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Steady-state responses in MEG demonstrate information integration within but not across the auditory and visual senses

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ABSTRACT

To form a unified percept of our environment, the human brain integrates information within and across the senses. This MEG study investigated interactions within and between sensory modalities using a frequency analysis of steady-state responses that are elicited time-locked to periodically modulated stimuli. Critically, in the frequency domain, interactions between sensory signals are indexed by crossmodulation terms (i.e. the sums and differences of the fundamental frequencies). The 3×2 factorial design, manipulated (1) modality: auditory, visual or audiovisual (2) steady-state modulation: the auditory and visual signals were modulated only in one sensory feature (e.g. visual gratings modulated in luminance at 6 Hz) or in two features (e.g. tones modulated in frequency at 40 Hz & amplitude at 0.2 Hz). This design enabled us to investigate crossmodulation frequencies that are elicited when two stimulus features are modulated concurrently (i) in one sensory modality or (ii) in auditory and visual modalities. In support of within-modality integration, we reliably identified crossmodulation frequencies when two stimulus features in one sensory modality were modulated at different frequencies. In contrast, no crossmodulation frequencies were identified when information needed to be combined from auditory and visual modalities. The absence of audiovisual crossmodulation frequencies suggests that the previously reported audiovisual interactions in primary sensory areas may mediate low level spatiotemporal coincidence detection that is prominent for stimulus transients but less relevant for sustained SSR responses. In conclusion, our results indicate that information in SSRs is integrated over multiple time scales within but not across sensory modalities at the primary cortical level.

Introduction

How does the human brain integrate information within and across sensory modalities to form a unified percept? This question has traditionally been addressed using transient stimuli, analysed in the time domain. Previous functional imaging studies have demonstrated integration of different types of visual information (e.g. form, motion or colour) in visual areas at multiple levels of the cortical hierarchy (Sarkheil et al., 2008; Seymour et al., 2010). Likewise, integration of information from multiple senses emerges in a widespread system encompassing subcortical, primary sensory and higher order association cortices (e.g.: Beauchamp et al., 2004; Calvert, 2001; Ghazanfar et al., 2008; Kayser et al., 2007; Lakatos et al., 2007; Noesselt et al., 2007, 2008; Noppeney et al., 2010; Sadaghiani et al., 2009; Schroeder and Foxe, 2002; van Atteveldt et al., 2004; Wallace et al., 1996; Werner and Noppeney, 2010a,b). Magnetoencephalography and electroencephalography (M/EEG) demonstrated that multisensory integration emerges very early at around 50–100 ms after stimulus onset. (Fort et al., 2002; Giard and Peronnet, 1999; Molholm et al., 2002; Raij et al., 2010; Schroger and Widmann, 1998; Talsma and Woldorff, 2005; Talsma et al., 2007; Teder-Salejarvi et al., 2002).

Identification of information integration and -interplay in the time and frequency domains—methodological considerations

In the time domain, integration of transient sensory stimuli is commonly determined by comparing the response to transient audiovisual (AV) stimuli to the summed responses for auditory (A) and visual (V) stimuli (i.e. $AV \neq A+V$). The rationale of this so-called super- or subadditivity criterion is that under the null-hypothesis of no audiovisual integration or interaction, the response to the audiovisual compound stimulus should be a linear combination (i.e. sum) of the responses to the two unisensory stimulus components when presented alone. However, despite its underlying rationale, this approach is often confounded by non-specific stimulus evoked processes such as arousal, anticipatory processes etc. (Goebel and van Atteveldt, 2009; Teder-Salejarvi et al., 2002). Since these general cognitive processes are elicited by each stimulus irrespective of its uni- or multisensory nature, they are counted twice

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for the sum of the two unisensory responses but only once for the bisensory response rendering the comparison unbalanced (Noppeney, 2011; Teder-Salejarvi et al., 2002).

Alternatively, integration of sensory signals within and across the senses can be studied in the frequency domain using steady-state responses (SSRs). The term 'SSR' refers to oscillatory brain activity that is elicited by and time-locked to periodically modulated sensory stimuli, such as amplitude modulated tones or luminance modulated visual stimuli (for a review on auditory SSRs see: Picton et al., 2003; for a review on visual SSRs see: Vialatte et al., 2010). Two sensory stimuli, modulated at frequencies f_1 and f_2, will evoke SSRs at fundamental and harmonic frequencies (i.e., n^*f_1 or m^*f_2, with m and n being any integer values). Critically, when perturbed concurrently with two periodically modulated sensory signals at two different frequencies, the brain can process and respond to them in two distinct ways: First, it may treat the two signals independently (Fig. 1A). In the time domain, we would then observe a linear combination (e.g. sum) of the two steady state responses that are individually elicited when the brain is presented with one signal alone. A frequency analysis of these steady state responses will then just reveal power at the fundamental and harmonic frequencies of the two component signals. Second, the brain may integrate the two sensory signals (Fig. 1B). In the time domain, integration is characterized by an interaction between the two sensory signals (i.e. a multiplication of the timecourses of the two component signals). Importantly, interactions of two sensory signals in the time-domain are expressed in terms of power at the crossmodulation frequencies (i.e. $n^*f_1 \pm m^*f_2$) in the frequency domain (Regan and Regan, 1988a, 1988b). Hence, crossmodulation frequencies provide an alternative way to identify integration of sensory signals within the human brain. For high frequency steady-state signals, multisensory integration can be much more clearly identified in the frequency- than in the time domain.

