Commentary on Mather, M., Clewett, D., Sakaki, M., & Harley, C.W. (in press). Norepinephrine ignites local hot spots of neuronal excitation: How arousal amplifies selectivity in perception and memory. Behavioral and Brain Sciences.

BBS-D-15-00895_ Mather_ Critchley & Garfinkel

Bodily arousal differentially impacts stimulus processing and memory: norepinephrine in interoception

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Abstract: Bodily arousal modulates stimulus processing and memory, contributing to expression of emotional salience. The 'glutamate amplifies noradrenergic effects' (GANE) model proposed by Mather and colleagues can be extended to account for differential impact of interoceptive (notably cardiac afferent) signals on sensory processing. However, some emotion-specific effects, e.g. for fear, may further depend upon functional anatomical organisation of affect-related brain structures.

Mather and colleagues provide a compelling account of how stimulus processing is selectively prioritised through interaction of central noradrenaline (norepinephrine) and glutamate release. Their model explains discrepancies regarding the impact of central arousal upon aspects of emotion, perception and cognition. Thus, arousal sometimes enhances the processing of salient stimuli at the expense of neutral or contextual information, while, in other circumstances, facilitates the processing of neutral stimuli and peripheral information. States of physiological arousal in the body evoked similar psychological effects, suggesting a common mechanism.

In presenting the GANE model, Mather and colleagues refer to studies of skydiving, threat response, processing of emotionally salient (alarming, exciting or disturbing) stimuli, and loud noises. States of running or even unanaesthetized wakefulness in animal

experiments are also considered. Arousal is proposed to be a common feature, operationally defined by noradrenaline release from the locus coeruleus. Such states of emotional and behavioural arousal are characterized by physiological changes in the periphery. Within the cardiovascular system, arousal is an embodied action-ready state: heart rate and blood pressure increases are brought about by enhanced sympathetic drive, parasympathetic withdrawal, and baroreflex inhibition. Bodily arousal feeds back to influence perception, cognition and emotion and cardiac and arterial baroreceptors, which fire cyclically on each heartbeat, are a major source of these interoceptive influences.

Relevant to the GANE model, brainstem noradrenergic nuclei including locus coeruleus are sensitive to afferent interoceptive signals concerning bodily arousal. These nuclei support both descending control of autonomic function (A1 and A2 groups within medulla) and ascending control of alertness (e.g. A4 and A6 groups, including nucleus coeruleus). Correspondingly, they react to behavioural challenges by increasing sympathetic drive to the body, and by increasing noradrenaline release in the brain via ascending projections from locus coeruleus to hypothalamus, thalamus and forebrain (cortex and amygdala). Cardiovascular arousal is conveyed to the brainstem in a pulsatile manner by vagus nerve and glossopharyngeal afferents carrying the phasic discharge of baroreceptors that encode the timing and strength of individual heartbeats. The firing of locus coeruleus neurons is regulated by baroreceptor firing (Svensson 1987), resulting in cyclical inhibition of neural activity at late diastole (Elam et al., 1984; 1986; Morilak et al., 1986; Murase et al., 1994). Cardiac afferents modulate activity of nearby brainstem reticular nuclei (Lambertz and Langhorst, 1995) and even the amygdala, where the effect is also influenced by state of alertness (Lambertz et al., 1995). Vagus nerve stimulation enhances release of noradrenaline within the amygdala (Hassert et al., 2004).

Fine-grained signals concerning bodily arousal can thus influence perception and cognition via brain regions governing alertness and central arousal: Baroreceptor signals occurring with each heartbeat impact stimulus detection (Park et al., 2014; Garfinkel et al., 2014), memory (Garfinkel et al., 2013) and emotional responses (Garfinkel et al., 2014). Yet when it comes to processing emotional information these physiological

arousal signals evoke selective effects. While cardiac systole inhibits the processing of pain stimuli (Gray et al., 2009), and attenuates the encoding into memory of words irrespective of valence (Garfinkel et al,. 2013), the processing of fear stimuli is enhanced (Garfinkel at al,. 2014).

