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Effects of aging on low luminance contrast processing in humans

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ABSTRACT

Luminance contrast is a fundamental visual cue. Using a dedicated neuroimaging framework, we sought to characterize typical Blood Oxygen Level Dependent (BOLD) responses in two subcortical regions, the superior colliculus (SC) and the lateral geniculate nucleus (LGN), and V1, the primary visual cortex area, and how they change over the lifespan. For imaging subcortical activity related to luminance contrast modulation, specific measurements were introduced to rule out possible signal contamination by cardiovascular activity and vascular alterations with age that could hamper the BOLD signal interpretation. Clearly, BOLD responses increased in these three regions with luminance contrast, with a statistically significant diminution in LGN and V1 for older compared to younger participants, while basal perfusion remained unchanged. Additionally, perceptual responses, as assessed with psychophysical experiments, were highly correlated to BOLD measures in the three studied regions. Taken together, fMRI and psychophysics results indicate an alteration of luminance contrast processing with normal aging. Based on this knowledge we can better recognize when age-related brain changes vary from these expectations especially during neurodegenerative diseases progression where the functioning of subcortical structures is altered. The proposed fMRI-physchophysics methodology allows performing such investigation.

Introduction

Besides cognitive impairments, visual deficits, frequently reported in normal aging, may impact daily life. Age-related visual decreases, including loss in sensitivity to motion, spatial frequency processing or luminance contrast sensitivity, are not solely due to changes in the optical properties of the eye (Elliott et al., 1990; Owsley, 2011). They probably result also from age-related neuronal changes occurring along the visual pathway, at retinal (photoreceptors and ganglion cells degeneration), subcortical and cortical levels. Indeed, electrophysiological studies in animal models demonstrate that many aspects of neural and behavioral responses, such as latency (Wang et al., 2005; Yu et al., 2005; Ball et al., 2007), color discrimination (Knoblauch et al., 1987, 2001), motion/speed tuning (Atchley and Andersen, 1998; Yang et al., 2009b) and contrast sensitivity (Yang et al., 2008a), change with aging along the multiple stages of the visual pathway. Knowledge about how in human, subcortical and cortical processing of retinal information is affected by normal aging is still missing.

Information from the retina is processed through two main pathways: the parvocellular (P) and magnocellular (M) pathways. Whereas the P pathway is responsive to chromatic and static stimulation of high spatial frequency and underlies form and chromatic discrimination along the L–M axis, the M pathway responds to achromatic stimuli with low spatial and high temporal frequencies and underlies motion and depth information processing. The majority of axons of the retinal ganglion cells (90%) that leaves the eye via the optic nerve projects to the Lateral Geniculate Nucleus (LGN), a small (5–10 mm) primary thalamic relay between the retina and the visual cortex (Sherman and Guillery, 2006). M and P pathways are mostly represented in the LGN (Felleman and Van Essen, 1991) and connected to corresponding sublayers in the primary visual area (V1). In addition to retinal afferent, LGN receives strong cortico-thalamic feedback projections from V1 (Sherman and Koch, 1986; Sherman and Guillery, 2006). This pathway is called the "retino-geniculo-striate" route. In parallel, a minority of fibers originating from the retina takes a secondary route and reachs the

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superficial layers of the Superior Colliculus (SC) (Kuypers and Lawrence, 1967; Hendrickson et al., 1970; Schiller and Malpeli, 1977). Additionally, these layers receive inputs from the striate and extrastriate cortex (Wilson and Toyne, 1970; Benevento and Fallon, 1975; Benevento and Yoshida, 1981; Fries, 1984) and the frontal eye field (Kuypers and Lawrence, 1967; Kunzle and Akert, 1977). There is also a projection coming from the dorsal and ventral LGN (Benevento and Fallon, 1975), especially from its M layers. In these layers visual neurons are organized in a topographical manner (DuBois and Cohen, 2000; Schneider and Kastner, 2005; Kaytal et al., 2010) and respond to transient or moving visual stimuli (Schiller and Koerner, 1971; Cynader and Berman, 1972; Marrocco and Li, 1977). This second pathway, bypassing V1 and sending projections to extrastriate areas, is called the "retino-tectal" route. Compared to the well-established P pathway alteration in normal aging (Owsley et al., 1983; Elliott, 1987; Elliott et al., 1990; Elliott and Werner, 2010), the influence of age on the M pathway is less documented. Even if some studies suggest that there are no alterations of this pathway with aging (Owsley et al., 1983), selective loss of contrast sensitivity to relatively low spatial frequency has nonetheless been documented (Lux et al., 2008; Elliott and Werner, 2010; Bordaberry et al., 2012; Allard et al., 2013). These controversial results about the preservation or not of the M pathway in normal aging could, in part, be due to the fact that only psychophysical data have been available. It is of interest, then, to introduce the fMRI technique for a finer non-invasive exploration of subcortical and cortical visual information processing along the M pathway and its possible alteration with age.

