

Short paper

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β -adrenergic modulation of oddball responses in humans

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Abstract

Detection of salient or motivationally significant stimuli is of adaptive importance. The neurophysiological correlates of this detection have been extensively studied in 'oddball' paradigms. Much theoretical data supports the role of noradrenergic systems in generating oddball responses. We combine psychopharmacology and functional neuroimaging to demonstrate modulation of neuronal responses to oddball nouns by the β -adrenergic antagonist propranolol. Critically, responses in regions implicated in oddball detection, namely right ventrolateral prefrontal cortex and temporoparietal junction (TPJ), were abolished by propranolol. Thus, oddball responses depend on modulatory adrenergic inputs, mediated via β -adrenergic receptors.

Background

Stimuli that violate the prevailing context, oddball stimuli, elicit a P3 event-related potential (ERP). A recent review [1] has highlighted the similarities between conditions evoking the P3 ERP and those evoking phasic responses in the Locus Coeruleus (LC), which provides the major ascending noradrenergic (NE) projection. Early studies combining animal intracranial recordings, lesion studies and human scalp-recorded ERPs provided evidence for the involvement of the LC-NE system in P3 generation [1,2]. The human electrophysiological response to oddball stimuli (P3) is dependent on the local and global probability of their occurrence [3,4]. In addition, P3s are elicited by motivationally significant stimuli, such as emotional stimuli [5]. In parallel, data from animal studies demonstrate increased phasic activity in LC neurones to novel, infrequent or threatening stimuli [6,7].

Thus, in the context of fMRI scanning, we presented subjects with two types of infrequent oddballs, perceptual and emotional, both known to elicit a P3 [1,3,5] and to

engage LC in animals [1,6,7]. To examine the role of the β -adrenergic system in oddball responses, 24 right-handed, native English speaking subjects were scanned in a double-blind placebo-controlled design with 12 subjects receiving a 40 mg dose of propranolol and 12 placebo. We scanned subjects while viewing nouns presented visually at a rate of one every 3 s. Subjects were presented with 38 lists of 14 nouns and were required to indicate with a push-button whether or not the first letter in the noun had an enclosed space (shallow encoding). For each list, 12 nouns were of the same semantic category, were emotionally neutral and presented in the same font, *i.e.* neutral control (C) nouns. A perceptual (P) oddball was presented in a novel font but was emotionally neutral and of the same semantic category as the neutral nouns. An emotional (E) oddball was aversive in content but of the same category and perceptually identical to neutral nouns. Thus, both oddball types had a frequency of 1 in 14 (global probability of occurrence 0.07). The first 5 nouns in each list were always neutral nouns, engendering low local probability of oddball occurrence.