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NEURAL MECHANISMS MEDIATING ASSOCIATION OF SYMPATHETIC ACTIVITY AND EXPLORATION IN DECISION-MAKING

H. OHIRA,[a*] M. MATSUNAGA,[b] H. MURAKAMI,[a,c] T. OSUMI,[a,d] S. FUKUYAMA,[e] J. SHINODA[e] AND J. YAMADA[e]

[a] *Department of Psychology, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8601, Japan*

[b] *Division of Cerebral Integration, Department of Cerebral Research, National Institute for Physiological Sciences, Okazaki 444-8585, Japan*

[c] *Department of Clinical Neuroimaging, Integrative Brain Imaging Center, National Center of Neurology and Psychiatry, Tokyo 187-8551, Japan*

[d] *Department of Psychology, Keio University, Tokyo 108-8345, Japan*

[e] *Kizawa Memorial Hospital, Chubu Ryogo Center, 590 Shimofurui, Furui-cho, Minokamo 505-8503, Japan*

Abstract—The somatic marker hypothesis asserts that decision-making can be guided by feedback of bodily states to the brain. In line with this hypothesis, the present study tested whether sympathetic activity shows an association with a tonic dimension of decision-making, exploratory tendency represented by entropy in information theory, and further examined the neural mechanisms of the association. Twenty participants performed a stochastic reversal learning task that required decision-making in an unstable and uncertain situation. Regional cerebral blood flow was evaluated using ^{15}O-water positron emission tomography (PET), and cardiovascular indices and concentrations of catecholamine in peripheral blood were also measured, during the task. In reversal learning, increased epinephrine during the task positively correlated with larger entropy, indicating a greater tendency for exploration in decision-making. The increase of epinephrine also correlated with brain activity revealed by PET in the somatosensory cortices, anterior insula, dorsal anterior cingulate cortex, and the dorsal pons. This result is consistent with previously reported brain matrixes of representation of bodily states and interoception. In addition, activity of the anterior insula specifically correlated with entropy, suggesting possible mediation of this brain region between peripheral sympathetic arousal and exploration in decision-making. These findings shed a new light about a role of bodily states in decision-making and underlying neural mechanisms.

Key words: decision-making, somatic marker hypothesis, exploration, entropy, positron emission tomography (PET), sympathetic arousal.

INTRODUCTION

The somatic marker hypothesis asserts that decision-making is guided by feedback of bodily states to the brain (Damasio, 1994, 1999). Among the various signals in the body, activity of the sympathetic nervous system is considered particularly important in generating and processing somatic markers that can influence decision-making (Bechara et al., 2000; Bechara and Damasio, 2005; Critchley, 2009). This notion has been verified by electrophysiological studies measuring skin conductance responses and levels (Denburg et al., 2006; Yen et al., 2012), a pharmacological study using beta-adrenergic receptor blockers (Rogers et al., 2004), neuropsychological studies of patients with damages to the amygdala and ventromedial prefrontal cortex (VMPFC) (Bechara et al., 1999; Gläscher et al., 2012), and clinical studies of pathological gamblers (Labudda et al., 2007) and patients with attention-deficit/hyperactivity disorder (Bubier and Drabick, 2008), who show attenuated sympathetic activity. Nevertheless, the specific role of the sympathetic nervous system in the somatic marker hypothesis remains controversial (Dunn et al., 2006), largely because sympathetic responses are too late to influence on-line trial-by-trial decision-making (Nieuwenhuis et al., 2010).

Considering kinetics of sympathetic nerves, we suggest that sympathetic activity might affect tonic states of decision-making that are maintained within relatively longer time periods, rather than a phasic and local moment of a specific decision. In particular, we suggest a well-known major dimension of decision-making, exploitation-exploration, might be a candidate for those tonic states. Exploitation is a strategy used by an organism to provide an option that is associated with the highest possibility of reward. By contrast, exploration involves deviations from this strict policy to seek for new and previously unexplored options. The balance between exploitation and exploration is critical for the survival of animals and humans, as exploitation is the

*Corresponding author. Tel/fax: +81-52-789-2220.
E-mail addresses: ohira@lit.nagoya-u.ac.jp (H. Ohira), matsunag@aichi-med-u.ac.jp (M. Matsunaga), hirokimura66@hotmail.com (H. Murakami), takahirosumi@hotmail.co.jp (T. Osumi), s-fuku@jasmine.ocn.ne.jp (S. Fukuyama), junshino@joy.ocn.ne.jp (J. Shinoda), yamada@kizawa-memorial-hospital.jp (J. Yamada).

Abbreviations: ACC, anterior cingulate cortex; CO, cardiac output; fMRI, functional magnetic resonance imaging; HF, high frequency of heart rate variability; HR, heart rate; HRV, heart rate variability; JPY, Japanese Yen; LC, locus coeruleus; LF, low frequency component of heart rate variability; M, mean; MBP, mean blood pressure; MPFC, medial prefrontal cortex; NTS, nucleus tractus solitaries; OFC, orbitofrontal cortex; PET, positron emission tomography; rCBF, regional cerebral blood flow; SD, standard deviations; SPM, statistical parametric map; TPR, total peripheral resistance.