Advances in fMRI technique have allowed the non-invasive functional investigation of subcortical nuclei in the human brain under certain conditions (Schneider and Kastner, 2005; Sylvester et al., 2007; Wall et al., 2009; Linzenbold et al., 2011). However, it remains difficult to measure the functional activity in SC (Poncelet et al., 1992; DuBois and Cohen, 2000) because of its small size, deep location and proximity to pulsating vascular structures that may hinder the BOLD signal measurement. Moreover, SC is highly sensitive to luminance changes with a response that rapidly saturates (Schneider and Kastner, 2005) restricting the conditions of stimulation. To overcome these difficulties, we developed a low luminance contrast varying stimulus to modulate the SC activity and accordingly, a specific fMRI setting to record and analyse the corresponding BOLD signal variations in SC, LGN and V1 regions of interest. We took specific care to rule out possible signal contamination by cardiovascular activity and vascular alterations with age. We used psychophysical tests to estimate luminance contrast perception. The strong correlation we observed between perceptual and BOLD responses clearly demonstrated the validity of our approach to non-invasively investigate the functional response of subcortical visual regions in human. We report an alteration of luminance contrast processing along the M pathway with normal aging beside the well-documented functional deficit of the P pathway. These control data and the proposed methodology allow detecting when age-related brain changes differ from these expectations in particular in neurodegenerative diseases (Rupp et al., 2012; Rolland et al., 2013; Hutchinson et al., 2014; Brace et al., 2015).

Materials and methods

Subjects

Thirty healthy subjects participated in this study. Three age-dependent groups were considered: *Young*, with 10 participants, 7 females, 26 ± 3 years; *Middle Age*, with 10 participants, 5 females, 47 ± 4 years and *Elderly*, with 10 participants, 7 females, 65 ± 3 years. A visual examination by an ophthalmologist was performed for middle age and elderly participants. They had normal or corrected-to-normal vision. Participants requiring visual correction wore the MediGoggle Adult Research Set (Cambridge Research Systems Ltd., England; http://crsltd.com/), interchangeable prescriptive goggles suitable for use in MR environment. All participants provided written informed consent before participating in the study and were screened according to standard MRI exclusion criteria. The study was approved by the local ethics committee (ID-RCB 2012-A00310–43).

Psychophysical procedure

Prior to the collection of imaging data, all observers performed a Maximum Likelihood Difference Scaling (MLDS) task (Maloney and Yang, 2003; Knoblauch and Maloney, 2008, 2012) to estimate the perceived magnitude of luminance contrast changes.

Stimuli conditions

The stimuli (Fig. 1) were composed of achromatic radial checkerboards (mean spatial frequency: 2.3 cpd, varying from 3 cpd in the center to 1.5 cpd at the periphery) with ten levels of luminance contrast from 2 to 20%, logarithmically spaced, displayed on a neutral grey background. These stimuli were generated using Matlab (MathWorks, MA, USA). A Python homemade program was used for displaying and running the experiment, using PsychoPy2 (Peirce, 2007, 2009) under the Windows 8 operating system. Spectral and luminance calibrations of the computer screen were performed with a PR650 SpectraScan Colorimeter (Photoresearch) and used for screen gamma-correction in stimulus specification. Stimuli had a mean luminance of 147 cd/m^2 equal to the grey background (CIE xy = 0.29, 0.30). Participants viewed the screen at a distance of 70 cm and the stimuli under a visual angle of 2.04°.

Experiment

In a dark room, each participant performed a three session experiment. Each session consisted in a 5 min random presentation of 120 trials. On each trial, a randomly selected triad of checkerboards was presented with three luminance contrasts (a, b, c), chosen from a series of ten contrasts described above, with a < b < c. Stimulus b was always the upper stimulus in the middle, and stimuli a and c were below randomly positioned on the left or right side, respectively (see Fig. 1). Stimuli were presented for 500 ms. The observer was instructed to fixate the fixation cross and respond with no limit of time when he/she could choose which of the bottom patterns (left or right) was most similar

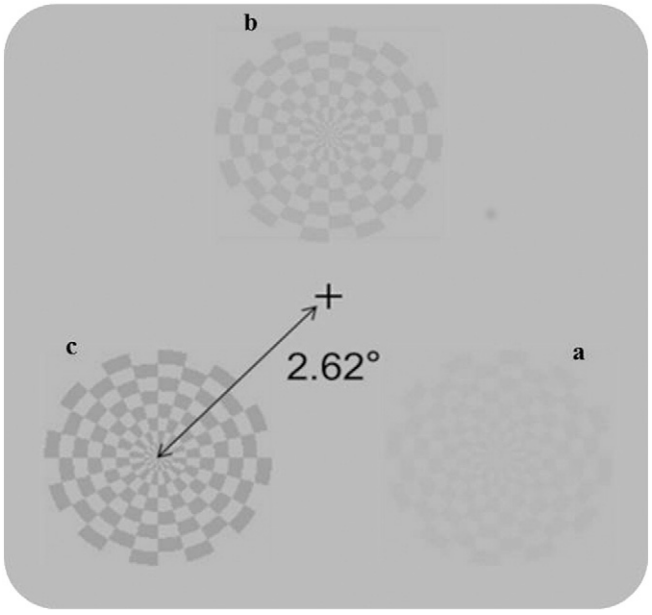

Fig. 1. MLDS experiment: example of a triad used in the psychophysical session before scanning. The observer had to fixate each pattern until he/she could choose which of the two bottom patterns (left or right) was most similar to the upper pattern with respect to the color of its interior region.