohol-dependent male adults were recruited during their third week of detoxification (Saint-Luc Hospital, Brussels, Belgium). They had all abstained from alcohol for at least 15 days, were right-handed as attested by the Edinburgh inventory questionnaire (Oldfield et al., 1971), and were free of