Ordo ab chaos

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Summary

From pre-Socratic to modern philosophers, many have debated about the role of the *sense of time* in our experience of the world. What is *time*, and how do we use it to structure our perception? Drawing a tight link between the use of *time* in physics and natural sciences and the *sense of time* in cognitive neuroscience, the research summarized in this thesis aims at understanding how our brain generates a *sense of time*, and how we employ *time* to coordinate perception and action.

With a series of basic, comparative and translational studies reported in Chapters 2 to 4, I discuss that neurophysiological activity in the brain may provide an exquisite sense of time: neural waves represent an internal ticking clock, generating an endogenous representation of time and able to keep track of the precise *timing* of external events. Thus, we discussed that neural waves at multiple time-scales (e.g., delta (δ; 1-4Hz) and beta (β; 12-20Hz)) encode the *when* of incoming sensory information, and predictively track the *when* of future sensory inputs by generating *predictions*. These expectations are formed by *detecting* temporal *regularities* in environmental stimuli: leveraging on learnt temporal *patterns,* neural waves prepare the organism to process the *next* stimuli, thus optimizing sensory processing, perception, and (re-)action. These so-called *dynamics of attending* are thought to play a fundamental role in our capacities to act and adapt in a dynamically changing environment. They rely on an extended cortico-subcortical network involving basal ganglia (BG) and cerebellum (CE), and are putatively linked to the development of higher order cognitive capacities in humans, such as music and speech.

Thus, in our research we asked: (i) do our close ancestors, macaque monkeys, process auditory temporal regularities similarly to humans? Next, (ii) can lesions in the BG and CE impact the capacities to encode, produce and synchronize with rhythms in the sensory environment?

In Chapter 2, we identified an adaptive δ-β neural code sampling the sensory environment by encoding, tracking and predicting basic auditory rhythms. In Chapter 3 we argued that striking similarities between humans and nonhuman animals (macaque monkeys) support the notion of shared basic rhythm cognition, challenging existing evolutionary hypotheses on the evolution of language and music in humans. Finally, in Chapter 4 we demonstrated that the δ-band neural computations employed to precisely encode the timing of auditory input are altered in BG and CE patients, who showed difficulties in processing the precise *when,* as well as in tracking and predicting upcoming sensory inputs. These difficulties were further reflected in behavioral data, showing impaired ability of these patients to produce and synchronize their own behavior (tapping) to externally presented rhythms.

Expanding this research line, in the second part of the thesis (Chapter 5) we discussed that the *sense of time* is further influenced by bodily physiological activity: heartbeat, respiration and gastrointestinal rhythms

provide yet another level of *time* in the body, next to brain activity. We thus, argued, that these complementary rhythms in the body and the brain may form a dynamic system of coupling oscillators, influencing sensory processing, perception and action. Our formulation of the Body-Brain Dynamic System (BBDS) incorporates the variability of human behavior, and explains it in function of inter-individual variabilities in physiological rhythms, as well as in body-brain coupling states. The BBDS opens to a plethora of new investigations on neurocognitive functioning in healthy and clinical populations: what is the modulatory influence of (altered) cardiovascular, respiratory and gastrointestinal activity on brain functioning and cognition? Some of the hypotheses formulated in the framework in Chapter 5 are tested in our new ongoing research line, in which we directly assess the link between body-brain rhythms, their dynamic coupling, and individual behavioral rhythms (e.g., rhythm of walking, speaking, listening preferences).

Altogether, the results presented in Chapters 2-4 speak in favor of a fundamental role of δ-β neural waves in rhythm processing, strengthen the notion that there exist similarities between human and nonhuman animal's rhythm cognition, and confirm the causal role of BG and CE structures in rhythm processing and production.

The second research line introduced in Chapter 5, suggests to expand the horizon of cognitive neuroscience research so to include body physiology and body-brain interactions in the equation. As such, our novel framework argues in favor of a fundamental shift in how we study human brain and behavior: holistic, systematic, individual assessments are critical to advance our understanding of human cognition, in health and pathology.

To conclude, we discussed that time generation and time processing, in the body and the brain, are fundamental to structure cognition: the *sense of time* allows to coherently process multisensory information, coordinating perception and (re-)action. *Ordo ab chaos*.