Université de Montréal

La vision aveugle suite à une ablation partielle du cortex visuel primaire : une étude en imagerie par résonance magnétique fonctionnelle

par Antonin Tran

Département Sciences Biomédicales
Faculté de médecine

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Résumé

La lésion du cortex visuel primaire mène à une perte de la vision dont l'étendue correspond à la taille et position de la lésion. Alors que la zone endommagée ou retirée ne traite plus l'information visuelle, certaines régions visuelles secondaires reçoivent toujours les entrées sensorielles en provenance de la rétine. Ces régions pourraient, dans une certaine mesure, permettre aux patients souffrants d'une lésion corticale de traiter l'information visuelle non perçue consciemment et de ressentir une certaine sensation associée à cette stimulation. La vision aveugle est un de ces phénomènes où le patient est capable d'effectuer des tâches de détection ou de discrimination sur des objets présentés au sein du scotome. Dans notre étude nous utilisons un paradigme de points en mouvement selon un design évènementiel chez une patiente de 30 ans souffrant d'une hémianopsie droite complète sans épargne maculaire et montrant des signes de vision aveugle. Nous mesurons les réponses comportementales et les activations cérébrales en utilisant l'imagerie par résonnance magnétique fonctionnelle (IRMf). Lorsque les stimulations étaient présentées dans l'hémichamp visuel fonctionnel les activations cérébrales et les résultats comportementaux étaient normaux alors que les résultats étaient significativement différents lorsque les stimuli étaient présentés dans l'hémichamp aveugle (activation bilatérale des colliculi supérieurs, temps de détection spontanée plus long). Ces résultats supportent une théorie basée sur l'expérimentation animale qui propose que la vision aveugle serait supportée par des voies secondaires et des structures sous-corticales telles que les colliculi supérieurs, le pulvinar et le corps genouillé latéral. Ces connaissances ouvrent la voie à de nouvelles techniques de réadaptation ciblant ces structures et voies spécifiquement.

Mots-clés : IRMf, vision aveugle, design évènementiel, étude de cas, hémianopsie, colliculus supérieur

Abstract

Brain injury occurring in the primary cortex may lead to a loss of vision that corresponds to the extent of the brain lesion. While the damaged area does not process the visual information, other surrounding regions are receiving retinal inputs and may allow brain-injured patients to process visual information unconsciously perceived and to experience a sense of awareness. Blindsight is one of such phenomenon where a brain-injured patient is able to detect or discriminate objects presented in the scotoma. In our study, we used functional magnetic resonance imaging (fMRI) with an event-related moving-dot stimulation paradigm in a 30 years old patient suffering a complete right hemianopia without macular sparing and showing strong signs of blindsight. The patient's vision ability was also assessed with behavioral tests. When the sighted hemifield was stimulated, fMRI activations and behavioral performances were normal. In contrast, brain activations induced by stimulation of the blind hemifield were significantly different showing a bilateral activity in the superior colliculi. In addition, the reaction time of the spontaneous detection of the movement was also longer when the stimulation was presented in the scotoma. These results support previous observations which reported that blindsight may be supported by secondary subcortical structures such as the superior colliculus, pulvinar and lateral geniculo-nucleus to process visual information. Our results may potentially impact the development of rehabilitation techniques to target subcortical pathways.

Keywords : fMRI, blindsight, event-related design, case study, hemianopia, superior colliculus

Table des matières

Liste des figures

Liste des sigles

AVC : Accident Vasculaire Cérébral

BOLD : Blood Oxygenated Level Dependent (signal)

CGL / LGN : Corps Genouillé Latéral / Lateral Geniculi Nucleus

CS / SC : Colliculus Supérieur / Superior Colliculus

DTI : Diffusion Tensor Imaging / Imagerie du Tenseur de Diffusion

HRF : Hemodynamic Response Function

IRMf / fMRI : Imagerie par Résonance Magnétique fonctionnelle

Functional Magnetic Resonance Imaging

MPRAGE : Magnetization Prepared Rapid Acquisition GRE

PUL : Pulvinar

RDK : Random Dots Kinematogram

SNR : Signal Noise Ratio

TE : Echo Time

TI : Inversion Time

TR : Repetition Time

Dead life, blind sight, poor mortal living ghost, Woe's scene, world's shame, grave's due by life usurped

Richard III - Shakespeare

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Introduction

La vision aveugle (« Blindsight ») est la capacité acquise à répondre, avec un taux de succès au-dessus du seuil de la chance, à la présentation d'un stimulus non vu (Weiskrantz, 1996). Cette capacité est particulièrement intéressante en sciences cognitives car il s'agit d'un important cas de dissociation entre conscience et performance (Heeks & Azzopardi, 2015) et apparaît exclusivement chez des patients cérébro-lésés montrant un certain degré d'adaptation structurale et physiologique (Bavelier, Achtman, Mani, & Föcker, 2012; Leh, Chakravarty, & Ptito, 2008).

Chapitre 1

La problématique de la conscience

La compréhension de l'origine de la conscience (à ne pas confondre avec l'état d'éveil) ainsi que des composantes qui en permettent l'émergence sont une des énigmes de la neuro-cognition moderne. Les premiers efforts de compréhension à fournir dans ce sens sont des efforts de définition et de segmentation des différentes expressions de « la conscience » (Block, 1995).

a. La conscience présentée comme « accès au phénomène » proviendrait d'un pattern d'activations corticales couplé à un mécanisme tel que la synchronie ou une limite temporelle (Salti et al., 2015) qui rendrait le phénomène accessible.
b. La conscience peut aussi être comprise comme l'accès à l'information sensorielle suivie de sa distribution au sein d'un réseau de travail global (Gaillard et al., 2009).
c. Enfin la conscience peut être approchée comme la capacité à auto-rapporter des perceptions, ainsi incluant le traitement phénoménologique et la capacité à le reporter (He, Cavanagh, & Intriligator, 1997).

D'après Bernard J. Baars (Baars, 2015) la conscience s'étudie sous la forme du contraste entre un état dit « inconscient » - le participant est incapable de donner des réponses et d'un état dit « conscient » - le patient est capable de donner des réponses. Le phénomène de conscience

est considéré comme subjectif et son évaluation est généralement basée sur la capacité d'un participant à répondre ou non à un stimulus donné.

Corrélats neuronaux de la conscience

Les corrélats neuronaux de la conscience reprennent la même définition que la conscience (Koch, Massimini, Boly, & Tononi, 2016), c'est-à-dire qu'ils correspondent au contraste entre pattern d'activations lorsqu'il y a conscience et pattern d'activations lorsqu'il n'y a pas conscience (dans des conditions similaires). Bien que l'activation d'un réseau fronto-parietal soit souvent associée à l'émergence de la conscience lors des tâches d'activation au cours de laquelle un participant rapporte un percept (Dehaene & Changeux, 2011) il faut garder en tête que l'activation de ces réseaux supporte aussi les activations neuronales liées aux fonctions cognitives entrainant la réponse du participant (de Graaf, Hsieh, & Sack, 2012). Dans les paradigmes où la réponse à la perception consciente n'est pas associée à une réponse du participant (il n'a donc pas de tâche à effectuer) le réseau associé à l'émergence de la conscience est beaucoup moins étendu. Dans une étude sur la rivalité binoculaire Frässle et al. (Frässle, Sommer, Jansen, Naber, & Einhäuser, 2014) montrent qu'en absence de réponse active des participants (ils enregistrent des paramètres musculaires oculaires) les régions préfrontales, cortico-motrices et certaines régions pariétales n'étaient plus activées, la majorité des activations évoquées étant postérieures (occipito-pariétales).

La perception visuelle chez l'humain

Le système visuel humain (Jacobson & Marcus, 2008), support de la perception visuelle, est constitué en entrée des yeux qui comprennent l'ensemble des capteurs de la lumière (cônes et bâtonnets) ainsi que le premier niveau de traitement de l'information visuelle via la réduction de l'information entrante (cellules bipolaires et cellules amacrynes) qui permet une ségrégation de l'information visuelle sous forme de champs récepteurs au niveau des cellules ganglionnaires. L'information est transmise via le nerf optique aux relais primaires de la vision après le chiasme optique. Au niveau du chiasme optique les champs récepteurs des deux yeux subissent une seconde ségrégation afin que l'ensemble des afférences visuelles soient réparties entre champ visuel gauche (traitées par les structures visuelles primaires de l'hémisphère droit) et champ visuel droit (traitées par les structures visuelles primaires de l'hémisphère gauche). Cette répartition sera préservée jusqu'aux stades avancés du traitement visuel où l'ensemble de l'information visuelle est traitée sous forme de scène. Après le chiasme optique plusieurs relais prennent en charge l'information visuelle, le corps genouillé latéral dorsal, partie du thalamus, est le principal. L'information visuelle est aussi dirigée vers les colliculi supérieurs (tronc cérébral) ou les noyaux suprachiasmatiques (hypothalamus) qui remplissent respectivement des rôles dans la coordination motrice des yeux avec les mouvements de la tête et la régulation des rythmes circadiens. L'information visuelle peut être divisée en deux composantes fonctionnelles qui correspondent à deux réseaux neuronaux distincts. La voie du « où » et la voie du « quoi » (Milner & Goodale, 2008).

