REVIEW ARTICLE

Towards a Dynamic Exploration of Vision, Cognition and Emotion in Alcohol-Use Disorders

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Abstract: Visuoperceptive impairments are among the most frequently reported deficits in alcohol-use disorders, but only very few studies have investigated their origin and interactions with other categories of dysfunctions. Besides, these deficits have generally been interpreted in a linear bottom-up perspective, which appears very restrictive with respect to the new models of vision developed in healthy populations. Indeed, new theories highlight the predictive nature of the visual system and demonstrate that it interacts with higher-level cognitive functions to generate top-down predictions. These models notably posit that a fast but coarse visual analysis involving magnocellular pathways helps to compute heuristic guesses regarding the identity and affective value of inputs, which are used to facilitate conscious visual recognition. Building on these new proposals, the present review stresses the need to reconsider visual deficits in alcohol-use disorders as they might have crucial significance for core features of the pathology, such as attentional bias, loss of inhibitory control and emotion decoding impairments. Centrally, we suggest that individuals with severe alcohol-use disorders could present with magnocellular damage and we defend a dynamic explanation of the deficits. Rather than being restricted to high-level processes, deficits could start at early visual stages and then extend and potentially intensify during following steps due to reduced cerebral connectivity and dysfunctional cognitive/emotional regions. A new research agenda is specifically provided to test these hypotheses.

Keywords: Alcohol-use disorders, visuoperceptive deficits, visual prediction, magnocellular pathway, parvocellular pathway, orbitofrontal cortex, bottom-up processes, top-down processes.

1. INTRODUCTION

Severe alcohol-use disorders (AUD) represent a substantial health and economic burden, and are associated with a large range of neurological and neuropsychological impairments affecting attentional, memory and executive functions [1-4], but also visuoperceptive abilities. Visuoperceptive deficits are often considered as one of the most severe and long-lasting impairments in the AUD literature. Actually, most recent reviews [1-4] document impaired performances in various neuropsychological tasks requiring efficient visuospatial skills, which may persist for several years after detoxification [5, 6]. However, visuoperceptive deficits of individuals with AUD (IAUD) have most often been explored using non-specific and multi-determined tasks, and are rarely taken into consideration when assessing cognitive and emotional abilities, despite their potential involvement in these higher-order deficits. Their exact extent and characteristics are therefore not well established.

Yet, vision is essential for environmental adaptation and is recruited in basically every aspect of our daily life. Through a continuous monitoring of our physical world, vision shapes our expectations and participates in building patterns of probability that guide our decision and actions [7]. A common implicit assumption is that sensory analysis and cognition constitute two distinct processes respectively corresponding to the extraction of visual information and the cerebral operations relative to attention, memory or decision-making, the latter being realized once the former has ended [7]. However, the new dominant paradigm considers that the visual system not only feeds the human brain with sensory information in a bottom-up manner, but also quickly interacts with higher-level cognitive functions in a top-down fashion, from the very start of visual stimulation [8, 9]. Thus, the boundary between perception and cognition might be purely artificial. Evidence suggests that vision is not an independent mechanism limited to sensory analysis but rather

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a proactive process integrating rapid cognitive and emotional predictions, these processing stages being interleaved [10]. Implications for neurological and psychiatric diseases are critical as this conceptualization implies that early visual sensory deficits can affect cognitive/emotional processes, and reciprocally that cognitive/emotional alterations can alter visual perception.

While preliminary results have been obtained in other pathological populations (*e.g*., schizophrenia or autism [11]), this perspective has not yet been explored in AUD. Given the combined presence of visuoperceptive, cognitive and emotional deficits in AUD [1-4], we suggest that current dynamic models of vision could be of particular relevance for studying this disease, and conversely that exploring impaired functioning in AUD might bring new insights to those models. Our main aim is therefore to stress the need to carefully investigate visuoperceptive deficits of IAUD, and then the mutual influences between these deficits and those regarding higher-level cognitive and emotional processes. To this end, we will first review evidence of visuoperceptive deficits in AUD and introduce the classically related bottom-up rationale. We will then briefly introduce the new theoretical framework of vision, with a specific focus on "prediction models". Finally, the specific implications for the study of AUD will be discussed, centrally underlining that the current neglect of visual top-down influences in AUD research leaves open central questions concerning our understanding of cardinal deficits described in patients. Accordingly, we will also propose new research avenues and practical ways to test new relevant experimental hypotheses directly emerging from this promising new field.

2. BOTTOM-UP PERSPECTIVE

2.1. Visuoperceptive Deficits in AUD

Visuoperceptive impairments have been documented for many decades in AUD. The interest for visual processing initially arose from the comparison between verbal and nonverbal skills, IAUD being generally more impaired in tasks using visuospatial material [12]. However, these early investigations often relied on poorly sensitive measures collected with broad intellectual tests [13-17], and on the mere comparison between verbal and nonverbal memory tasks [18, 19]. Other studies investigating the cerebral asymmetry of deficits in AUD obtained inconsistent results [6, 20-22], preventing any conclusion in favor of a selective impairment of the right hemisphere (presumably specialized in visuospatial processing). More importantly, these studies used non-specific tasks encompassing a large variety of visuoperceptive abilities and higher-level cognitive processes, and could hardly help to draw specific conclusions about the origin of the deficits. Subsequently, more specific studies revealed alterations in the ability to perceive motion and speed [23, 24] as well as higher temporal frequency thresholds (*i.e*. lower perception of quick changes of luminance) among IAUD [25, 26], while others showed that they do not process global visual information as efficiently as healthy individuals [27-31]. IAUD also appear impaired when processing eccentric targets [21], which suggests that they could explore the peripheral visual field less accurately.

