cortex xxx (2017) 1–15

Available online at www.sciencedirect.com

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

Clinical neuroanatomy

Reach and grasp deficits following damage to the dorsal pulvinar

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ARTICLE INFO

Article history:
Received 26 January 2017
Reviewed 08 June 2017
Revised 17 July 2017
Accepted 2 October 2017
Action editor David Carey
Published online xxx

Keywords:
Pulvinar
Reaching
Grasping
Saccades
Visuomotor
Perceptual choice
Ataxia

ABSTRACT

Expansion of the dorsal pulvinar in humans and its anatomical connectivity suggests its involvement in higher-order cognitive and visuomotor functions. We investigated visuomotor performance in a 31 year old patient with a lesion centered on the medial portion of the dorsal pulvinar (left > right) due to an atypical Sarcoidosis manifestation. Unlike lesions with a vascular etiology, the lesion of M.B. did not include primary sensory or motor thalamic nuclei. Thus, this patient gave us the exceedingly rare opportunity to study the contribution of the dorsal pulvinar to visuomotor behavior in a human without confounding losses in primary sensory or motor domains. We investigated reaching, saccade and visual decision making performance. Patient data in each task was compared to at least seven age matched healthy controls. While saccades were hypometric towards both hemifields, the patient did not show any spatial choice or perceptual deficits. At the same time, he exhibited reach and grasp difficulties, which shared features with both, parietal and cerebellar damage. In particular, he had problems to form a precision grip and exhibited reach deficits expressed in decreased accuracy, delayed initiation and prolonged movement durations. Reach deficits were similar in foveal and extrafoveal viewing conditions and in both visual hemifields but were stronger with the right hand. These results suggest that dorsal pulvinar function in humans goes beyond its subscribed role in visual cognition and is critical for the programming of voluntary actions with the hands.

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https://doi.org/10.1016/j.cortex.2017.10.011

1. Introduction

Evolutionary history and ontogenetic development together with fronto-parietal connectivity of the dorsal pulvinar suggest its contribution to higher cognitive functions and in particular to primate-specific abilities such as complex visuomotor transformations that require the integration of visual with eye and hand position information (Grieve, Acuna, & Cudeiro, 2000; Preuss, 2007). The pulvinar is a typical association nucleus with strong reciprocal connections to a multitude of modality specific and multimodal cortical areas (Benarroch, 2015; Gutierrez, Cola, Seltzer, & Cusick, 2000). The pulvinar is a heterogeneous structure for which different parcellations schemes have been proposed, depending on the anatomical techniques that were used such as cyto-, myelo- or chemoarchitecture (Jones, 2007). However, most authors agree on at least four major subdivisions in human and non-human primates, consisting of anterior pulvinar (PuA), medial pulvinar (PuM), lateral pulvinar (PuL) and inferior pulvinar (PuI). Together, the medial pulvinar and the dorsal portion of the lateral pulvinar form the so called ‘dorsal pulvinar’, which roughly occupies the region dorsal to the level of the brachium of the superior colliculus (BSc) (Gutierrez et al., 2000; Kaas & Lyon, 2007). The majority of pulvinar studies have investigated its ventral aspect, which is retinotopically organized and is connected with striate and extrastriate visual cortices in monkeys and humans (Arcaro, Pinsk, & Kastner, 2015; Saalmann & Kastner, 2011). In contrast to the ventral pulvinar, the dorsal pulvinar portion does not contain an orderly retinotopic or visuomotor topography (Benevento & Port, 1995) and is reciprocally interconnected with cortical regions that underlie the coordination of visually-guided movements, such as posterior parietal and prefrontal cortices (Arcaro et al., 2015; Barron, Eickhoff, Clos, & Fox, 2015; Gutierrez et al., 2000; Jones, 2007; Rosenberg, Mauguiere, Catenoix, Faillenot, & Magnin, 2009). Response properties of dorsal pulvinar neurons resemble the complexity found in fronto-parietal cortices, i.e., neuronal firing correlates with visual attention, subjective perception, decision confidence as well as the planning and execution of eye- and hand movements (Bender & Youakim, 2001; Benevento & Port, 1995; Dominguez-Vargas, Schneider, Wilke, & Kagan, 2017; Komura, Nikkuni, Hirashima, Uetake, & Miyamoto, 2013; Magarinos-Ascone, Buno, & Garcia-Austt, 1988; Wilke, Mueller, & Leopold, 2009; Yirmiya & Hocherman, 1987). There is also evidence from pulvinar lesion studies in monkeys (Komura et al., 2013; Robinson & Petersen, 1992; Wilke, Kagan, & Andersen, 2013; Wilke, Turchi, Smith, Mishkin, & Leopold, 2010; Zhou, Schafer, & Desimone, 2016) and humans (Arend, Rafal, & Ward, 2008; Karnath, Himmelbach, & Rorden, 2002; Rafal, McGrath, Machado, & Hindle, 2004; Snow, Allen, Rafal, & Humphreys, 2009; Van der Stigchel, Arend, van Koningsbruggen, & Rafal, 2010; Ward, Danziger, & Bamford, 2005; Zihl & von Cramon, 1979) that the pulvinar is a critical contributor to a wide range of higher-order visual and oculomotor functions including attentional orienting, visual search, emotion recognition and saccadic decision making. At the same time, although an initial dorsal pulvinar inactivation study in monkeys suggests its critical contribution to the programming of reach and grasp movements (Wilke et al., 2010), there is a marked paucity of studies that tested basic visuomotor functions involving hand usage in humans (Benarroch, 2015; Bridge, Leopold, & Bourne, 2016).