La voie du quoi est impliquée dans l'identification et la reconnaissance d'objets. Elle est supportée par le réseau neuronal passant par le corps genouillé latéral, extension postero-ventro-

médiane du thalamus, vers le cortex strié (V1) puis V2, V3 V4 puis les régions multisensorielles associatives temporale et pariétale ainsi que les régions frontale et préfrontale. Inversement, la voie du où ne passe pas par le corps genouillé latéral, elle est impliquée dans la localisation spatiale d'objets. Cette voie est définie par les projections issues du tractus optique qui se rendent dans le tectum (partie postérieure du mésencéphale) dans les colliculi supérieurs. Des colliculi supérieurs les fibres projettent vers les noyaux postéro-latéraux du thalamus, spécifiquement dans la région inférieure du pulvinar. Enfin les fibres projettent vers V5/MT et la voie dorsale. C'est cette dernière voie qui serait impliquée dans le phénomène de blindsight. Dans le cas du présent mémoire nous nous intéresserons à des paradigmes qui mettent en évidence les processus de dissociation entre conscience et perception, spécifiquement par l'utilisation de stimuli visuels.

Paradigmes pour l'étude de la vision aveugle

Dans leur étude Eimer et al. (Eimer & Schlaghecken, 2003) utilisent un paradigme d'amorçage subliminal dans le but d'observer l'impact d'une amorce visuelle sur une réponse motrice. L'amorce visuelle qui donnait un indice sur la réponse demandée était masquée après 16ms de présentation et donc complètement « invisible » dans le sens ou le participant n'était pas capable de donner la nature de l'amorce. Cependant l'amorce avait un effet négatif (temps et précision par rapport à des essais neutres) lorsque l'amorce et la cible étaient incompatibles et, dans le cas contraire, un effet positif. Les auteurs concluent qu'un effet d'amorçage inconscient peut influencer des processus décisionnels de contrôle moteur contrairement aux tâches d'inhibition (tâche « go-nogo » ou « stop-signal ») qui demandent une discrimination consciente d'évènement pour entrainer une inhibition. Ce processus d'inhibition aurait lieu à une étape du traitement de l'information très précoce. Cependant la dissociation entre perception

et conscience peut aussi apparaître dans un traitement tardif de l'information comme c'est le cas dans le clignement attentionnel.

Nous pouvons étudier le clignement attentionnel en utilisant un paradigme visuel mettant en évidence l'impact attentionnel sur la capacité à détecter une cible visuelle. Lorsque deux cibles visuelles sont présentées à 200-500ms d'intervalle, la première cible est perçue alors que la seconde passe généralement inaperçue. Cependant lorsqu'il est demandé au participant d'ignorer la première cible, la seconde cible peut être détectée sans difficulté. Shapiro et al. utilisent ce phénomène dans un protocole d'amorçage (Shapiro, Driver, Ward, & Sorensen, 1997) et observent qu'une cible (lettre majuscule ou mot) non perçue (car masquée par une cible précédente) peut avoir un impact sur la réponse (identité, lettre minuscule ou mot de la même famille). Dans les deux protocoles le clignement attentionnel entraîne une meilleure identification. De plus, le traitement inconscient de l'information n'est pas que limité au contenu perceptuel, mais s'effectue également au niveau du contenu sémantique. Ainsi, le traitement sémantique de l'information pourrait avoir lieu au niveau pré-attentionnel.

Ces études nous montre qu'il est possible de réagir à une stimulation visuelle en l'absence de rapport subjectif vis-à-vis à celle-ci. Il s'agit donc d'une dissociation entre la perception et la prise de conscience. Le Blindsight est un type de dissociation entre perception et conscience, cependant les patients qui présentent cette dissociation sont partiellement à entièrement aveugles. Ainsi, contrairement aux paradigmes précédents ou les stimuli pouvaient dans certaines circonstances être visibles, les patients qui présentent du Blindsight sont dans l'incapacité totale (et permanente) d'accéder au contenu de ce qui leur est présenté dans leur champ visuel défectueux.

Cet effet est pour le moment non reproductible chez des participants sains malgré des essais prometteurs. Afin de séparer l'objet de perception (le percept) et la performance chez des participants sains, Lau et Passingham (Lau & Passingham, 2006) utilisent un paradigme de métacontraste qui consiste en une tâche de discrimination visuelle (carré ou diamant blanc sur fond noir) suivi de très près par la présentation d'un masque présentant les deux formes surimposées négativement (forme noire contour blanc). Les auteurs rapportent, pour 2 intervalles inter-stimuli entre masque et stimulus (*stimulus onset asynchrony, SOA*), une différence du taux de détection auto rapportée pour une performance identique (nature de la forme présentée). Ainsi pour des SOA de 33ms et 104ms les participants ont la même performance en détection de la nature des stimuli mais rapportent avoir plus de difficulté à les détecter lorsque le SOA est plus petit. Selon les auteurs, il s'agit là de la preuve d'une performance en absence de conscience (vision aveugle relative). Les résultats de cette étude sont cependant discutés sachant qu'ils n'ont pas pu être reproduits et ont été attribués à des biais méthodologiques et d'analyses (Balsdon & Azzopardi, 2015).

La vision aveugle étant un phénomène jusqu'à présent strictement observée chez des patients cérébro-lésés, elle s'inscrit comme un phénomène émergeant post-lésionnel. Ici la plasticité neuronale est donc d'importance et a plusieurs conséquences sur les tissus endommagés et les régions avoisinantes. Ceci implique 1) une perte des fonctions supportées par la région touchée au sein du réseau visuel (Binda, Thomas, Boynton, & Fine, 2013), 2) la possible apparition de fonctions modifiées ou nouvelles (de Gelder et al., 2008), et 3) la création ou le renforcement de réseaux ou voies visuelles vers des régions qui supportent peu ou pas ces fonctions (Bridge, Thomas, Jbabdi, & Cowey, 2008). Bien que les changements qui suivent une lésion occipitale sont souvent considérés comme une perte permanente de la vision par les

patients et les thérapeutes, il est important de noter que le scotome pourrait héberger des fonctions, certes inconscientes mais quand même importantes, qui pourraient être utilisées dans des thérapies de restauration de la vision (de Haan, Heutink, Melis-Dankers, Tucha, & Brouwer, 2013) d'où l'importance d'explorer des performances telles que la vision aveugle et ses bases neurales.

Description et apparition de la vision aveugle

La vision aveugle peut apparaître suite à une perte partielle de la vision, généralement un hémichamp (hémianopsie) ou un quart de champ (quadranopsie) allant parfois jusqu'à la perte totale de la vision lors d'une lésion des deux cortex visuels. Il existe un ensemble de conséquences qui découlent de cette perte de la vision, allant de la difficulté à s'orienter dans l'espace (stratégies de recherche atteintes), se déplacer dans l'espace (particulièrement à l'extérieur), difficultés à lire (retour à la ligne approximatif, difficulté à reconnaître les mots), ainsi qu'un ralentissement et des performances moindres dans les fonctions visuelles en général (Perez & Chokron, 2014).

Les conditions d'apparition de la vision aveugle mis à part la destruction du cortex visuel primaire restent inconnues, notamment parce que c'est un phénomène principalement inconscient et que les patients le reportent rarement d'eux même. Les causes de destruction du cortex primaire sont variées, la majeure cause étant les AVC occipitaux qui représentent 30% du total des AVC (Ali et al., 2013), on retrouve aussi ces conséquences lors de certaines chirurgies occipitales ou plus rarement lors de traumatismes cranio-cérébraux. Pour la recherche sur la vision aveugle les patients ayant un AVC sont donc plus nombreux mais en contrepartie la lésion est plus diffuse et difficile à évaluer et délimiter.

Cette capacité peut se présenter sous de nombreuses formes qui sont classées soit en fonction de l'état de conscience du patient envers les stimuli visuels (type 1 : absence totale de conscience, mais performance au-dessus du niveau de la chance, et type 2 : sensation de présence sans être capable de donner d'information sur le stimulus) soit en fonction du type de manifestation pour le patient (« action blindsight » lorsque le patient est capable d'effectuer une action motrice vers une cible non vue en fonction des caractéristiques physiques telles que la taille ou l'orientation, et « attention blindsight » lorsque le patient est capable de porter son attention au stimulus et d'en donner des caractéristiques telles que la couleur ou la valence émotionnelle) (Cowey, 2010; Danckert & Rossetti, 2005; de Gelder et al., 2008; Pegna, Khateb, Lazeyras, & Seghier, 2005; Van den Stock et al., 2014).