Findings from psychophysical studies further showed that IAUD display impaired color vision [32-36] in the absence of any visual acuity difference [36] or eye anatomic change [33]. These results should however be interpreted carefully as contradictory results have been reported [37] and as color vision deficits might be related to alcohol-related metabolic diseases or nutritional deficits rather than AUD *per se* [38-40]. Interestingly, results from behavioral studies suggest that IAUD could display residual impairments in visuospatial functioning even after long-term abstinence [5, 6, 41]. Time-dependent visuoperceptive recovery could be particularly limited in older IAUD [42] and may also differ across different skills. While basic processes might resolve rapidly [43], more complex perceptive deficits might remain for years [44]. To date, the exact rate and extent of recovery of visuoperceptive deficits remain debated [45-47].

At the cerebral level, neuroimaging data disclosed the presence of structural and functional brain changes, among which smaller gray matter volumes [48, 49] and lower metabolic activity [50, 51] in the occipital lobe. In particular, studies found reduced activation in striate and extra-striate visual cortices [52] and a specific link between metabolic alterations in V1 and performances of IAUD in visuoperceptive tasks [53]. Additional work highlighted white matter microstructural alterations in the fronto-occipital fasciculus [54, 55], namely the long associative white fiber tract that connects parieto-occipital regions with dorsolateral premotor and prefrontal areas [56], which correlated with the visuoperceptive performances of IAUD [54]. In agreement with this, functional data suggest that reduced blood flow in occipital cortex of IAUD usually occurs concurrently with hypo-perfusion in the frontal lobe [57]. Finally, numerous studies used event-related potentials (ERP) to investigate the electrophysiological correlates of AUD. Some of them found reduced P3 amplitude, related to decision-making processes [58, 59], during visual target detection tasks [58, 60-62]. Importantly, others highlighted disruption of the P1, a component representing the activity of extrastriate visual areas [63]. This ERP component, sensitive to the basic properties of the visual inputs and task demands [64], has been found to be delayed [65] and reduced in amplitude [66-68] in IAUD. Alterations of the N170, an early occipito-temporal negative component linked to visual expertise, among which face processing [63, 69], have also been reported [67, 70].

As a whole, although these results clearly suggest the presence of visuoperceptive deficits in AUD, no integrative proposal has been put forward to explain this specific pattern of visual deficits. In particular, the few studies that have considered the consequences of visual deficits in AUD so far have focused on a bottom-up perspective.

2.2. Classical Interpretation of Visual Deficits: Vision as a Bottom-up Process

One way to picture the adverse consequences of low-level visual deficits is to consider that they might impair the subsequent cognitive and emotional cerebral processing stages, lowering the related behavioral performance. This "sequential" interpretation, relies on a bottom-up or feed-forward conceptualization of vision, which long prevailed in the perception field. This approach was initially guided by the stratified architecture of the visual cortex, containing different areas dedicated to increasingly sophisticated perceptual processes [71, 72]. It considered vision as a hierarchical system working linearly to provide a perceptual content that can only be influenced by high-level cognitive and emotional factors at a later and distinct stage, once the perceptual analysis is fully completed.

Various data have shown that modifying the properties of visual sensory inputs can influence cognitive and emotional abilities. One very simple example is that attention can be exogenously captured by the high visual salience (*e.g.*, abrupt onset, color, shape or movement) of a stimulus [73-75], with functional consequences for the concurrent or subsequent tasks. Moreover, having to process degraded visual stimuli can also require a greater allocation of resources at early sensory extraction stages, leading to increased cognitive workload [76, 77]. Basic features of a visual stimulus, such as its spatial frequency content (*i.e.* the level of detail constrained by the alternations of light and dark bars that compose an image) can also affect memory [78] or executive control by modulating, for instance, inhibition abilities in a Stop-Signal task [79]. Variations in spatial frequencies can also influence emotional facial expression (EFE) discrimination by facilitating or hampering the processing of relevant cues (*e.g.*, global facial configurations or details of the mouth/ eyes regions) [80-83].

So far, only a few studies have considered the potential consequences of AUD visuoperceptive impairments on higher-level cognitive and emotional functioning [67, 70, 84-86]. These studies, often based on ERP paradigms and emotional tasks, generally adopted a bottom-up rationale. For instance, some authors suggested that early visual deficits (P1 and N170 impairments) during EFE processing might impair the whole continuum of cognitive processing by: (1) creating a time-lag that lasts during all subsequent processing stages (delayed P3 latency); (2) weakening decisional processes (reduced P3 amplitude) [67, 70]. Beyond these emotional studies, nothing is known about the impact of visual deficits on other higher cerebral functions. Even the role of visual deficits in emotional tasks remains an open question since IAUD do not always differ from healthy controls when processing non-emotional facial features (*e.g.*, gender, race, age) [85, 87]. Actually, some deficits may not be detectable at the behavioral level [70] and/or an additional emotional-related factor may also affect early and/or late processing stages.

This last proposal stresses the need to consider the presence of early top-down connections between vision and other cerebral systems, such as affect-processing regions. In fact, while interesting, the bottom-up conceptualization of vision appears too restrictive when considered in isolation. By considering vision as a close system, it cannot explain how mental states and contextual knowledge, for instance, are able to affect low-level sensory processing [88, 89], thereby occulting other complementary visual mechanisms. Additional top-down processes and feedback loops indeed contribute to the efficiency of vision, and should be considered when investigating its role in AUD. Fig. **1** illustrates this paradigm change.

3. TOP-DOWN PERSPECTIVE

3.1. New Approaches on Vision: the Proactive Brain

Human visual pathways not only convey crucial external perceptual information but also rapidly interact with various cognitive and emotional systems in a top-down manner [90-92]. Several recent papers reviewed the presence of early modulations of vision, thereby overcoming the long-lasting debate regarding the cognitive and emotional "permeability" of vision [8-10, 93-95]. The human visual system is considered as a predictive system creating quick visual percepts depending on the situation. In order to efficiently guide future behavior, it analyzes incoming visual inputs and exploits past experiences to make rapid predictions concerning stimuli [7, 91, 96]. This predictive function, consistent with the principle of optimization in neuroscience [97], requires vision to communicate bi-directionally with other cerebral systems. Crucially, new theoretical models show how the inner anatomo-functional dissociation of human visual pathways can sustain these interactions.