This is particularly surprising given that multimodal signals from a wide range of well-studied cortical visuomotor areas converge in the dorsal pulvinar and it has thus been proposed to facilitate cortico-spinal control over movements and possibly better parietal-premotor integration for the flexible control of goal-directed movements (Cappe, Morel, Barone, & Rouiller, 2009; Grieve et al., 2000; Guillery & Sherman, 2002). In the present study, we investigated visuomotor functions with a focus on reach performance in a patient with a circumscribed lesion centered on the medial portion of the dorsal pulvinar. This patient provided the unique opportunity to unravel the contribution of the pulvinar to proper visuomotor behavior without lesions in functionally pertinent first-order thalamic nuclei (Sherman, 2016), and without primary sensory or motor deficits. Based on our previous dorsal pulvinar inactivation study in monkeys (Wilke et al., 2010), we hypothesized that the patient would show reach inaccuracies and initiation delays, possibly with a stronger effect for the (right) hand and space located opposite to the more pronounced pulvinar lesion (left). From an optic ataxia we expected reaching errors to be stronger in extrafoveal-as compared to foveal reaches (Andersen, Andersen, Hwang, & Hauschild, 2014; Perenin & Vighetto, 1988), a comparison not available from pulvinar lesion studies in monkeys.

2. Material and methods

2.1. Participants

2.1.1. Patient M.B

Patient M.B. is a right-handed 31 year old male with an atypical cerebral manifestation of a systemic Sarcoidosis (Hoitsma, Drent, & Sharma, 2010). Sarcoidosis is a rare disorder that shows CNS manifestations in 2–26% of the cases with many atypical lesion locations (Fritz, van de Beek, & Brouwer, 2016). In patient M.B. the neural manifestation of the sarcoidosis affected the thalamic pulvinar on both sides. The patient's symptoms started with walking problems, headache and loss of appetite. These symptoms improved after an initial high dose corticosteroid therapy. Several weeks later, his symptoms relapsed and he was referred to our hospital. The diagnosis of Sarcoidosis was secured by thoracic biopsies together with pathological CD4/CD8 ratio in the bronchoalveolar-lavage and histopathological documentation of epithelioid-cell granulomas that followed the detection of suspicious lymph nodes in the abdominal-CT and FDG-PET-CT (Fritz et al., 2016). All examinations described in this paper were done in February 2016, within the two weeks when the disease cause was just diagnosed.

2.1.1.1. Localization of the lesion. The pulvinar lesion was larger on the left side than on the right and included large portions of the medial pulvinar as well as a small portion of the anterior pulvinar. On the right side, initially only a small portion of the medial pulvinar was affected (Fig. 1). This right