Corrélats neuronaux de la vision aveugle

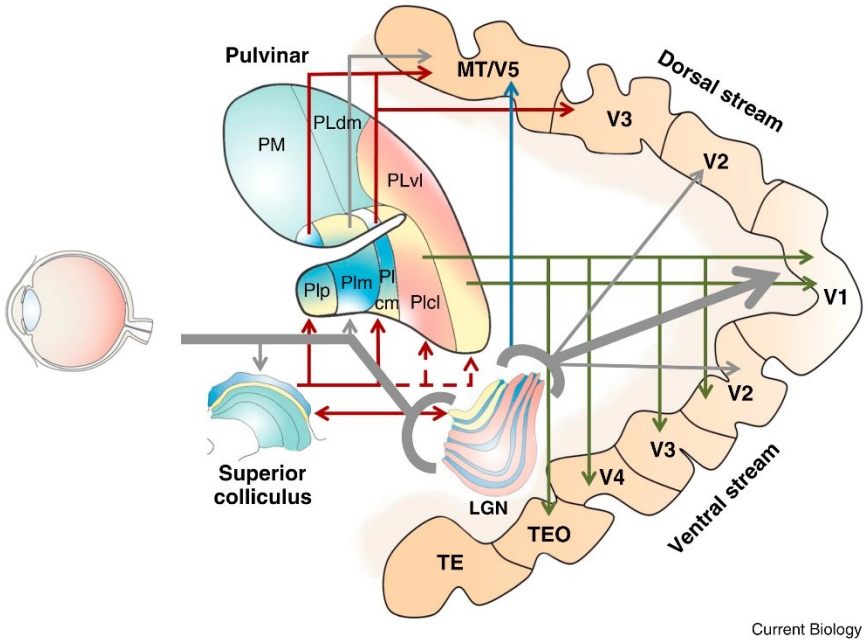

Figure 1. Connections from the eye to the visual cortex involving intermediate relays in LGN, superior colliculus and pulvinar dans (Tamietto & Morrone, 2016)

Les bases neurales qui supportent ces capacités sont cependant peu comprises pour le moment. Les études chez le chat et le singe ont montré une claire implication des aires extra-striées telles que le gyrus temporo-médian (MT/V5), du sillon latéral et de structures sous-corticales (Ciaramitaro, Todd, & Rosenquist, 1997; Sherman, 1977). Cependant chez l'humain l'étude de la vision aveugle a surtout été phénoménologique et s'est relativement peu penchée sur l'implication des structures sous-corticales dans le fonctionnement de ce phénomène (principalement par manque de moyens techniques non invasifs). Jusqu'à présent peu d'études en imagerie par résonance magnétique (IRM) ont montré une implication claire entre l'activité de structures sous-corticales telles que les corps genouillés latéraux (CGL), les colliculi supérieurs (CS) et les pulvinar (PUL) ou des régions corticales telles que le cortex visuel primaire et extrastrié (V1, V3 et MT-V5) avec les différentes performances en vision aveugle.

Une étude récente chez des participants cérébro-lésés (Ajina, Pestilli, Rokem, Kennard, & Bridge, 2015a) a montré l'existence d'un faisceau de matière blanche entre le CGL et V5 spécifique à la présence de vision aveugle chez les patients. Bien que ce faisceau soit souvent rapporté dans la littérature humaine et animale (macaque) (Schmid et al., 2011), l'existence des faisceaux ayant pour origine le PUL et le CS ne semblent pas corréler avec la performance en vision aveugle. D'autres études chez les mammifères montrent cependant une implication plus importante de ces deux dernières structures dans le phénomène de vision aveugle (Fredes, Vega-Zuniga, Karten, & Mpodozis, 2012; Jiang, Stein, & McHaffie, 2015; Piché et al., 2015; Villeneuve, Kupers, Gjedde, Ptito, & Casanova, 2005). Ces résultats sont cohérents avec certaines recherches chez l'humain (Tamietto et al., 2010).

Les colliculi supérieurs sont 2 petites structures positionnées à l'extrémité rostrale du tronc et fortement connectées aux noyaux thalamiques. Elles représentent chez l'homme un rôle majeur en vision et sont le deuxième relai visuel le plus important après le CGL. Cependant, leur petite taille et la proximité avec les vaisseaux sanguins sont deux grandes limitations au niveau de leur détection à l'IRM fonctionnelle (IRMf), la seule technique d'imagerie non-invasive permettant un accès aux activités physiologiques en profondeur du cerveau. La plupart des études en IRMf qui enregistrent l'activation des CS utilise un champ de vue en cerveau entier dont l'analyse statistique ne favorise pas la détection des activités provenant de structures de petite taille et/ou de courte durée. Ces activités sont catégorisées comme étant du bruit et ainsi cachent une portion du signal lié à la tâche d'activation. Ce biais est d'autant plus accentué lors de l'utilisation d'un design dit en bloc (Wall, Walker, & Smith, 2009). Il est ainsi probable que l'utilisation combinée de l'analyse cerveau entier et l'utilisation d'un design en bloc soit la raison pour laquelle des structures telles que le CS le CGL ou le PUL ne soient pas reportées comme supportant la performance de vision aveugle chez l'homme (Perez & Chokron, 2014). Pour contourner ces limitations, il est possible de de modifier le champ de vue de spatial en IRMf pour orienter l'acquisition de données sur les structures plus petites et profondes du cerveau. De plus, la recherche actuelle s'est aussi portée sur une autre séquence d'imagerie, l'imagerie anatomique de connectivité (DTI) (Tamietto & Morrone, 2016) laissant la question du lien structure-fonction du phénomène non traitée à ce jour.

Chapitre 2

Objectifs et hypothèses

Le but général de mon mémoire est d'explorer les substrats neuronaux impliqués dans le phénomène de la vision aveugle chez un patient cérébro-lésé afin de comprendre l'implication de voies visuelles secondaires dans le phénomène de vision. Cette compréhension permettra à l'avenir de construire des méthodes de réhabilitation en vision en se basant sur une compréhension holistique des réseaux visuels.

Objectif spécifique 1

Via l'utilisation d'imagerie non invasive (IRMf), il s'agit d'explorer les patterns d'activation de structures sous-corticales et régions corticales lorsque le patient présente le phénomène de vision aveugle. Ces régions forment des relais au sein de réseaux visuels largement distribués au travers du cerveau.

Hypothèse 1

Un ensemble de structures sous-corticales (colliculus supérieur ; pulvinar ; corps genouillé latéral) montrent des patterns d'activations différents en fonction de la latéralité du stimulus visuel (présentation à droite ou présentation à gauche). On s'attend à ce que ceux-ci soient similaires à ceux rapportés dans la littérature chez l'humain sain lorsque l'hémichamps sain du patient cérébro-lésé est stimulé et soient différents lorsque l'hémichamps aveugle est stimulé. Puisqu'il s'agit avant tout d'une étude exploratoire, les patterns d'activations émergeants suite à la stimulation de l'hémichamps lésé sont inconnus, cependant on peut s'attendre à observer des phénomènes compensatoires liés aux phénomènes de plasticité.

Objectif spécifique 2

Investiguer les différences comportementales (phénoménologiques) émergeantes entre des situations de vision normale ou de vision aveugle.

Hypothèse 2

Lorsque questionné, le patient rapporte une expérience différente entre vision normale et vision aveugle. De plus, ses performances objectives (chance de succès, temps de détection) sont différentes entre vision normale et vision aveugle.