Cortical visual processing is classically divided into an occipito-temporal "ventral" stream and an occipito-parietal "dorsal" stream, respectively mediating visual recognition and visuospatial processing [98]. The ventral stream is supposed to be mainly fed by incoming information from the parvocellular (PC) cells of the lateral geniculate nucleus, which are connected to the cone photoreceptors of the retina. It slowly conveys detailed (*i.e.* high spatial frequency, HSF) visual information and is mostly focused on central vision [99]. Conversely, the dorsal stream, is primarily connected to the magnocellular (MC) cells and rod photoreceptors. It rapidly conveys coarse (*i.e.* low spatial frequency, LSF) information and is especially tuned to the periphery [99]. Despite this dorsal/ventral streams segregation has been nuanced [11], neurophysiological studies [100, 101] have demonstrated that neural processing follows a "Coarse-to-Fine" analysis of visual inputs, which are initially processed at a coarse spatial scale (MC-related analysis) to guide consecutive visual examinations at a finer scale (PC-related analysis) [102, 103]. The "visual prediction" model [90-92] builds on this proposal and postulates that MC-related visual content is rapidly transmitted from early visual regions to the orbitofrontal cortex (OFC, defined here as encompassing the entire orbital section of the prefrontal cortex) where a first visual prediction is computed. This prediction, resulting from analogical mapping and associative processing [7, 91, 104], preactivates relevant representations in memory and is then relayed to the inferotemporal cortex, facilitating conscious visual recognition. In parallel, LSF information is also quickly projected to the parahippocampal and retrosplenial cortex, where it triggers experience-based contextual guesses [105]. These contextual predictions are then back-projected into the inferotemporal cortex and contribute, with the help of object-based predictions, to the activation of the most likely single visual identity.

The “affective prediction” hypothesis [106] further extends this model by stating that the affective content of an image is an essential part of visual predictions as it helps to prioritize relevant information for survival and well-being. It suggests that the OFC could also constitute a crucial area for

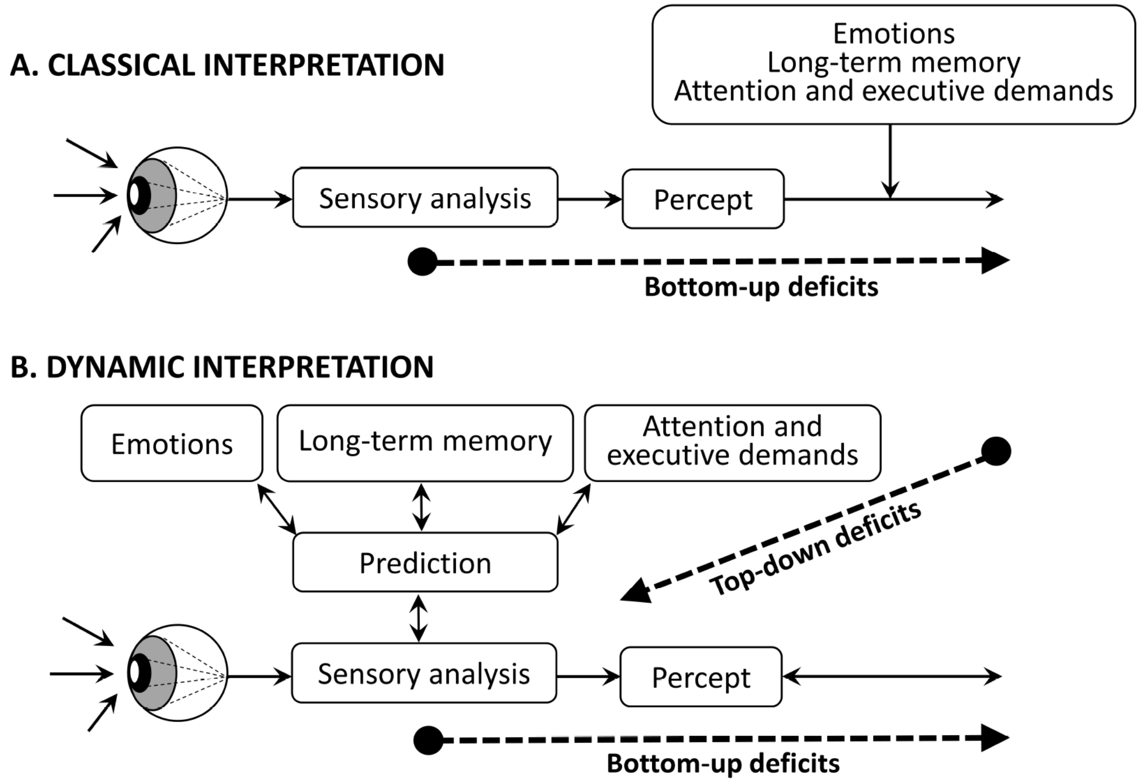

Fig. (1). Paradigm shift between: (**A**) a classical bottom-up interpretation of the origin and consequences of visual deficits in AUD, and (**B**) a dynamic explanation combining both bottom-up and top-down mechanisms. Rather than being restricted to strictly bottom-up disturbances starting at the sensory analysis level, the visuoperceptive deficits of IAUD could also be affected by higher-level impairments since emotions, memory, attention and executive functions also influence basic visual processing in a top-down and reciprocal manner. The dashed lines therefore represent the potential multiple origins and directionalities of the deficits.

vision-emotion interactions, as it is the convergence point of neuroanatomical connections from visual areas, other affective regions (amygdala, insula) and autonomic centers [107]. Affective predictions generated on the basis of MC-input into the OFC could explain how emotional cues can influence perception very early on [108], even unconsciously [109]. Therefore, it challenges the classical and linear conception that emotional processing is restricted to amygdala responses, modulating visual cortices from which it previously receives visual input. It rather appears as an alternative to short-cut models suggesting that some MC-inputs could quickly reach the amygdala *via* a subcortical pathway through the superior colliculus and pulvinar, bypassing V1 [110, 111].

