Parietal connectivity mediates multisensory facilitation

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ABSTRACT

Our senses interact in daily life through multisensory integration, facilitating perceptual processes and behavioral responses. The neural mechanisms proposed to underlie this multisensory facilitation include anatomical connections directly linking early sensory areas, indirect connections to higher-order multisensory regions, as well as thalamic connections. Here we examine the relationship between white matter connectivity, as assessed with diffusion tensor imaging, and individual differences in multisensory facilitation and provide the first demonstration of a relationship between anatomical connectivity and multisensory processing in typically developed individuals. Using a whole-brain analysis and contrasting anatomical models of multisensory processing we found that increased connectivity between parietal regions and early sensory areas was associated with the facilitation of reaction times to multisensory (auditory–visual) stimuli. Furthermore, building on prior animal work suggesting the involvement of the superior colliculus in this process, using probabilistic tractography we determined that the strongest cortical projection area connected with the superior colliculus includes the region of connectivity implicated in our independent whole-brain analysis.

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Introduction

Our senses provide us with independent and sometimes dissimilar information, yet we need to detect, localize, and respond to events in the world based on unitary and coherent percepts. This perceptual unity is achieved through multisensory integration, which combines and facilitates the processing of temporally and spatially congruent information from different sensory modalities (e.g., Stein et al., 1993). The redundant-target paradigm (e.g., Brang et al., 2012; Cappe et al., 2010; Hershenson, 1962; Miller, 1982) demonstrates a basic and well-replicated finding that participants are faster to respond to a multisensory stimulus (a sound and a light combined) relative to a unisensory target (the sound or light in isolation), due to the facilitatory effects of multisensory integration. This facilitation is generally attributed to integration at the level of individual neurons, such that the response to a multisensory stimulus is greater than the response to either unisensory stimulus in isolation[1], and has been proposed as a driving force behind the evolution of multisensory processes in both animals and humans (for a review see Stein and Stanford, 2008).

Multisensory integration reliably occurs in brain areas that receive inputs from multiple primary sensory modalities, including the cortex,

midbrain, and thalamus (Jones and Powell, 1970) with the extent of integration varying according to task demands and stimulus complexity. Cells in the superior colliculus (SC) in particular are involved in orienting to a multisensory stimulus and initiate directed eye and head movements through projections to brainstem motor nuclei (Gandhi and Katnani, 2011; Krebs et al., 2010). Temporal, parietal, and frontal association areas have demonstrated multisensory integration during a wide array of tasks both with functional imaging (Macaluso and Driver, 2005) and single unit recordings (e.g., Bruce et al., 1981) and lesions to these regions are typically associated with deficits in multisensory processing (e.g., Teuber, 1966).

Several mechanisms have been proposed to underlie multisensory integration, differing in the anatomical pathways involved and the modulatory role of connectivity. Multisensory convergence models argue that information is relayed from the primary sensory modalities through afferent connections to multisensory neurons in temporal, parietal, and frontal cortical regions (Driver and Noesselt, 2008; Jones and Powell, 1970) leading to behavioral facilitation though projections to the primary motor cortex (Molholm et al., 2006) and the superior colliculus (Jiang et al., 2001). A second, direct anatomical model attributes multisensory integration to direct anatomical connections between the primary sensory modalities, including between unimodal visual and auditory cortical areas (Beer et al., 2011; Falchier et al., 2002, 2010; Lewis and Noppeney, 2010; Romei et al., 2009). Questioning the necessity of anatomical connections between the senses in mediating multisensory integration, recent evidence suggests substantial multisensory processing occurs in areas typically considered unisensory (Ghazanfar and Schroeder, 2006), including primary and

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[1] Multisensory neurons exhibit different ranges of summed activity, with less than a quarter of neurons in the SC showing superadditivity and the majority showing subadditive integration (Perrault et al., 2005).

secondary auditory cortex (Kayser et al., 2008). Indeed, laminar profiles of auditory cortex show both feedforward and feedback projections from visual cortex, indicating that visual information is relayed to auditory cortex in the initial bottom-up flow of processing (Schroeder and Foxe, 2002).

These classes of models make different predictions regarding the effect intraindividual variability in anatomical connectivity has on multisensory processing. As both increased connectivity and increased myelination are related to increased processing speed (Turken et al., 2008) both multisensory convergence and direct anatomical models predict that multisensory processing would be facilitated by high white matter coherence along anatomical pathways, but differ on where in the brain these critical connections lie. On the other hand, processes relying on multisensory responses in unisensory regions assign less importance to variations in long-range anatomical connectivity and predict relatively little effect of individual differences in connectivity on multisensory processing. Here we examine the role of anatomical connectivity, as assessed with diffusion tensor imaging (DTI), in human multisensory facilitation. Multisensory facilitation was quantified with a redundant-target paradigm in which subjects responded as quickly as possible to auditory, visual, and auditory–visual stimuli. Subjects typically respond faster to multisensory targets than the timing predicted by statistical summation of the unisensory targets (exceeding what is known as the race-model prediction; Miller, 1982); the degree to which subjects' average multisensory response speed exceeds that of the race-model reflects their level of multisensory facilitation.

