Effect of parasympathetic stimulation on brain activity during emotional processing

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Introduction. Many physiological conditions, such as physical activity, mental stress and emotional stimuli, are associated with cardio-vascular modifications, detectable by carotid baroflex testing. Cardiovascular parameters such as heart rate, blood pressure and peripheral vascular resistances are continuously regulated by the sympathetic and parasympathetic branches of the autonomic nervous system (ANS), where afferent signals from peripheral sensors are processed at central level. So far, the anatomical location of autonomic receptors and the need of invasive procedures for physiological assessments, have made it difficult to study the central processing and control of ANS in humans. We recently developed an automated neck suction device, to induce a non-invasive, bilateral stimulation of the mechanoreceptors in the carotid sinus of humans. Such a device, used synchronously with functional Magnetic Resonance Imaging (fMRI), can be used to detect *in vivo* changes of brain activation as a function of the direct perturbation of ANS (1). In a previous investigation (2), we demonstrated that ANS perturbation impacts on brain activity at rest as well as during performance of a cognitive task. Aim of this fMRI study was to investigate the role of ANS (through parasympathetic perturbation) modulating the activation of the brain while engaged in emotion processing.

Methods. Thirteen right-handed healthy volunteers [all men; mean (SD) age=29.0 (6.4) years] underwent an fMRI investigation at 3T (Siemens Allegra system). An automated neck suction device, operated synchronously with fMRI acquisition, was used to induce bilateral stimulation of the mechanoreceptors in the carotid sinus (Fig.1). During fMRI experiments, the autonomic effect was controlled on a trial by trial basis by peripheral ECG recording. Efficacious (E) and non-efficacious (NE) stimuli were preliminary defined to identify the lowest suction pressure inducing peripheral autonomic response (-60 mmHg) and the highest pressure not inducing any autonomic response (-15 mmHg) (2). Subjects were unable to differentiate between efficacious and non-efficacious stimuli. Echo-planar (EPI) T2* sequence with BOLD contrast (TR=2080 ms, TE=30 ms, Matrix size=64 x 64,32 slices, thickness=2.5 mm) covering the whole brain was used for fMRI acquisitions. A Modified Driven Equilibrium Fourier Transform (MDEFT) scan (TR=1338 ms, TE=2.4 ms, Matrix = 256x 24, n. slices=176, thick. 1 mm) was also acquired and served as anatomical reference. While subjects performed an emotional paradigm, fMRI data were collected using an event-related design (Fig.2). Subjects were shown with four, randomly occurring, facial expressions (neutral, angry, sad and happy, duration = 2 sec, each) and asked to label faces' emotional valence (neutral vs emotionally loaded) by button pressing. Meanwhile, 40 efficacious and 40 non-efficacious neck suction stimuli (with a duration of 8 sec each and separated by 4 sec intervals to avoid mechanoreceptor accommodation) were randomly administered across the experiment (500 echo-planar imaging volumes, total duration= 32 min). Using SPM8, a within subjects ANOVA modeling the 8 conditions of the 2x4design (ANS stimulation: E/NE x Task: 4 different emotions) was employed to investigate the interaction between carotid stimulation and brain activation during emotion processing.
In all fMRI analyses, statistical threshold was set to p values cluster level corrected<0.005.