The "visual prediction" model, which has received experimental support in healthy participants [9, 104, 112-114], thus suggests that perception is not a neutral, cognitively "impenetrable", process since a first cognitive value is ascribed to the early MC-related percept and can influence the slower PC analysis [96, 115]. Importantly, top-down visual feedback might incorporate various cognitive and emotional-related information (see Fig. **2** for an integrated view of the model), which will be the focus of the next section. Most of the work done in the field pertains to visual recognition and relates to predictions regarding the identity of stimuli, but these predictions can be extended beyond identity and concern multiple features of the stimuli. The proactive nature of vision, presented here in the context of the visual prediction model, thus refers to a more general brain function mode [116].

3.2. Illustrations of Top-down Interactions between Vision, Cognition and Emotions

3.2.1. Attention

Early visual areas are influenced by top-down attentional mechanisms. Attention can be directed endogenously to prioritize the processing of sensory information of highest motivational relevance [117]. It acts at a very early stage by facilitating the perception of spatial frequencies [118-120], brightness [121] and contrast [122-124]. Attention could alternatively enhance the quality of the perceptual representation (signal enhancement proposal) and/or reduce the impact of sensory information outside its scope [125]. Activity in the primary visual cortex can be recorded even in the absence of visual stimulus when individuals have to maintain attention during a lap of time in anticipation of a visual target [126], further illustrating these top-down influences.

3.2.2. Memory

Visual illusions nicely illustrate the modification of visual perception by a proactive construction relying on heuristic guesses [127, 128]. Perception is guided by long-term memory, which can for instance trigger a preparatory brain activity in the visual cortex that enhances perceptual sensi-

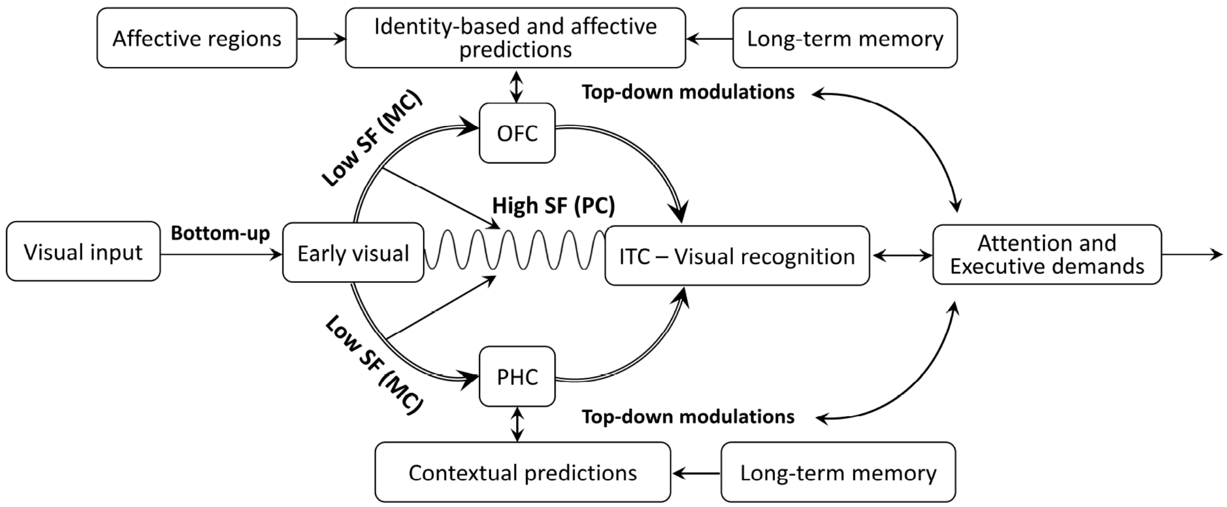

Fig. (2). Integrated proposal of visual mechanisms. The incoming visual input reaches early visual areas in a bottom-up fashion. Coarse low SF input from the MC pathway quickly interacts with the slower high SF input of the PC pathway but is also rapidly transmitted to the OFC where a first prediction about the identity and affective value of the stimulus is computed with the contribution of information stored in long-term memory and activations from other affective regions. In parallel, low SF input also reaches the PHC where contextual predictions are initiated. Together, these predictions help to refine the fine-grained analysis performed in the ITC on the basis of high SF cues, facilitating recognition in a top-down manner. In the meantime, attentional and executive processes also modulate these top-down mechanisms by biasing the processing of specific low-level visual features according to the requirement of the task. ITC: inferotemporal cortex; MC: magnocellular; OFC: orbitofrontal cortex; PHC: parahippocampal cortex; PC: parvocellular; SF: spatial frequencies. Figure adapted from the visual and affective prediction models from Bar and colleagues [91, 105, 106].

tivity for targets presented at a memory-predicted location [129]. In the same line, several studies showed that expectations shape the activity of the primary visual cortex and especially that predictable visual stimuli evoked reduce V1 responses [130, 131]. Perceptual learning can influence the very early C1 ERP component [132], reflecting V1 activity [133, 134], while previously encoded contextual information modulates early bilateral occipital activations [104]. Expectations and predictions, based on previous experiences stored in long-term memory can modulate early visual sensory processing by: (1) reducing the need to repeatedly process stable environmental features; (2) facilitating the interpretation of ambiguous stimuli by relying on contextual probabilities [135]. As a result, the processing of anticipated visual information could require less neural activation [130].