Chapitre 3 : article

Neuronal Mechanisms of Motion Detection Underlying Blindsight Assessed with Functional Magnetic Resonance Imaging (fMRI)

Antonin Tran[1,2,3*], Michèle W. MacLean[2,6,*], Vanessa Hadid [1,2,], Latifa Lazzouni[2], Dang Khoa Nguyen[1,4], Julie Tremblay[3], Mathieu Dehaes[3,5,**], and Franco Lepore[2,3,6,**]

[1]Department of Biomedical Sciences, Université de Montréal, Montréal, QC, Canada

[2]Centre de Recherche en Neuropsychologie et Cognition (CERNEC), Montréal, QC, Canada

[3]Centre Hospitalier Universitaire Sainte-Justine, Montréal, QC, Canada

[4]Centre Hospitalier Universitaire de Montréal, Montréal, QC, Canada

[5]Department of Radiology, Radio-oncology and Nuclear Medicine, Université de Montréal, Montréal, QC, Canada

[6]Department of Psychology, Université de Montréal, Montréal, QC, Canada

[*] Equal contribution as co-first- author

[**]Equal contribution as co-senior author

Abstract

Brain imaging research offers a valuable model of functional brain plasticity by showing how sensory inputs reshape cortical activations after a visual impairment. Following a unilateral post-chiasmatic lesion affecting the visual cortex, patients may suffer a contralateral visual loss referred to homonymous hemianopia. Nevertheless, these patients preserve the ability to unconsciously detect, localize and discriminate visual stimuli presented in their impaired visual field. To investigate this paradox, known as *blindsight*, we have conducted a study using functional magnetic resonance imaging (fMRI) of blood oxygenation level dependent (BOLD) using an event-related moving-dot stimulation paradigm to evaluate the structural and functional impact of such lesion in a 33-year old patient (ML), who suffers a complete right hemianopia without macular sparing and showing strong evidences of blindsight. We thus performed whole brain and sliced thalamic fMRI scan sequences during resting state and a motion detection task. In addition, ML underwent a series of visual tasks to correlate blindsight performances with neural activity. Accurate performance demonstrated the presence of residual vision and the ability to unconsciously perceive motion presented in the blind hemifield, although her reaction time was significantly higher when compared to her performance in the intact visual field. When the normal hemifield was stimulated, we observed significant contralateral activations in primary and secondary visual areas as well as motion specific areas, such as the supramarginal gyrus and middle temporal area. We also demonstrated sub-thalamic activations within the superior colliculi (SC) and pulvinar. These results suggest a role of secondary subcortical structures in normal spontaneous motion detection. In a similar way, when the lesioned hemifield was stimulated, we observed contralateral activity in extrastriate areas with no

activation of the primary lesioned visual cortex. Moreover, we also observed activations within the SC when the blind hemifield was stimulated. However, we observed unexpected ipsilateral activations within the same motion specific areas, as well as bilateral frontal activations. These results highlight the importance of abnormal secondary pathways bypassing the primary visual area (V1) in residual vision. This reorganization in the structure and function of the visual pathways correlates with behavioural changes, thus offering a plausible explanation for the blindsight phenomenon. Our results may potentially impact the development of rehabilitation techniques to target subcortical pathways.

Keywords: Functional magnetic resonance imaging (fMRI), Blood Oxygenation Level Dependant (BOLD), Motion Detection, Event-Related Stimulation Paradigm, Homonymous Hemianopia, Blindsight, Cerebral Plasticity

Introduction

Blindsight is the ability to detect, localize, and discriminate objects presented in the blind hemifield without having consciousness of seeing the objects (Weiskrantz, 1996). Portraying a rare case of dissociation between consciousness and performance, this phenomenon has raised strong interests in cognitive neurosciences (Heeks & Azzopardi, 2015). Behavioral approaches to study blindsight showed a wide variety of types and manifestations (Cowey, 2010; Danckert & Rossetti, 2005), ranging from the ability to discriminate forms, emotional content (Pegna et al., 2005; Van den Stock et al., 2014), and the capability to perform actions toward unseen targets (de Gelder et al., 2008). We distinguish Type 1 blindsight, where the subject has no awareness or conscious perception, and Type 2 blindsight, where the subject has awareness of visual presentation in the blindfield without visual qualia (Hadid & Lepore, 2017; Leopold, 2012).

Representing over half a million Americans, homonymous hemianopia (HH) patients frequently demonstrate blindsight abilities. HH refers to a post-chiasmatic lesion of the primary visual cortex (V1), in the right or left hemisphere, leading to contralateral cortical blindness (Barleben et al., 2015; Leh et al., 2008). Most commonly caused by a stroke, HH represents the leading cause of cortical deficits causing visual field loss and resulting in a significantly reduced quality of life (Goodwin, 2014; Perez & Chokron, 2014; Urbanski, Coubard, & Bourlon, 2014). Following this post-chiasmatic lesion, neuronal plasticity with various degrees of structural and physiological adaptation, and major changes in brain circuitry were previously observed: 1) loss of function in the impacted region (Binda et al., 2013), 2) reinforcement of spared pathways or formation of new pathways to strengthen the original connections (Bridge et al., 2008), and 3) emergence of new or modified functions (de Gelder et al., 2008). While occipital cortical

connectivity may change following a lesion, this plasticity is seldom associated with regaining of visual function. However, when subcortical – thus unconscious – visual processing emerges, restoration therapies might be calibrated to exploit these alternative pathways (de Haan et al., 2013). In particular, neuroimaging studies of visual field defect patients demonstrated a reorganization of the cerebral neuronal networks following visual training – see a review in (Perez & Chokron, 2014). More specifically, on the one hand there is evidence of a connection between the lateral geniculate nucleus (LGN) and the middle temporal areas, specific to the performance of blindsight (Ajina, Pestilli, Rokem, Kennard, & Bridge, 2015b), yet on the other hand experiments in mammals have also suggested the role of the pulvinar and the colliculi (Fredes et al., 2012; Jiang et al., 2015; Piché et al., 2015; Villeneuve et al., 2005) which were coherent with human research(Tamietto et al., 2010). In addition, studies in cats and monkeys showed implications of extrastriate areas such as the middle temporal (MT), visual area 5 (V5), the Sylvian sulcus and subcortical structures (Ciaramitaro et al., 1997) as well as a pathway connecting LGN neurons to the extrastriate cortex(Yu, Atapour, Chaplin, Worthy, & Rosa, 2018). Given this body of research, we hypothesized the superior colliculi (SC) to be highly connected to the thalamic structures and motion specific areas, thus acting as the second visual relay after the LGN.

Currently, few functional magnetic resonance imaging (fMRI) studies have shown consistent associations between blindsight performance, specific structures and functional networks. However, the implication of subcortical structures in the functioning of residual vision in humans is yet to be fully understood. To our knowledge, this blindsight study is the first to propose the use of an event-related paradigm to measure blood oxygenation level

dependent (BOLD) activations in the subcortical structures of an HH individual. Our approach included behavioral testing and imaging techniques to evaluate the structural and functional impact of the striate cortex lesion. Our goals were 1) to assess the anatomical state of the brain by imaging structures that are likely damaged by the lesion; 2) to represent cortical activations external to the lesion with a fMRI whole brain analysis scan and 3) to determine the implication of subcortical structures in blindsight using an event-related fMRI design that focused around the thalamus. Hence, we anticipated to observe an increase in the projections from the superior colliculi to the middle temporal areas acting as the second visual relay after the LGN. As the main visual pathways are lesioned, these alternative pathways could represent the underlying mechanisms of blindsight.

Materials and methods

This study was approved by the *Comité d'Ethique de l'Unité de Neuroimagerie Fonctionnelle* (UNF) of the *Centre de recherche de l'Institut universitaire de gériatrie de Montréal* (IUGM), Montréal, Canada.

Patient history

The patient is a 33-year old woman who in 2004, at the age of 17, was diagnosed with left occipital lesions that required a stereotaxic biopsy. Post-biopsy examination scans showed the appearance of a 3.7 cm by 3 cm anterio-posterior left occipital hematoma and subarachnoid hemorrhage. A burr hole and a ligature of an important blood vessel were also observed. In 2005, a porencephalic cyst next to the occipital horn was also diagnosed. MRI follow-up

examination showed a small lesion with T1-weighed imaging hyposignal and T2-weighed imaging hypersignal in the posterior portion of the lenticular right core, resulting in a possible lesion post-ischemia. Since the surgery, the patient's health state is stable and she presents no cognitive disorder other than a right homonymous hemianopia without macular sparing. She reports notably "forgetting her things in her right field of view and bumping into objects". Vision in the left hemifield was clinically assessed and did not require any correction with surgery or lenses.

Blindsight evaluation

The patient underwent a first testing prior to MRI examination to evaluate the visual residual abilities. The behavioral tests showed performances at chance level for static stimuli suggesting no sign of blindsight. However, when the blindfield was stimulated with moving stimuli, the patient was able to spontaneously detect the stimuli. The patient reported that she "was unable to see the moving stimulus, but she only had a vague feeling that something just happened in her blind field, without being able to describe it". This ability refers to Type II blindsight (Leopold, 2012).

Stimuli – Peripheral Motion Detection Paradigm

Visual stimuli were presented using Presentation® software (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA) on a screen located behind the MRI magnet and reflected through the mirror of the head coil. Prior to data acquisition, the position of the mirror was adjusted and located such as the field of view ($150\times110mm^2$) was sufficiently large to display all stimuli. Visual stimuli consisted of static dots presented bilaterally, which moved either in the right or

left hemifield. Three conditions were analyzed: 1) static condition, i.e. static dots presented bilaterally, 2) right visual motion, i.e. dots in motion on the right side of the screen, and 3) left visual motion, i.e. dots in motion on the left side of the screen.