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most adaptive strategy where the environment is stable and contingencies between options and outcomes are fixed, while exploration is more adaptive where the environment is unstable and contingencies between options and outcomes are uncertain. In this context, exploration is linked to increased response variability (Stocco, 2012). In recent studies on decision-making (Lee et al., 2004; Seo and Lee, 2008; Baek et al., 2013; Takahashi et al., 2013), the degree of response variability is represented by a concept in information theory, termed entropy (Shannon, 1948). Furthermore, brain regions such as the cingulate cortex and pre-supplementary motor area (Goñi et al., 2011) and neurotransmitters such as norepinephrine (Aston-Jones and Cohen, 2005; Nieuwenhuis et al., 2010), dopamine (Humphries et al., 2012), and acetylcholine (Stocco, 2012), have been reported to be involved in response variability in decision-making reflected by entropy.

Sympathetic activity can influence activity of the brain and central neurotransmitters, in part via visceral ascending routes in which signals of peripheral hormones such as epinephrine are conveyed into the brain though the afferent vagus nerve, nucleus tractus solitaries (NTS), locus coeruleus (LC)-norepinephrine system, the basal forebrain cholinergic system, amygdala, and insula (Berntson et al., 2003, 2011). Specifically, intraperitoneal administration of epinephrine was reported to enhance the auditory-evoked brain potential as an index of cerebral processing in rats (Knox et al., 2004) and enhance memory performance in rats (Williams and McGaugh, 1993; Cahill and McGaugh, 1998; Clayton and Williams, 2000) and humans (Cahill and Alkire, 2003). These phenomena caused by peripheral epinephrine are mediated by NTS and LC activity (Berntson et al., 2003). Once elevated sympathetic activity and increased peripheral epinephrine enhance NTS and LC activity, it is plausible that increased release of epinephrine may act as a somatic marker to modulate behavioral exploration in decision-making (Aston-Jones and Cohen, 2005; Nieuwenhuis et al., 2010). In turn, these effects of sympathetic activity may become more dominant in an unstable and uncertain situation, where exploration is required. Thus, the primary goal of this study was to test this hypothesis.

Furthermore, we aimed to elucidate the neural basis mediating the possible association between sympathetic activity and exploration in decision-making. In this context, our primary brain region of interest was the anterior portion of the insula. The insula receives visceral and somatosensory inputs, and is thought to play a significant role in integrated representation of bodily states and emergence of interoception (Craig, 2009; Critchley, 2009). The insula also has reciprocal interconnections with the prefrontal cortex and limbic regions such as the amygdala and anterior cingulate cortex (ACC) (Augustine, 1996), and thus plays a role in multiple emotional and cognitive processes, including decision-making. With respect to decision-making, the insula was reported to be involved in anticipation and delivery of reward and loss (Rolls et al., 2008; Chua et al., 2009; Liu et al., 2011), recognition and processing of risk (Preuschoff et al., 2006; Mohr et al., 2010; Symmonds et al., 2011; Rudorf et al., 2012), detection of salient events (Metereau and Dreher, 2013), and switching functions of neural networks to allocate attention and working memory (Menon and Uddin, 2010). Given this strategic location of the insula, we hypothesized that this brain region might modulate behavioral exploration, at least in part, via the influence of peripheral sympathetic activity.

To examine these hypotheses, we simultaneously measured regional cerebral blood flow (rCBF) with ^{15}O-positron emission tomography (PET) and catecholamine (epinephrine and norepinephrine) in blood, and cardiovascular activity, during a version of stochastic reversal learning that requires cognitive and behavioral flexibility. This task was composed of two stages, initial learning and reversal learning. During the initial learning stage, participants learn the contingency between stimuli and outcomes, while, in the following reversal learning stage, the option-outcome contingency becomes inverted, without explicit instruction. One merit of this paradigm is that the brain regions responsible for performance in this task are known: the medial prefrontal cortex (MPFC), orbitofrontal cortex (OFC), and several striatal nuclei (Cools et al., 2002; Remijnse et al., 2005, 2006; Xue et al., 2008; Jocham et al., 2009; for a review, Kehagia et al., 2010). In addition, this method provides high test–retest reliability for both behavioral performance and brain activation (Freyer et al., 2009). Participant's exploratory tendencies were estimated by calculating entropy on the basis of their decisions, as well as conventional indices of decision-making, response bias and reward acquisition. Introduction of reversal between options and outcomes and their stochastic nature will implicitly inform participants of unstable and uncertain characteristics of the task structure. Thus, we hypothesized that exploration reflected by entropy would be enhanced and the association between sympathetic activity and exploration would be strengthened in the stage of reversal learning. Brain regions showing correlations between their activation and sympathetic activity, and entropy in decision-making, were explored.

EXPERIMENTAL PROCEDURE

Participants

Twenty right-handed males who were healthy and were not taking any medications were recruited (mean (*M*) ± standard deviations (*SD*); 33.95 ± 7.09 years). The participants reported that they had no past history of psychiatric or neurological illness, and gave written informed consent in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of the Kizawa Memorial Hospital. Data from one participant were excluded from analyses because of technical problems in measurements and recording.

Task and experimental procedure

Participants performed eight blocks of a task: three blocks of an initial learning condition, three blocks of a reversal