3.2.3. Executive Functions

Executive functions, and centrally inhibition, can also influence visual processing. For example, an fMRI study showed that inhibition time is related to the strength of the connections between the prefrontal and visual cortex [136], suggesting that these connections could control the flow of visual information in a top-down fashion in order for the inhibitory processes to be completed before the individual selects a response based on visual cues. Considering the privileged relationship between the MC pathway and the prefrontal cortex, a specific role for LSF information could be hypothesized. In support of this proposal, results from another study using the Stop-Signal paradigm showed that the removal of LSF information of faces yielded the strongest effects on stopping performances [79]. Thus, perceptual processes could constitute a central component of both reactive and proactive control of response inhibition and decision-making [137] and MC processing may be of particular importance in visuo-cognitive interactions, especially in top-down prefrontal feedbacks necessary to control planned actions.

3.2.4. Emotions

The affective content of a stimulus also influences early vision by eliciting a visual trade-off between MC- and PC-related processing [138, 139]. Depending on the situation, emotions improve fast visuomotor responding on the basis of LSF information or accurate visuo-attentional selection of HSF information in a way that allows to take the most out of both visual channels [140]. Parallel research on how social knowledge influences perception also showed that the emotional valence attributed to a neutral face based on the emotional surrounding context (short text) can influence visual ERPs, as faces associated with negative actions (*e.g*., rape) trigger reduced N170 [141] compared to faces associated with positive actions (*e.g*., child rescue). Even more notably, the pattern of cerebral activation appears to be very similar to that observed for faces actually displaying positive or negative EFE. Finally, in line with the affective prediction hypothesis, the OFC quickly processes the emotional load of the stimuli [142], possibly through LSF information [143, 144], and mediates the influence of peripheral affective stimuli on the subsequent processing of foveal information [145].

3.3. Implications for the Study of AUD: A Specific Deficit for MC Pathways?

The previous examples show how early cognitive and emotional predictions can bias human vision and demonstrate that vision can no more be considered as a linear bottom-up process but should conversely be explored as a bidirectional dynamic and proactive system. However, the experimental exploration of vision in AUD, mostly developed during the 80-90s, appears limited with regard to the evolution of new dynamic models of human vision. Very little research has taken the role of visual deficits into account in AUD and no integrated view of patients' impairments has been put forward with respect to these models. Notably, studies reporting visuoperceptive deficits in AUD have not made any clear proposal in terms of structural and functional integrity of the two main visual pathways.

Yet, even though specific investigations are lacking, we already reviewed deficits for global rather than local visual configurations [27-31], motion [23], speed [24], peripheral targets [21] and high temporal frequencies [25, 26], namely specific MC-related visual properties. In addition, fMRI studies [86, 146] revealed a differential pattern of activation of the ventral and dorsal visual streams between IAUD and healthy controls in a spatial working memory task, suggesting that IAUD could rely on extra PC activation to compensate MC alterations. At the structural level, AUD is also associated with grey matter shrinkage in the parietal lobe (correlated with reduced spatial processing performance), without changes in the temporal lobe [49]. Signs of reduced cerebral flow [147, 148] and volume loss [149] have also been reported with respect to the OFC. Together with impaired fronto-occipital connectivity [54, 55], these results indicate a deterioration of the cerebral substrates of visual top-down predictions in AUD, characterized by specific MC pathway and OFC impairments. Thus, we suggest that IAUD could present with both altered MC pathways and OFC, but overall preserved PC pathways and inferotemporal cortex. Following this assumption, they could display a dissociation between the two pathways postulated by the visual prediction model. Hence, we hypothesize that: (1) the rapid but coarse MC visual analysis could be impaired in IAUD; (2) as a result, they might not efficiently benefit from facilitation of visual recognition through OFC predictions; (3) together, these two phenomena could contribute to their cognitive and emotional deficits.

We thus suggest that alcohol could have a specific neurotoxic effect on the visual system, and especially on the MC pathway. This neurotoxicity could induce early visual impairments that in turn accentuate preexistent or co-induced cognitive and emotional impairments, thereby contributing to their maintenance. In other words, visuoperceptive deficits could be indirectly implicated in the emergence and perpetuation of excessive alcohol consumption. This indirect influence, which is less obvious than those of the well-studied cognitive and emotional deficits, may explain why visual deficits have often been overlooked in the literature. However, top-down modulations of early vision have important theoretical and clinical implications as they might actually lead to a deep reinterpretation of the deficits [150], and more broadly to a reconceptualization of brain dysregulations in AUD. Centrally, exploring visual and affective predictions could help to better understand core features of AUD, such as attentional bias towards alcohol-related stimuli, loss of inhibitory control and EFE decoding deficits.

4. TOWARDS A DYNAMIC EXPLANATION OF VISUAL, COGNITIVE AND EMOTIONAL DEFICITS IN AUD

Together, attentional biases, executive impairments and emotional decoding deficits constitute three well-established mechanisms contributing to the maintenance of the addiction by feeding the vicious circle of consumption. On the one hand, attentional bias towards alcohol-related stimuli increases consumption risk by increasing craving: as craving increases, substance-related cues become even more salient, thereby eliciting more uncontrolled substance-seeking behaviors due to reduced inhibitory control [151-153]. This latter executive factor thus acts as a cement that holds the pattern of drinking habits. On the other hand, affective deficits put IAUD at high risk for interpersonal conflict [154], reinforcing their social isolation as well as their feeling of shame and auto-stigma, which in turn enhance their negative affects. In that context, they integrate the behavioral response of drinking as a way to escape and release the negative affects associated with interpersonal distress, therefore introducing a negative reinforcement mechanism [154-156]. As they keep drinking, their affective skills also keep deteriorating, leading to the onset of a vicious circle [157]. In view of the contribution of attentional, executive and affective processes in the maintenance of the disease, it appears necessary to assess the role that vision could potentially play in these intertwined mechanisms. We defend a dynamic explanation of the deficits, starting at early visual stages and then expanding and potentially magnifying during following steps due to reduced cerebral connectivity and combined visual, cognitive and emotional alterations.