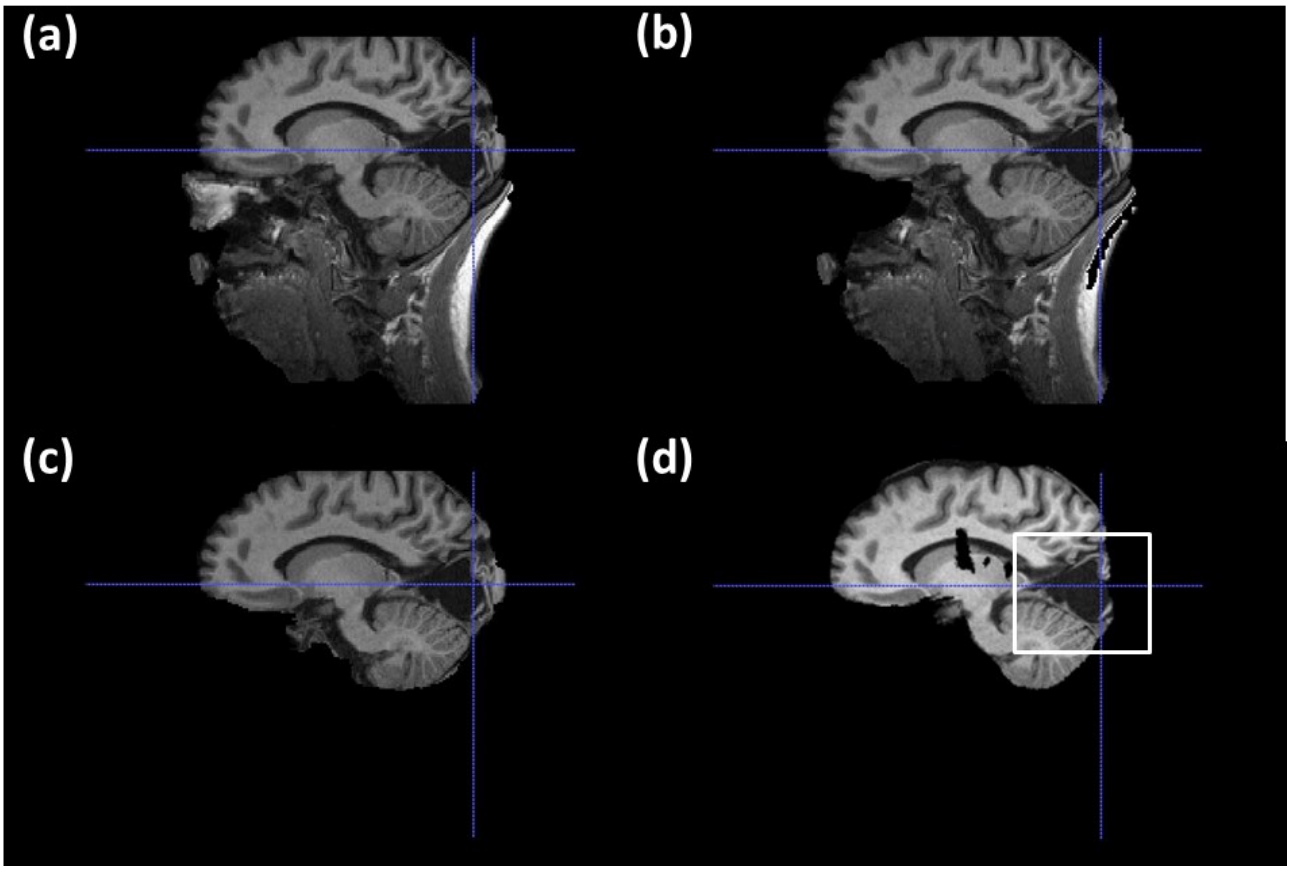

Figure 2. Iterative brain extraction tissue in the patient: (a) Initial phase of gross removal of non-cerebral tissues, (b) eye extraction and (c) neck extraction. (d) Non-accurate brain extraction tissue obtained using another algorithm (Lutkenhoff et al., 2014).

at the left or the right of the fixation cross at 8° of eccentricity (Figure 2). The diameter of each dot was 0.75º and the number of dots was 150. The speed of each dot was 12º/s with a limited lifetime of 150ms. The dots moved with 100% coherency.

An event-related block design was selected to present the three conditions. Thirty-three (33) events were distributed randomly per trial. Inter-stimulus interval (ISI) duration was 6s on

average, varying following a Poisson distribution (Hagberg, Zito, Patria, & Sanes, 2001) while the duration of each stimulus was 3s.

The task consisted in detecting as fast as possible the moving dots in the left or right hemifield. The accuracy rate and the reaction time (RT) (when < 3s) were collected for behavioral analyses. The subject's response was collected through a button box connected to the data acquisition software. The box was built with two buttons: one located on the right and the other on the left side. The left button was associated with events occurring in the left hemifield while the right button with the right hemifield. The subject's responses were always recorded with the right hand. Through the entire scanning session, none of the details about the nature of the stimuli, their duration or location were provided to the subject. After completing the imaging session, the patient was interviewed about the nature of the stimuli and her ability to detect them.

Data acquisition

Prior to data acquisition, stimuli were presented to the blindfield (right hemifield) of the patient to ensure she was unable to see the visual stimuli. During fMRI scans, eye movements were recorded with a MRI-compatible optical eye-tracker device (IScan RK-464B, ISCAN Inc., Woburn, MA, USA). Only time-series data where the visual gaze was kept focused on the center of the screen were considered for data analysis. MRI data were acquired with a Siemens 3T Trio system (TrioTim, version Syngo MR B17) using a 12-channel array head coil.

The total scanning time was 39 minutes which included a high-resolution T1-weighted anatomical scan of 5 minutes as well as two fMRI sequences of 17 minutes each, one with a field of view (FOV) of the whole brain and another one with a FOV focused on subcortical structures. The fMRI scan that focused on subcortical structures was designed with 17

continuous axial interleaved slices centered on the thalamus. The position of the slices was selected manually to ensure inclusion of all subcortical structures in the FOV. The fMRI sequence parameters were the following: repetition time (TR) 1500ms, echo time (TE) 36ms, no delay time in TR, FOV 192×192mm^2, slice thickness 3mm, spacing between slices 3mm, flip angle 80°, acquisition matrix 64×64mm^2. The structural T1-weighted 3D magnetization prepared rapid gradient echo sequence (MPRAGE) was acquired with the following parameters: voxel size of 1×1×1.2mm^3, acquisition matrix size 240×256, flip angle 9°, TR 2300ms, TE 2.91ms, inversion time (TI) 900ms, FOV 256×256mm^2, 160 slices.

Data analysis

Behavioral data

Behavioural tests were analyzed using IBM SPSS Statistics (IBM Corp., New York, USA, 2012). The number of correct answers for both conditions was acquired by recording each response associated with the presentation of global motion on either side. A hit corresponded to the correct button press (left or right) when motion occurred; a false alarm corresponded to a button press during the static condition. Reaction times were compared between the left and right visual motion, and analyzed with *t*-tests. Significance level was set to $p < 0.05$.

Imaging the whole brain

A first analysis was performed to assess cortical activations of the whole brain. Functional MRI data of the whole brain were preprocessed and analyzed with SPM12 (Statistical Parametric Mapping, Wellcome Trust Centre for Neuroimaging, London, UK) using MATLAB (MathWorks, Natick, MA, USA). Preprocessing of functional images for the three conditions

included: discard of the four initial volumes(Wall et al., 2009), realignment of functional time series with the first image as a reference to correct for head motion, co-registration of functional and anatomical data with the subject's anatomy, spatial normalization in the Montreal Neurological Institute (MNI) space, and spatial smoothing with a three-dimensional isotropic Gaussian kernel (8mm full-width at half-maximum, FWHM).

Subsequent to preprocessing steps, fMRI model specification was performed. Changes in brain regional responses were modeled using the convolution of a boxcar function (onsets and duration of stimulation) and the canonical hemodynamic response function (HRF). The general linear model was used to account for changes in brain response explained by changes in the experimental conditions. Movement parameters derived from realignment of the functional volumes (translations and rotations around the three directions) were also included. Removing artefactual low-frequency trends was performed using high-pass filtering with a discrete cosine basis function and a cut-off period of 128s.

Statistical parametric maps were generated for the main effects of visual motion presented on the left or right contrasted by the static image. Further analysis was performed to describe common regions activated by the combination of left and right visual motion conditions. In addition, the analysis of specific effects were performed and presented through a list of regions showing significant activations, i.e. movement presented on one (left or right) side contrasted by movement on the opposite side combined with static images (defined by the left and right contrast, respectively).

Statistical inferences were adjusted for multiple comparisons with the family-wise error (FWE) correction for the entire brain volume. Unpaired sample *t*-tests were performed between each contrast. We labeled significant clusters with structural neuroanatomy information using

an available brain atlas (Tzourio-Mazoyer et al., 2002) to ease the location and identification of activated regions. However, to enhance spatial accuracy and visualization of activated regions in the midbrain, a specific pipeline implemented through FSL (FMRIB Software Library, Oxford, UK) (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012; Woolrich et al., 2009) was performed.