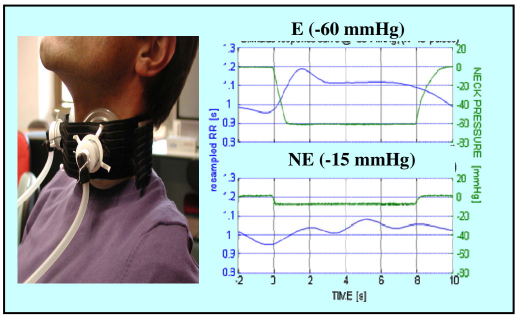
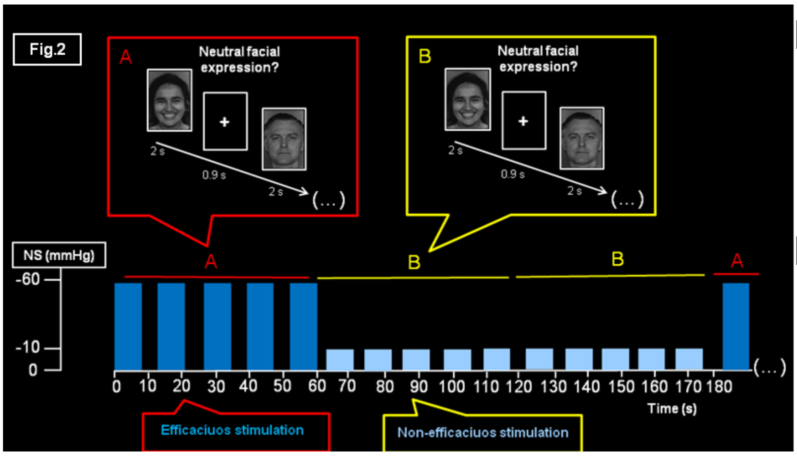


Fig. 1. Neck suction device (left); Efficacious (E) and non-efficacious trials (NE) as assessed by continuous ECG recording (right).



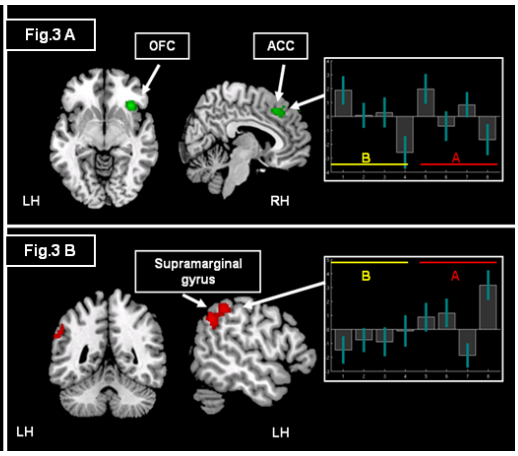


Fig 2. Emotional paradigm: subjects had to indicate by button pressing whether the face showed a neutral or an emotionally loaded facial expression. A=efficacious carotid stimulation; B=not-efficacious carotid stimulation. Fig 3. (A) Main effect of emotional conditions; (B) positive modulation of brain activation due to interaction between efficacious carotid stimulation and emotional processing. Plots on the right show the BOLD signal changes in the ACC (Fig.3A) and in the left supramarginal gyrus, for neutral, angry, sad, and happy expressions, respectively, in not-efficacious and efficacious stimulation.

Results. Behavioral results showed that subjects performed well in emotional discrimination, though longer reaction times (RTs) were required when confronted with neutral facial expressions within the efficacious (mean(SD)=1072(101.8)ms), versus non-efficacious carotid stimulation (mean(SD)=1114(98.5)ms). A similar trend, though not reaching full statistical significance (p=0.08), was observed for all emotional stimuli in the efficacious condition, as compared to the non-efficacious one. Overall, a significant emotional effect was observed within the right orbitofrontal cortex (OFC), extending to the insular cortex, and in the right anterior cingulate cortex (ACC) (see Fig.3A). A significant interaction between carotid stimulation and emotions (effect dominated by happy facial expressions) was observed in left supramarginal gyrus (parietal lobe) (see Fig.3B).

Discussion. Our results provide evidence that the autonomic perturbation of the parasympathetic system modulate both behavioral responses (increased RTs) and brain activity during emotional processing. This effect is similar to that previously observed in subjects performing a cognitive task (2). A possible interpretation relies on a compensatory mechanism (increased brain activity) allowing the maintenance of satisfactory task performance. The current study is relevant not only for neurophysiological speculations, but also to increase our pathophysiological understanding of many disorders (e.g., hypertension; Parkinson disease, stroke, etc) for which the implication of ANS seems to be crucial (3).

References

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