4.1. Attentional Bias towards Alcohol-related Stimuli

Attentional biases in AUD refer to the automatic tendency to preferentially process alcohol-related cues and are generally assessed by the Posner paradigm or the dot-probe task [151]. These tasks evaluate to what extent resources are preferentially allocated to the processing of alcohol-related pictures by measuring to what extent a participant benefits from a spatial cue according to whether it is congruent or incongruent with the location of an alcohol-related versus non-alcohol-related stimulus presented earlier. So far, results have classically been interpreted as reflecting a purely attentional deficit. However, attentional biases implicate early visual processes, among which predictive MC-related mechanisms, as MC inputs: (1) help to control spatial orientation by feeding the dorsal visual stream [117]; (2) rapidly reach the superior colliculus, a brain area involved in covert attention [158] and in the production of saccadic eye movements [159]. Assuming the presence of MC alterations in AUD, visual disturbances and impaired visual predictions could thus contribute to the so-called "attentional" biases of patients. In addition, IAUD display increased P1 [160] and N170 [161] amplitudes for alcohol-related stimuli, which suggests that a perceptive rather than attentional process could drive the bias. The increasingly high incentive and affective value that is attributed to alcohol-related stimuli could especially facilitate the primary visual bias in view of the early connections between visual and emotional regions.

In sum, the visual and emotional deficits of IAUD could conjointly dysregulate their early visuo-affective predictions, leading to an excessive automatic resource allocation and approach response towards alcohol that could partly be sustained by MC-related attentional functions.

4.2. Loss of Inhibitory Control

Action control involves different processes among which visual detection, action selection and action execution [137, 162]. Disrupted detection and processing of visual cues can lead to longer perceptual processing time and to reduced executive efficiency, notably in tasks requiring the fast and efficient processing of perceptive cues. More importantly though, IAUD present with a disruption of the fronto-occipital tract [54, 55], found to monitor the inhibition of planned responses [136]. The well-documented frontal damages in AUD may particularly impair the balance between visual target analysis and executive processing (*e.g.*, inhibition of a motor responsis), so that response selection and execution may actually occur before the inhibitory process is completed, due to delayed visual processing and/or reduced control over visual-based decisions. Moreover, recent findings suggest that IAUD might need more visual resources than healthy controls to inhibit alcohol pictures. In agreement with a compensatory hypothesis, an increase of activity has been observed in different areas related to visual processing (occipital regions) and impulse regulation (anterior cingulate gyrus, medial frontal gyrus, and medial orbitofrontal cortex) in the absence of behavioral disparity in a Go/NoGo task using alcohol-related stimuli [163]. An ERP study also reported increased N170 amplitudes in IAUD for alcohol-related pictures in No-Go conditions [161]. Alternatively, it could be postulated that part of the inhibitory deficits of IAUD may be due to the OFC inability to compute optimal MC visual predictions (used to sensitize the most relevant visual identity), which leads to an increased influence of non-relevant competing visual candidates. Consequently, IAUD may be more influenced by distractive visual information, which could have additional deleterious consequences for executive control. In line with this set of arguments, studies showing intra-visual functional modifications in IAUD in higher-level cognitive tasks, such as spatial working memory [86, 146] provide further evidence that visual processes can adapt to executive demands and intervene in high-level deficits.

4.3. Emotional Facial Expression Decoding Deficits

In this renewed framework, emotional decoding deficits may be partially explained by visual alterations. Considering that IAUD may exhibit a primary MC deficit, they may not be able to correctly process the LSF content of emotional visual stimuli, which has been found to trigger early vision-emotion interactions [144, 164], and to increase amygdala activity [165, 166]. As a result, they may not rely on the most appropriate visual cues to build a rapid "first impression", which in turn influences the more extensive and detailed parallel PC analyses. At the same time, the structural [167] and functional [168, 169] changes observed in their limbic system may also influence the emotional tone ascribed to this first visual gist. Several preliminary findings highlight the need to consider visual alterations when assessing emotional functioning in AUD. First, as mentioned above, alterations of early visual (P100) and face-processing (N170) stages have been reported in IAUD while processing EFE [67, 70]. Second, reduced activation of OFC has been reported during emotion decoding [148] along with white matter abnormalities suggesting that AUD may be associated with decreased visual/affective connectivity [170]. Specifically, alterations of the cingulate bundle of the limbic system [171] evoke possible connectivity impairments between OFC and parietal areas of the dorsal visual stream. Reduced functional connectivity between areas of the ventral visual stream and frontal regions has also been highlighted during EFE categorization [172].

5. EXPERIMENTAL AND CLINICAL PERSPECTIVES IN AUD

The theoretical considerations and experimental data discussed in this paper raise a number of hypotheses that will have to be empirically tested. In order to reassess the role that visuoperceptive impairments may play in AUD, we suggest the following two research axes (graphically summarized in Fig. **3**), which should be successively conducted.

5.1. Clarifying Basic Visuoperceptive Deficits and Coarse-to-Fine Processing

A first axis should focus on: (1) clarifying the low-level visual deficits of IAUD to determine the origin and extent of their difficulties; (2) exploring PC and MC contributions in the framework of coarse-to-fine visual analysis.

First, studies should test the hypothesis of a primary MC deficit by means of more precise experimental tasks distinguishing PC and MC properties. To this end, basic parameters such as spatial/temporal frequency, contrast, luminance and eccentricity could be manipulated. Psychophysical tasks measuring perceptual thresholds for sinusoidal gratings (Gabor patches) of varying contrast levels and spatial/temporal frequency content displayed in central and peripheral vision could help to determine which parameters might differentially influence visual performances between IAUD and healthy controls (see Fig. **3**, section A). In order to control for the correct perception of the gratings, participants usually have to report whether the visual pattern is tilted to the right or left. Pokorny and Smith's 3-step pedestal paradigm [173, 174] also measures MC and PC-mediated contrast discrimination and has yielded interesting results with regard to acute alcohol intoxication [175]. Other techniques such as spatial filtering [176], exposure to red or green diffuse light [177-179] or manipulation of luminance and color [180] have been used successfully to dissociate MC and PC pathways in healthy participants.