Imaging the midbrain

A second analysis was performed to assess cortical activations in the midbrain. Functional MRI volumes of the midbrain were preprocessed and analyzed with FSL. Preprocessing included discard of the four initial volumes, realignment of functional time-series using FSL linear motion correction and noise correction. Functional data were not registered in a stereotaxic template and were kept in the native space. This strategy allowed to preserve fMRI data as non-linear transformation used to co-register data may induce signal loss. Anatomical data were then registered in the functional space using FSL FLIRT routine with 6 parameters rigid body fitting technique. Three iterations of brain tissue extraction were performed using FSL BET (Smith, 2002) and applied to anatomical data using a measure of fractional intensity threshold. This strategy was used to preserve accurate tissue segmentation, which can be affected by T1 signal inhomogeneity due to the presence of the lesion. The skull was first removed with an initial fractional intensity threshold of 3.0. Eye removal was then performed with a fractional intensity threshold of 2.0. To complete brain extraction, the neck was removed with a fractional intensity threshold of 1.0. Brain tissue surrounding the lesion was then preserved at the proximity of the skull. The resulting BET mask was applied to functional data. Our technique was compared against an automated script (OptiBET) (Lutkenhoff et al., 2014) that failed to segment correctly

brain structures around the lesion (Figure 2). Statistical analyses were then performed in masked functional volumes.

Functional data were analyzed using FSL FEAT pipeline (Woolrich et al., 2009). Changes in BOLD regional responses were estimated using a general linear model that included three regressors, i.e. one regressor for each condition (left and right visual motion, and static images). While a high-pass filter of 0.11Hz was applied to functional data, spatial smoothing was not performed because the size of the sub-structures of interest was close to the functional voxel size (3 to 9mm^3). Two explanatory variables were included in the model, i.e. one for each moving stimuli (left and right visual motion). A double gamma HRF was used to model the stimuli and to further fit fMRI data. This selection allowed a higher number of degrees of

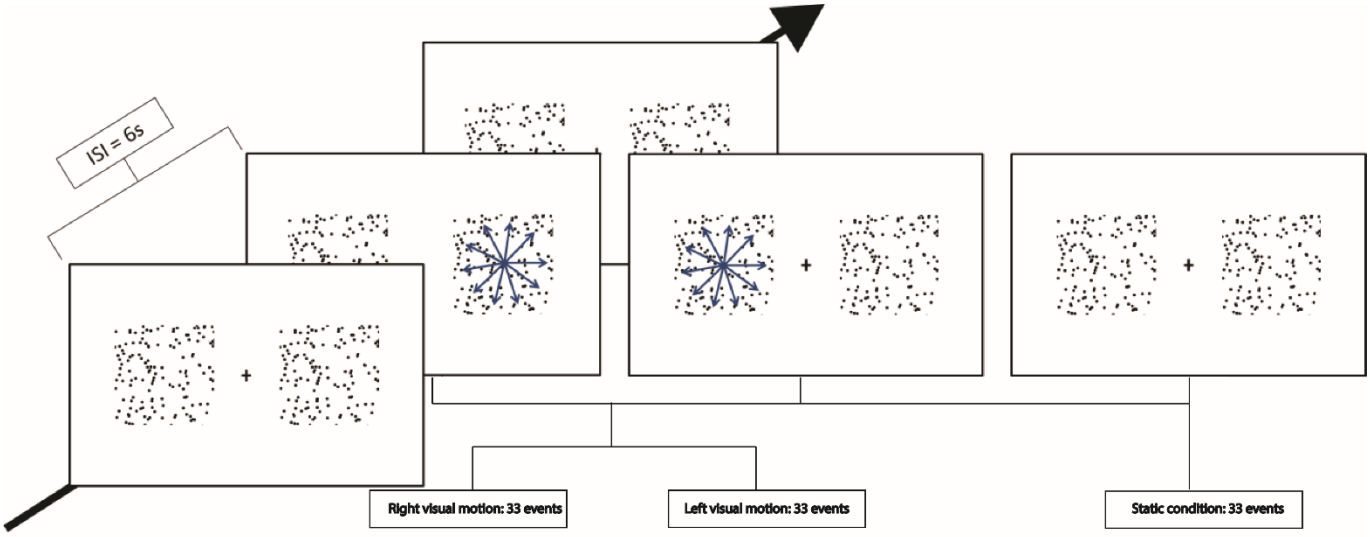

Figure 3. Event-related stimulation design displaying moving (blue arrows) and static dots. Each condition (left visual motion, right visual motion and static condition) is presented for a duration of 3s and for 33 times with an inter-stimulation interval (ISI) average duration of 6s.

allowed reducing the risk of removing signals from sub-cortical structures and their neighboring voxels that fit highly constrained HRF models. Results included BOLD activation maps

estimated for left and right contrasts defined above. As for whole brain analysis, activation maps were corrected for multiple comparisons.

Results

Behavioral results – performance and reaction time

Fig. 3 shows reaction time (ms) for spontaneous detection of visual motion in both hemifields. For stimuli presented in the left hemifield (intact vision), the performance was optimal, i.e. 100% detection rate accuracy with a mean RT of 665.09ms (standard deviation 131.35ms). In the right hemifield, detection rate was 93% with a mean RT of 1590.42ms (standard deviation 587.49ms). RT of detection of stimuli presented in the right hemifield (left hemisphere motion processing/lesion side) was significantly slower than RT in the left hemifield (right hemisphere motion processing/intact side) ($p < .0001$).

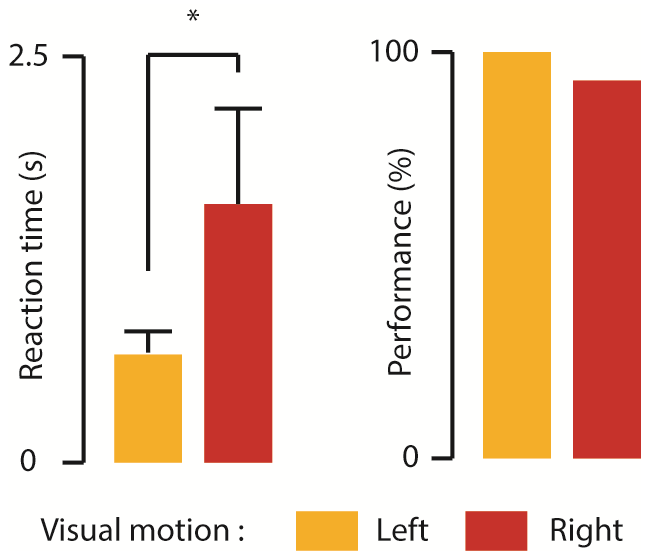

Figure 4. Patient reaction times (s) on the left axis and performance (%) on the right axis to spontaneous detection of moving targets for left visual motion (orange) and right visual motion (red) (** $p < .01$). ML was significantly faster when stimuli where presented on the left side (normal hemifield) of the screen compared to the right side (blind hemifield). However, ML's response accuracy was comparable between conditions.

During the semi-structured interview, the patient reported no awareness of the nature of the stimuli presented in her blind (right) hemifield with a clear perception of the stimuli presented in her left hemifield. However, the patient deduced stimuli of both hemifields to be of the same nature. The patient also reported a total lack of confidence in her performance with respect to the right stimuli presentation. The patient described randomly pressing the right button arguing that even if she felt something happened in her blindfield, it was very faint. The patient described this feeling such as Eigengrau patches in the middle of the scotoma (Ladd, 1894).

Functional results – imaging the whole brain

Fig. 4 shows cortical BOLD activation maps analyzed with the whole brain approach across different conditions and contrasts. Fig. 4 A (a)-(c) shows axial view slices, separated by $12mm^3$, for the left and right visual motion conditions, and for both conditions together, respectively. Fig. 4 B (a)-(f) shows specific axial, sagittal and coronal views of axial slice $z = 4$ and $z = -8$, for left and right visual motion stimuli, respectively. Table 1 shows the list of significant cortical regions (as clusters) corresponding to the BOLD activations depicted in Fig. 4. Clusters are described with their name, size (in voxels), MNI peak coordinates, significant *t*-value and corresponding z-score, and specific brain areas that are included in the cluster. Only cluster sizes > 10 voxels are presented in the table.