Fig.1

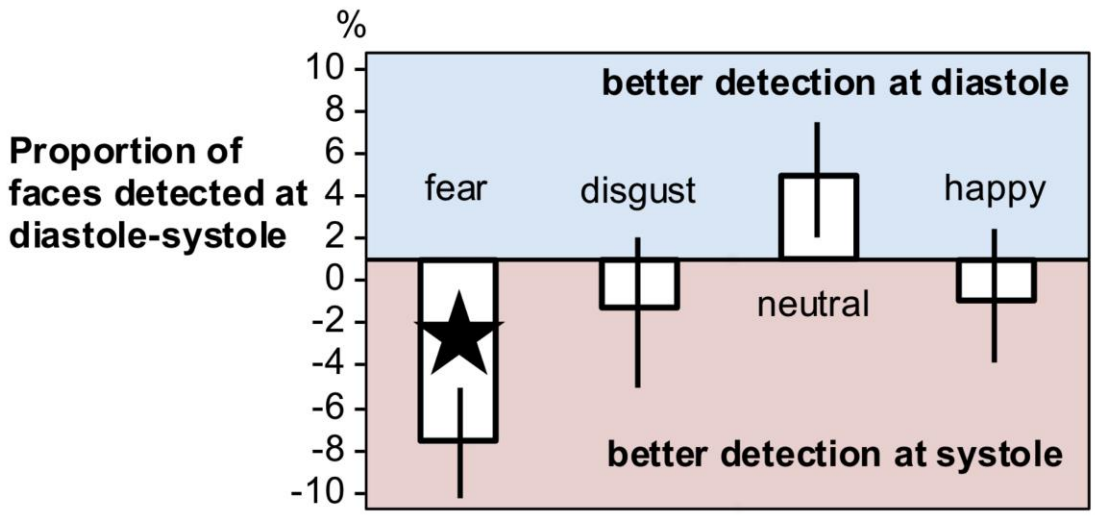

Figure 1: Cardiac modulation of emotional face detection
An attentional blink paradigm presents two target stimuli within a stream of masking distractors, pushing attentional resources to the limit for the perception of the second target stimulus presented during an 'attentional blink' (around 300ms after the first target). Detection of this second target is much better if the stimulus is emotional, reflecting intrinsic affective salience, and blocked by central β-adrenoreceptor antagonists. The presentation of the second target (here faces) to coincide with cardiac systole (when arterial baroreceptors are active) compared to diastole (between these cardiac afferent signals) enhances the detection of fear stimuli, but has no effect on other emotion stimuli. Adapted from Garfinkel et al. (2014).

The emotional attentional blink paradigm illustrates the prioritised processing of emotional stimuli. At the limit of perceptual awareness, emotional stimuli can overcome a perceptual block, the attentional blink effect, breaking through to awareness by capturing attention. This index of emotional salience is adrenergically mediated, being enhanced by administration of the noradrenergic reuptake inhibitor reboxetine and abolished by β-adrenoreceptor blockade with propanolol (De Martino et al., 2007). This prioritized processing of emotional stimuli also depends on the functional integrity of the amygdala (Anderson and Phelps, 2001). The additional impact of afferent signals concerning cardiovascular arousal on early affective processing can be measured by timing the presentation of target stimuli to distinct phases (systole and diastole) of the cardiac cycle. Here the outstanding observation is a selective cardiac enhancement of fear processing, manifest in the emotional attentional blink task as better detection of fearful faces presented at systole, compared to diastole. This cardiac cycle effect is not seen for disgusted, happy or neutral faces (although there is a trend for neutral faces to be better detected at diastole) (Fig 1; Garfinkel et al., 2014). Moreover at systole, increased amygdala activity to fear compared to neutral stimuli, predicts increased subjective rating of fear intensity and underscores the selective contribution of cardiac afferent signals to amygdala-mediated processing of salient stimuli (Garfinkel et al., 2014).

Thus interoceptive signals concerning cardiovascular arousal can both increase (e.g. fear) and decrease (e.g. words, pain) stimulus processing. This is differentiated by the type of task or the emotion class of the stimulus. While the GANE model explains much of the differential impact of cardiac afferent signals on sensory processing, it only partially accounts for emotion specificity and (task-related) behavioural demand that can further differentiate and guide the directionality of arousal effects. Encompassing physiological state within the concept of arousal reveals levels of interaction and a selective impact of the arousal signal itself. The glutamate component of the GANE model takes into account prioritisation of certain stimulus types, yet it underplays the degree to which this specificity must also depend on the differential anatomical organisation of critical brain structures supporting emotion-related response repertoires.

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