Second, PC and MC contributions should be assessed in the framework of coarse-to-fine visual analysis to examine the proposal of disrupted early interactions between visual streams among IAUD. To this end, previous studies have used pairs of pictures filtered in LSF and HSF to mimic coarse-to-fine (LSF followed by HSF) or fine-to-coarse (HSF followed by LSF) visual sequences [181]. For instance, participants could be asked to decide whether both pictures belong or not to the same semantic category (Fig. **3**, section B). Results obtained among healthy individuals [181] showed that coarse-to-fine sequences quickly increase activity in the OFC and temporo-parietal areas in response to LSF cues before enhancing HSF analysis in the primary cortex and ventral regions. In AUD, we hypothesize that early OFC and temporo-parietal activity will be reduced because of MC and/or OFC damage. Such tasks will also allow to measure behavioral correlates of visuoperceptive deficits (*e.g*., reduced facilitation for semantically-related pictures pairs, especially in coarse-to-fine condition).

This first research axis will help clarifying the extent of visuoperceptive deficits and will lay the groundwork for the development of a new screening battery assessing specific components of visual perception in AUD. It will also investigate how both visual streams act together toward the construction of a coherent visual percept, thereby offering the first integrated view of MC, OFC and/or PC-related deficits in this population.

5.2. Exploring Dynamic Interactions between Vision and Cognitive/Emotional Systems

The second research axis should concentrate on visuo-cognitive predictions/interactions and visuo-emotional predictions/interactions.

A first cluster of studies should focus on cognitive top-down modulations of vision by means of paradigms assessing visual predictions based on long-term memory content. In order to manipulate the cognitive prediction/load attributed to a visual stimulus, one option could be to use semantic/spatial visual primes in visual detection and judgment tasks (Fig. **3**, section C). For instance, low-luminance contrast and achromatic (MC-biased) or chromatically defined and isoluminant (red-green; PC-biased) pictures of objects (*e.g*., a dresser) could serve as spatial or semantic cues according to whether one would expect objects (*e.g*., a photo frame) to be placed above/under it in real life conditions or to be found in the same visual context [182]. Participants would have to determine whether the target appearing right after is a real or non-existing object. In such paradigms, IAUD should benefit less from the memory-based associative and analogical activation postulated by the visual prediction model, especially when primes are valid and MC-biased. It is worth mentioning that the use of prime stimuli introduces an attentional component in the task. The impact of attention on visual prediction could be more precisely measured by using distinct primes types (*e.g*., abstract/meaningful, central/peripheral, MC/PC/non-biased, informative/non-informative) that might differentially prepare and influence visual processing, and ultimately recognition. The executive demands of the tasks could also be modified by adding distractive visual noise or emphasizing speed/accuracy.

A second cluster of studies should examine affective predictions. It is possible to explore the effects of emotional priming on MC and PC functioning by measuring distinct MC- and PC-related visual functions, such as temporal and spatial sensitivity (see, for this purpose, the temporal and spatial gap detection tasks illustrated in Fig. **3**, section D), after the presentation of emotional stimuli (unfiltered or LSF/HSF filtered). Such tasks allow to examine the close connections between MC pathways and emotional regions since visual modulations are selectively triggered by LSF emotional content [144, 164]. Contrary to healthy controls [138], we expect emotions not to improve fast temporal (MC) vision at the expense of fine-grained spatial (PC) vision in LSF and unfiltered conditions in IAUD. IAUD might thus not better perceive two rapidly appearing circles as distinct rather than fused (an ability that requires a high temporal sensitivity) and might not present impaired detection of the presence/absence of a very tiny gap in a small circle (which requires a good spatial sensitivity) after viewing emotional stimuli. In order to measure the impact of visual disturbances on explicit emotional judgments, and especially EFE decoding, participants would also have to identify EFE under MC or PC visual conditions, or in coarse-to-fine and fine-to-coarse sequences. We predict IAUD to display longer reaction times and/or lower accuracy scores, especially in the LSF and coarse-to-fine conditions. P1 and N170 modulations observed in response to spatial frequency and emotional content are also expected to differ.

This second research agenda would constitute the first direct exploration of cognitive and emotional top-down visual interactions in IAUD. It would allow to assess the contribution of vision in various experimental tasks and to examine whether perceptive deficits may explain, at least partially, some of their cognitive and/or affective difficulties. More extensive research could then be conducted to determine the applicability of the findings in critical situations encountered by IAUD, and notably for processing alcohol-related cues.

In sum, we suggest to endorse a continuous perspective by exploring each visual pathway separately before assessing their interactions, and ultimately introducing an additional cognitive and/or emotional variable. This methodology, notably capitalizing on ERP's high temporal resolution, will help to identify at which stage(s) the deficits occur, which components might be impaired and whether very mild visual, cognitive or emotional deficits may only be measurable in addition to each other.

5.3. Clinical Considerations

From a clinical standpoint, the high relapse rates observed among IAUD [183] suggest that current treatments, and corollary their underlying theoretical models, remain unsatisfying. Based on the need to account for visuoperceptive deficits, we suggest that an early individual screening of perceptive abilities could help identifying patients who might initially benefit from visual skills remediation rather than immediately more complex cognitive and emotional remediation. This preliminary rehabilitation program may, in turn, accelerate the recovery of higher-level functions. In agreement with this proposal, recent data suggested that training LSF sensitivity by means of low-level visual material can improve the use of LSF information when processing faces [184]. Training basic visual features could thus transfer from elementary stimuli to complex objects and high-level visual perception, thereby offering new thoughts on how to upgrade face-specific training programs [184].