Left visual motion stimuli elicited activity in the following regions : temporal inferior (858 voxels) including the right calcarine, right middle temporal (MT), left occipital inferior (94 voxels), right lingual (44 voxels) including the right calcarine, right supramarginal (47 voxels) and right middle temporal (13 voxels), while right visual motion stimuli activated the left occipital middle and inferior (376 voxels), left calcarine (57 voxels), left (21 voxels) and right frontal inferior orbital (61 voxels), left (14 voxels) and right temporal middle (22 + 11 voxels),

right lingual (34 voxels), and right frontal middle (12 voxels). When controlling for static condition (subtracting the condition from left and right visual motion conditions separately), the right calcarine (1202 voxels), right postcentral (149 voxels) including right parietal inferior and superior in the cluster, left rolandic operculum (166 voxels), right supramarginal (36 voxels) remained activated for the left visual motion stimuli while for the right visual stimuli, left occipital middle (325 voxels), right insula (93 voxels), right frontal superior (34 voxels), left insula (128 voxels), right frontal middle (63 + 41 voxels), right supramarginal (48 voxels) right MT (10 voxels) were activated (Table 2). When combining both left and right conditions, common activated regions included left occipital inferior, right middle temporal and right lingual areas with respective voxel counts of 94, 22 and 24 (Table 3). In addition, BOLD activations resulting from the left contrast included the right occipital superior, right MT and right lingual (calcarine and fusiforme) areas (280, 53 and 114 voxels, respectively) while for the

right contrast, activated clusters included the left frontal inferior orbital and right insula with respective (63 and 96 voxels, respectively, Table 3).

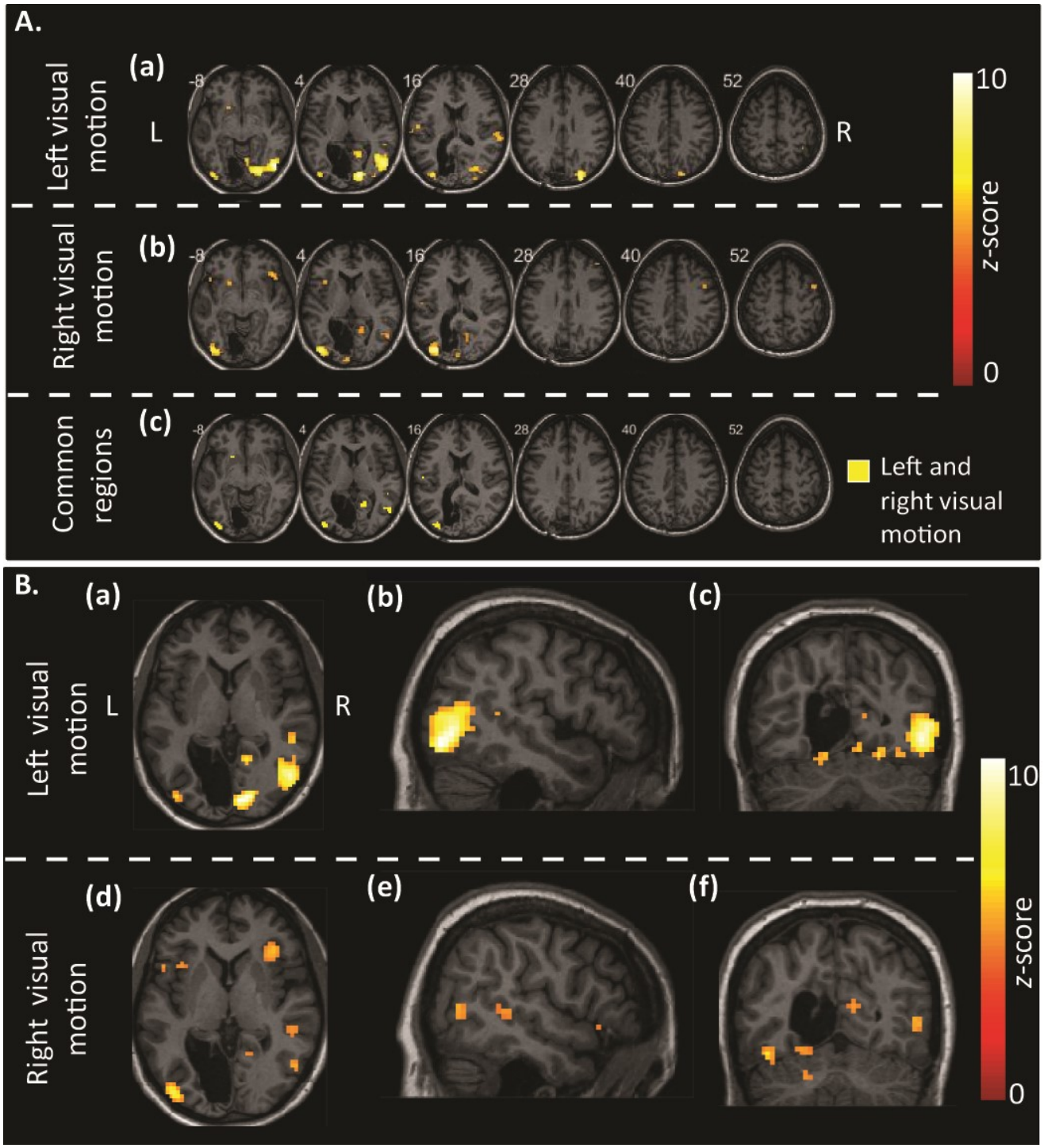

Figure 5. Patient cortical blood oxygen level dependent (BOLD) activations in the whole brain sequence scan. BOLD activations are reported for **A**. six different transverse slice views separated by 12mm^3 for optimal visualization and for **B.** the left stimuli and right stimuli shown by a (a-d) transverse slice, (b-e) sagittal slice and (c-f) coronal slice. (pcorr < .05 FWE). *Results are presented in tables 1, 2, & 3.*

Functional results – imaging the midbrain

Fig. 5 shows BOLD activation maps resulting from the midbrain analysis and estimated for left and right visual motion conditions contrasted with static stimuli. For left visual motion, Fig. 5 (a) and (b) show significant activated regions in the bilateral medial temporal gyri (MT+/V5) and V1, respectively. In addition, Fig. 5 (c) and (d) show significant activations in the bilateral SC and the left lateral PUL, respectively. For right visual motion, Fig. 4 (e) and (f) show significant activations in the right MT+/V5 regions and the right calcarine sulcus, respectively. In addition, Fig. 5 (g) shows significant activations in the left SC.

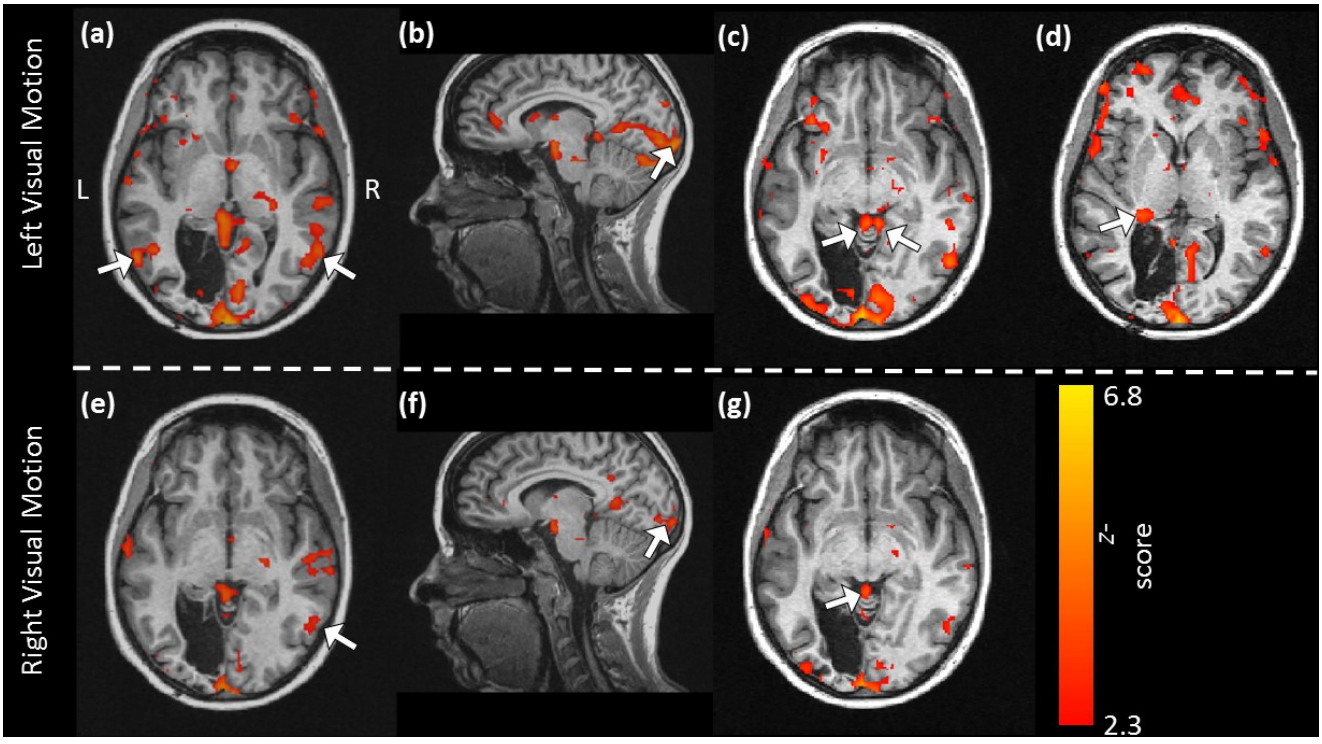

Figure 6. Patient cortical and subcortical blood oxygen level dependent (BOLD) activations in the midbrain sequence scan for the left (a)-(d) and right (e)-(g) stimulations. For the left stimulation, BOLD activations are observed in the (a) bilateral medial temporal gyri (MT+/V5), (b) right calcarine sulcus, (c) bilateral superior colliculi, and (d) left pulvinar. For the right stimulation, BOLD activations are observed in the (e) right MT+/V5, (f) right calcarine sulcus, and (g) left superior colliculus. Corrected significant results are reported, p <.05.