Materials and methods

Subjects

Twenty-seven subjects (22.7 ± 3.2 years, fifteen females, 24 right-handed) participated in the study. Subjects had no history of neurological disorders, and gave their informed consent to participate in the experiment.

Individual differences in multisensory facilitation

Redundant-target paradigm

Participants were seated in front of a PC screen (refresh rate 100 Hz) with their eyes 57 cm from the center of the screen. The stimuli were delivered using E-Prime software (Psychology Software Tools, Inc.). Participants pressed the space bar on a PC keyboard to start each trial. Trials began with a 1.5 second fixation cross followed by a variable random delay (500–1500 ms) preceding either a salient visual stimulus (a red "X", 12 cd/m^2 presented at fixation subtending 0.7° of visual angle, presented for 100 ms against a white background, 65 cd/m^2), a salient auditory stimulus (a 3500 Hz 64 dB tone presented for 100 ms via headphones), or both targets simultaneously in the multisensory condition. Catch trials were also included to discourage anticipatory responding. Participants were instructed to respond via E-prime's Serial Response box with the index finger of their dominant hand as soon as they perceived a stimulus. There were 4 blocks of 74 trials; each block began with 4 randomly selected trials that were treated as practice trials and excluded from analysis, followed by 20 trials in each condition (auditory, visual, and multisensory) plus 10 blank catch trials. As such, each participant generated 80 reaction times for each experimental condition.

Redundant-target paradigm analysis

As the multisensory condition presented participants with two targets compared to a single target presented in either the auditory or visual conditions, some facilitation of reaction times is attributable to two independent stimuli contributing to response generation and execution. To calculate the extent of multisensory benefit in addition to that which is predicted by the redundant nature of the multisensory condition, the independent race model was used as a comparison for multisensory benefits compared to the joint probability of responses from either sensory stimulus alone (Laurienti et al., 2006; Miller, 1982, 1986). The independent race model utilizes cumulative distribution functions (CDFs) to compare relative probabilities for each condition within 1 ms time windows and is constructed from the joint probabilities of the auditory alone and visual alone conditions [(Pr Auditory + Pr Visual) − (Pr Auditory ∗ Pr Visual)]. If the cumulative distribution function for the multisensory condition exceeds that which would be predicted by the race-model then the model is violated. These violations of the race model are thought to reflect true multisensory integration at the neural level (Laurienti et al., 2006; Miller, 1982). Accordingly, each subjects' data were divided into 1 ms reaction time bins, used to create individual CDFs for each condition (auditory, visual, and multisensory). Next, the race-model predictions at each time bin were computed for each subject based on the auditory and visual CDFs. Finally, average race-model predictions were calculated for each subject from the mean of the response times in the race-model CDFs for comparison against the raw multisensory response times. To confirm that subjects' multisensory response times were faster than those of the race model we compared the conditions using a two-tailed independent t-test. Multisensory facilitation for each participant was defined as the difference between mean race-model prediction minus the observed mean response to multisensory stimuli.

Whole-brain analysis

MRI acquisition

MR imaging was acquired on a General Electric 1.5 T Excite HDx MRI scanner. The T1-weighted anatomical dataset was acquired in the sagittal plane with a 3D MPRAGE sequence (TR = 10.73 ms, TE = 2.8 ms, TI = 1000 ms, FOV = 25 cm, flip angle = 8°, whole brain, slice thickness = 1 mm, 176 slices). DTI was acquired along 51 directions with a b-value of 1000 s/mm^2 (as well as one image with no diffusion weighting) with a voxel-size of $1.875 \times 1.875 \times 2.5$ mm^3 (TR = 13.2 s, TE = 80.4 ms, FOV = 24 cm, 47 oblique slices AC/PC aligned encompassing the whole brain, and 2.5 mm slice thickness).

DTI analysis

DTI measurements yield information about white matter coherence within a region. The most consistent measure derived from DTI is fractional anisotropy (FA), with higher values reflecting greater numbers of axons, reduced axonal diameter, reduced fiber crossing, and increased myelination (Johansen-Berg and Rushworth, 2009). FA was calculated using FMRIB Software Library (FSL; Smith et al., 2004) and we conducted a whole-brain voxel-wise statistical analysis of the FA data using TBSS (Tract-Based Spatial Statistics; Smith et al., 2007; part of FSL). First, FA images were created by fitting a tensor model to the raw diffusion data using FDT, and then brain-extracted using BET (Smith, 2002). All subjects' FA data were then aligned into a common space (MNI152) using the nonlinear registration tool FNIRT (Andersson et al., 2007) which uses a b-spline representation of the registration warp field (Rueckert et al., 1999). Next, the mean FA image was created and thinned to create a mean FA skeleton that represents the centers of all tracts common to the group. Each subject's aligned FA data were then projected onto this skeleton and the resulting data fed into voxel-wise cross-subject statistics. Voxel-wise permutation-based testing and inference was performed using Randomise in FSL (10,000 permutations) to test for a relationship between FA and multisensory facilitation. Statistical maps were family-wise error corrected using $p < .05$ using FSL's threshold-free cluster enhancement (TFCE) metric (Smith and Nichols, 2009), in which raw voxel-wise t-statistics are adjusted based on local spatial clusters, producing whole-brain corrected volumes. Raw data from significant regions are displayed in Fig. 2 where coefficients are reported as descriptive values only as these values were selected