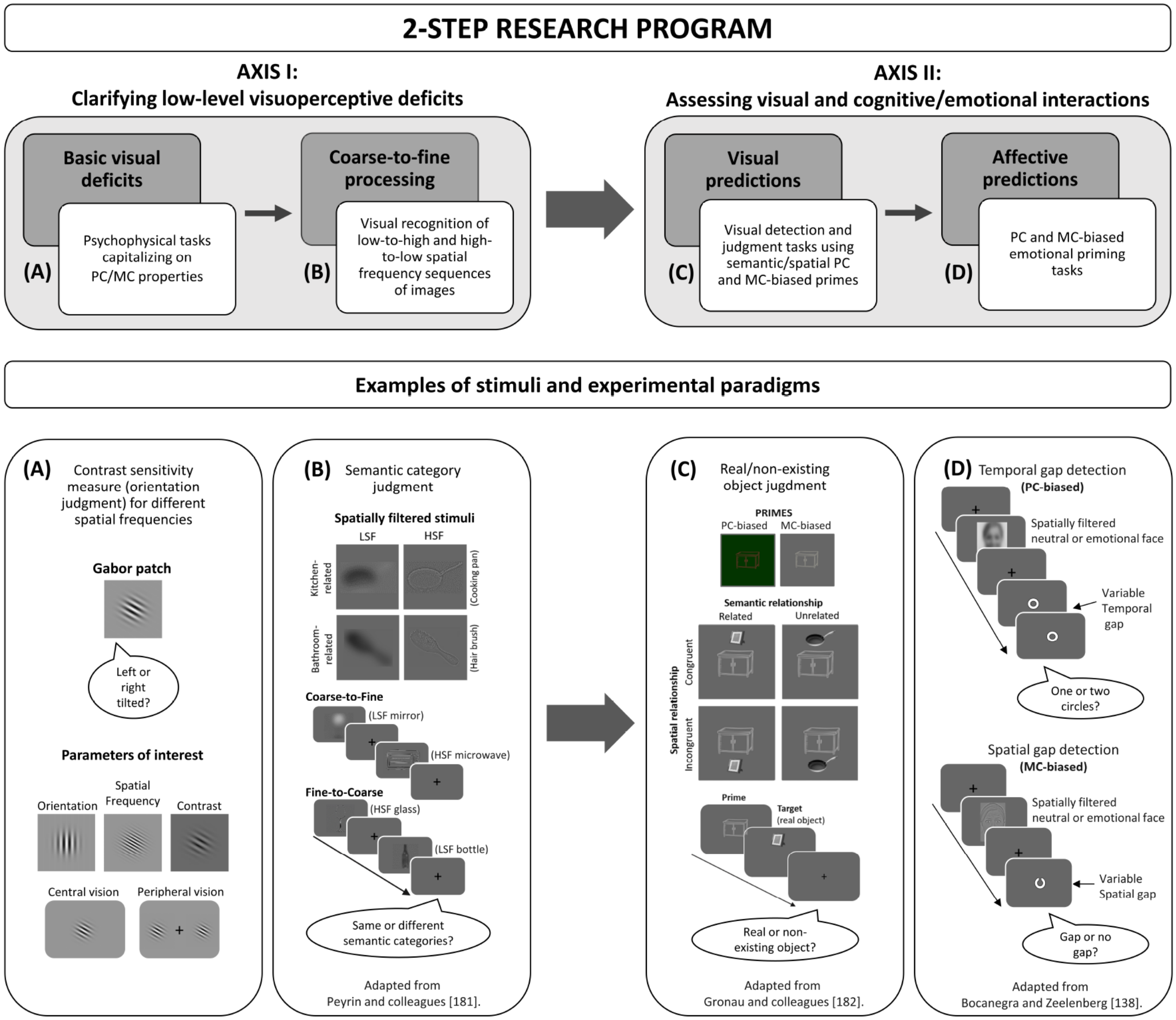

Fig. (3). Schematic summary of the proposed two-step research agenda. The first axis focuses on low-level visual properties and basic visual recognition, while the second axis addresses the concurrent role of additional cognitive (attentional, mnemonic, executive) and emotional processes. The lower part of the Figure offers an example of stimuli and task for each part of the research program. These tasks are further described in sections 5.1. and 5.2. of the paper. HSF: high spatial frequency; LSF: low spatial frequency; MC: magnocellular; PC: parvocellular; SF: spatial frequencies.

Including low-level perceptual tasks in the neuropsychological assessment of IAUD could help clinicians to specify the needs of the patients and to develop efficient therapeutic tools targeting the adequate sensory, cognitive and/or emotional processes.

CONCLUSION

In conclusion, the lack of recent studies exploring visuoperceptive deficits in AUD, leading to the absence of integration of these deficits in the dominant models, currently hampers to obtain an integrative and exhaustive description of the disease. According to recent predictive models of vision, visual disorders may affect the whole continuum during information processing, in such a way that the many cognitive and affective impairments largely documented in AUD (*e.g*., attentional, executive, or EFE decoding difficulties), could at least partly rely on basic sensory deficits, and, reversely, intensify visual deficits. While heuristic, these models have, however, not yet been explored directly in this population. Such investigations could help to renew the field of AUD with crucial implications in terms of both theoretical contributions and clinical prospects while providing significant input to theoretical models developed in healthy individuals.

LIST OF ABBREVIATIONS

AUD = Severe Alcohol-Use Disorder

IAUD = Individuals with Severe Alcohol-Use Disorder

EFE = Emotional Facial Expressions

ERP = Event-Related Potentials

HSF = High Spatial Frequency

LSF = Low Spatial Frequency

MC = Magnocellular

OFC = Orbitofrontal Cortex

PC = Parvocellular

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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