Discussion

Behavioral and fMRI results suggest that visual information presented in the blindfield is processed through different pathways and/or structures, notably through the geniculo-extrastriate pathway and the colliculo-pulvinar-extrastriate pathway depending on the visual residual abilities found in the blind hemifield - see review by (Hadid & Lepore, 2017). However, while previous blindsight studies have employed block designed whole brain fMRI analysis – see review by (Urbanski et al., 2014) -, our study was the first to provide a functional description of a single V1-lesioned patient using an event-related fMRI design focused on cortical and subcortical areas. In addition, this design allowed us to associate the sense of awareness the patient presented in the blindfield with BOLD activations, providing unique new insights on Type II blindsight. In fact, the patient triggered a response every time she had a sense that something was happening in her blind hemifield inducing highly accurate performances for detecting moving stimuli. Subsequently, the responsiveness to stimuli in the sighted hemifield was not significantly different than the one in the blind field. However, there was a downside to this accuracy; the reaction time to stimuli in the blind field was significantly longer than in the normal field. We postulate that due to the fact that her decision making was based on subjective criteria, it is less robust than decision making based on perceptual evidences, thus potentially inducing longer reaction times (Kang, Petzschner, Wolpert, & Shadlen, 2017) which could account for behavioral differences in blindsight.

Motion detection in the normal left hemifield induced significant BOLD activity in the right calcarine (visual primary areas) (Tootell et al., 1995; Watson et al., n.d.), as well as activations in the contralateral right MT visual area, thought to be specific to motion (Dukelow

et al., 2001). Activations of the visual cortex were only contralateral when the static condition was subtracted from the left visual motion condition, cancelling out ipsilateral activity observed in visual areas. Bilateral activations were found in parietal regions possibly reflecting shift of attention between the left and the right hemifield (Saygin & Sereno, 2008) and in the supramarginal gyrus known to be responsive to visual motion (Dupont, Orban, De Bruyn, Verbruggen, & Mortelmans, 1994). Therefore, in agreement with previous literature on motion detection and perception, activations following stimulation of the normal hemifield were consistent.

However, when we compared activations of the [left - static] condition to the [right - static] condition, we observed that stimulating the blind hemifield did not induce activity in the left calcarine, which was expected due to the lesion in the left primary visual area. This result led us to reject the hypothesis that the surviving residual V1 islands are responsible for blindsight, as left calcarine activity was observed in the right visual motion condition because it implies bilateral stimulation of static dots. Nonetheless, motion in the right hemifield [right - static] induced significant BOLD activity in the left striate, i.e. calcarine, and extrastriate visual areas including the inferior and middle occipital gyri, which showed that visual information was received by the typical contralateral visual areas. However, these activations were not strong enough to trigger a response in MT within the same hemisphere. Nonetheless, activations were observed in the ipsilateral MT instead of the contralateral counterpart which could explain implicit motion detection in the blind hemifield. Moreover, when either hemifield was stimulated [left-static] or [right-static], activations were found in the right inferior parietal lobe, notably the right supramarginal gyrus, which is likely responsible for attentional capture even

in the absence of awareness (Hervais-Adelman et al., 2015) specific to visual motion processing (Dupont et al., 1994).

Common regions observed when combining left and right visual motion conditions were found in the right calcarine, left inferior occipital and right MT, indicating that mechanisms of compensation driven by visual areas were used allowing for some processing of information when the blind hemifield was stimulated. Therefore, we hypothesize that a secondary residual pathway that prioritizes the use of the "healthy" hemisphere may be used to allow performances above chance level in the absence of consciousness. When compared with the blind hemifield [left contrast], the normal hemifield exhibited significantly higher responses within the right striate and extrastriate visual areas and MT, which was expected. Interestingly, in the [right - static] condition, the presence of activity in the frontal areas and in the insula (contralateral left frontal operculum and frontal inferior orbital) could explain why the patient preserved the sense that something happened within the blind regions and the high performances she exhibited (Persaud et al., 2011).

Taken together, these results could indicate that abnormal activations of ipsilateral MT areas are able to drive some insular and frontal activity which could explain the lack of real visual percept. Therefore, we speculate that frontal activations would not have been generated without MT responses which could have been driven by subcortical structures as the superior colliculus.

In fact, stimulation of the normal field was accompanied by a bilateral activation of the colliculi, as well as activations in the left pulvinar region and stimulation of the blind field elicited responses in the contralateral colliculus. Why the pattern differs when one hemifield is stimulated compared to the other is yet to be understood. The activation pattern following

stimulation of the normal hemifield observed in the ipsilateral superior colliculus and pulvinar appears to be abnormal, because collicular activations should be essentially contralateral (Wall et al., 2009). Therefore, if we admit that in normal behavior, a subcortical pathway from the contralateral SC to the contralateral MT could induce perception of motion, it leads us to postulate that the activity found in the ipsilateral colliculus and pulvinar is not typical. One hypothesis would be that stimulation of the normal hemifield induces ipsilateral activations. These activations act as a system destined to stimulate the colliculus so that it does not degenerate and contribute to processing motion stimuli even in the absence of visual awareness. Therefore, the SC is thought to project to the ipsilateral MT, which is consistent with the activity we observed after stimulating the right hemifield. In other words, when the blind field (right) is stimulated, the contralateral SC (left) is activated in association with the ipsilateral MT (right) which is likely to respond to stimulation of the normal hemifield (left). These observations may contribute to the understanding of the human blindsight literature and suggest that the lesion disturbs not only the ipsilesional brain circuitry but also impacts the functional contralateral network. Therefore, understanding and guiding cortical plasticity could allow the rehabilitation and restoration of visual functions following a lesion in the occipital areas. Thus, investigating the neural and vascular basis of blindsight is of importance to enable personalized clinical treatments, such as specific visual trainings to improve exploration and visual-orientation abilities, with long-term effects.

fMRI is a relevant tool to study subcortical functional activations evoked by external stimulation in a non-invasive setting. However, SNR in small deep brain structures remain a limitation due to MRI physics. Nevertheless, this limitation can be mitigated by using precise analysis and experimental designs. On an experimental perspective, event-related designs are

also challenging as they require a higher number of stimulation events and longer acquisition time than block-averaged designs for equivalent performance. Also, the presence of blood vessels in close proximity to the subcortical structures may affect the quality of images with additional physiological noise and distortions.

Finally, our results are likely limited with regards to explaining different types of blindsight, performances and phenomenology – see review by (Hadid & Lepore, 2017), due to the uniqueness nature of the patient lesion. As an example, contralateral activation of MT could occur in blindsight, but would be associated with a different form of blindsight, as Type I blindsight, due to the fact that the signal would be too weak to propagate through the dorsal pathway and create a sense of awareness.

Further work will need to compare different lesions and behavioral performances in a cohort of hemianopic patients with a delimited lesion of V1 using event-related fMRI design to assess the role of subcortical structures and increase the effectiveness of rehabilitation approach based on subcortical pathways.

Conclusion

In conclusion, a subcortical dorsal pathway implicating the contralateral SC, ipsilateral MT and contralateral frontal areas may mediate Type II blindsight for motion detection. The SC could have an essential role in allocating attention, enhancing perceptual sensitivity in the blind field and sending visual information directly to MT of the non-lesioned hemisphere (right) or indirectly to MT (right) circulating in priority through the extrastriate visual areas of the lesioned hemisphere (left). Because this pathway is not commonly used in conscious vision in humans,

the visual signal sent could be less rich in information or not appropriate to be processed by cortical areas to generate explicit vision. Nonetheless, we hypothesized that MT was able to process visual properties linked to motion explaining performance above chance level, but then again with less accuracy and precision keeping the level under the threshold of consciousness. Propagation of the signal through the dorsal pathway and to frontal areas could induce a sense of awareness without reaching the threshold of visual awareness allowing for the phenomenon of Type II blindsight. Thus, the role of plasticity in our case study shows that stimulation of the normal hemifield, which leads to activation of the ipsilateral SC to enhance perception in the blind field may potentially help to develop rehabilitation approach based on subcortical pathways.

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