In addition to this 'true' signal integration, two signals may influence each others' processing in a non-specific fashion in the time-domain; for instance, one signal may increase the saliency of another signal via stimulus evoked arousal and related attentional mechanisms. These non-specific modulatory effects are reflected in an amplification (or suppression) of the amplitude of the fundamental and harmonic frequencies in the frequency domain and will not induce any crossmodulation frequency terms.

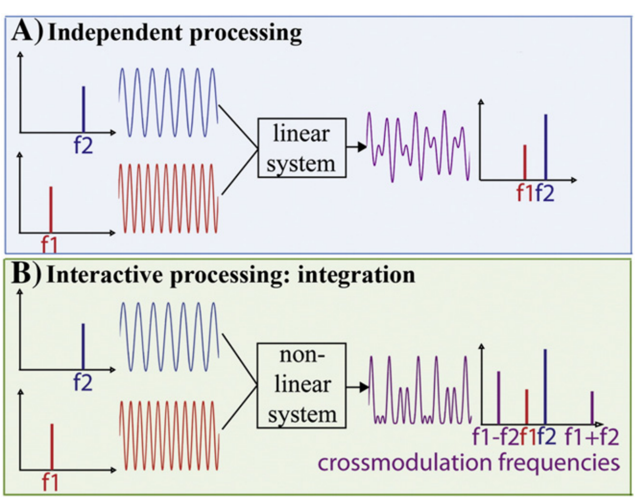

Fig. 1. Responses to two sinusoidal signals in the time and frequency domain: A, Independent processing: If two sinusoidal inputs at frequencies f_1 and f_2 are processed independently (= linear system), the output is a linear combination (e.g. sum) of the two component signals (with potential changes in phase and amplitude). Hence, in the frequency domain, power is observed only at frequencies f_1 and f_2. B, Interactive processing (= integration): If two sinusoidal inputs at frequencies f_1 and f_2 are processed interactively (= non-linear system), the output signal represents the multiplication of the two input signals. Hence, in the frequency domain, power is observed also at the crossmodulation frequencies, i.e. the sums and differences of the input frequencies ($f_1 \pm f_2$).

EEG and MEG evidence for information integration within and across the senses using SSRs

Over the past decade, SSR paradigms have accumulated evidence for signal integration within a single sensory modality on the basis of crossmodulation frequencies. Within the auditory modality, several MEG and EEG studies have demonstrated the emergence of crossmodulation frequencies when the auditory stimuli were amplitude modulated at two frequencies or simultaneously modulated in amplitude and frequency suggesting that information about a signal's amplitude and frequency interact along the auditory processing stream (Dimitrijevic et al., 2001; Ding and Simon, 2009; Draganova et al., 2002; Luo et al., 2006, 2007). Likewise, within the visual modality, crossmodulation frequencies indicated interactions of brain signals induced by multiple visual objects that were flickering at multiple different frequencies (Fuchs et al., 2008; Ratliff and Zemon, 1982; Regan and Regan, 1988a; Sutoyo and Srinivasan, 2009).

In contrast, there is only sparse evidence for non-linear interactions across modalities. In fact, to our knowledge only one study has identified interactions between auditory and visual steady-state signals based on audiovisual crossmodulation frequencies (Regan et al., 1995). Yet, this very early study did not report statistics, effect sizes or number of participants limiting the conclusions that can be drawn from it. Hence, a new more thorough study is needed to investigate whether crossmodulation frequencies emerge when the brain is perturbed with two steady state signals in two sensory modalities.

Relevance of SSRs in cognitive neuroscience

The characterization and identification of crossmodulation frequencies as a useful index for multisensory integration would open new research avenues for tracking the influence cognitive processes in multisensory integration. Thus, since SSRs and their crossmodulation frequencies are determined by the periodicity of the stimulating signal, they can be used to 'tag and track' multiple brain signals simultaneously. For instance, frequency tagging has been used to investigate the influence of awareness of several simultaneous signals during binocular rivalry. Presenting two distinct images that were flashed at two different frequencies to the two eyes demonstrated that the SSRs' magnitude elicited by each visual stimulus is modulated by its perceptual dominance (Cosmelli et al., 2004; Kamphuisen et al., 2008; Srinivasan, 2004; Sutoyo and Srinivasan, 2009; Tononi et al., 1998). Along those lines, crossmodulation frequencies would then offer a unique opportunity to study the effect of consciousness or attention on integration of specific signals or information within and across the senses non-invasively within the human brain. For instance, one could easily and very precisely address the question whether visual signals that the subject is not aware of can interact with auditory signals that the subject is aware of.

Experimental design and hypotheses

Previous studies have demonstrated that cue integration and interplay differs when the sensory cues are from the same or from different modalities (Duncan et al., 1997; Hillis et al., 2002). Most prominently, Hillis et al. (2002) demonstrated that single cue information is lost only for integration within but not across the senses.

This MEG study was designed to investigate information integration within and across the senses. Therefore, we employed a 3×2 factorial design, manipulating (1) modality: auditory, visual or audiovisual (2) temporal dynamics: single or double modulated. In the single modulated conditions, subjects were presented with an auditory signal modulated in frequency at 40 Hz and/or with a visual grating modulated in luminance at 6 Hz. In the double modulated conditions, the visual grating was additionally modulated at 0.2 Hz in size and the auditory tone at 0.2 (or 0.7) Hz in amplitude. This design enabled us to investigate crossmodulation frequencies that are elicited when two stimulus features are