Arousal, exploration and the locus coeruleus-norepinephrine system

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Chapter 8

Summary

The studies described in this thesis address a range of topics related to arousal, exploration, temporal attention, and the locus coeruleus-norepinephrine (LC-NE) system.

Chapters 2 and 3 reported two studies that investigated the central tenets of the adaptive gain theory of LC function in human participants. According to the adaptive gain theory, the LC-NE system is critical for optimizing behavioral performance by regulating the balance between exploitative and exploratory control states. However, crucial empirical tests of this theory in humans have been lacking. Recent studies have suggested that, under controlled circumstances, pupil diameter provides an indirect index of LC activity. Inspired by this evidence, we used pupillometry to examine whether the relationship between pupil diameter, control state and task-related utility is consistent with the assumptions of the adaptive gain theory (Chapter 2). The results from this study provide indirect evidence for the idea that LC mode regulates the exploration-exploitation trade-off, and that transitions between LC modes are driven by assessments of task-related utility.

To provide a more direct test of the adaptive gain theory's assumption that the tonic LC mode promotes an exploratory control state, we investigated the effects of a pharmacological manipulation of the LC-NE system on measures of exploration and task (dis)engagement (Chapter 3). Contrary to predictions of the adaptive gain theory, we found no evidence that the elevated NE levels induced by our pharmacological manipulation were associated with increased task disengagement or exploratory behavior in our experimental tasks. In contrast to the results reported in Chapter 2, these results suggest that the LC-NE system may not be involved in the regulation of the exploration-exploitation trade-off in humans, at least not within the context of a single task. These results leave open the possibility that the LC-NE system is involved in random exploration exceeding the current task context. Possible reasons for the discrepancy between the conclusions of our pupillometry study and our pharmacological study are that (i) the difference in baseline pupil size preceding exploitative versus exploratory choices did reflect something else than a difference in tonic LC activity; (ii) our pharmacological manipulation did not produce a net increase in tonic NE levels; (iii) our pharmacological manipulation had unexpected effects on the phasic LC response or on other neuromodulatory systems. These and other possible explanations remain to be explored in future studies.

Chapter 4 reported a study on neurocognitive function in patients with dopamine-β-hydroxylase (DβH) deficiency, a rare genetic disorder characterized by the absence of NE in the peripheral and the central nervous system. NE levels in DβH-deficient patients can be restored by the administration of a synthetic precursor of NE. Informal clinical observations suggest that DβH-deficient patients do not have obvious cognitive impairments, but systematic studies on neurocognitive function in DβH deficiency have been lacking. We tested five DβH-deficient patients and a healthy control group on a comprehensive neurocognitive task battery; the patients were tested once on and once off medication. We found that the patients' neurocognitive performance was largely spared, even when they were off medication, which is striking given the

important role of NE in normal cognition. The results from this study suggest that other neuromodulators have taken over the function of NE in the brains of these patients.

Exploratory behavior in both animals and humans is often driven by curiosity. Chapter 5 reported a study on the neural correlates of human perceptual curiosity, using functional magnetic resonance imaging (fMRI). We found that the induction of perceptual curiosity, through the presentation of ambiguous visual input, activated brain regions sensitive to conflict and arousal. The relief of curiosity, through visual disambiguation, activated regions of the striatum that are involved in reward processing. In addition, the relief of curiosity was associated with increased hippocampal activation and enhanced incidental memory. Our results suggest that perceptual curiosity evoked by ambiguous visual input is an aversive condition. In addition, our results suggest that termination of this condition is rewarding and promotes learning. The results from this study provide compelling neurobiological evidence for Berlyne's (1954, 1966) classic psychological theory of curiosity.

Chapter 6 and 7 reported several experiments investigating the effects of accessory stimuli (Chapter 6) and temporal preparation (Chapter 7) on information processing, using scalp electrophysiology and sequential-sampling models of decision making. The results from these experiments suggest that both accessory stimulation and temporal preparation affect nondecision processes (stimulus encoding and/or response preparation) but have little effect on the two main components of the decision process: decision-threshold setting and the rate of evidence accumulation.

Attention and decision making are essential components of cognition that are involved in almost all aspects of behavior. In the last decades, reward-based decision making and spatial attention have been topics of extensive investigation among cognitive neuroscientists. However, other less specific dimensions of decision making and attention, such as arousal, exploration and temporal attention, have received less recognition and interest. The research described in this thesis aims to contribute to a better understanding of these constructs. Taken together, the studies reported in this thesis suggest that arousal, exploration and temporal attention are closely related, which is likely due to a shared neural basis.