Where's the example?

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Abstract: Lewis has missed an excellent opportunity to concisely demonstrate that a dynamical system can provide a bridge between emotion theory and neurobiology.

Lewis proposes constructing a bridge between emotion theory and neurobiology by using concepts from dynamic systems (DSs). Our major criticism is that the author has missed an excellent opportunity to concisely demonstrate what he has tried to explain with pages of words. First, we observe that nowhere in this target article are there any examples of a DS. Second, the diagrams given are very schematic, usually consisting of several boxes with lines and arrows connecting them in all possible manners and directions, and yet they lack the specificity needed to construct a DS. Thus these diagrams do not clarify, but rather simply say that "anything is possible." Third, there are no quantitative comparisons given anywhere, so the mathematically oriented reader is left without any means for judging the validity of the ideas presented.

This target article would have been much improved by the inclusion of just one example of a DS. Ideally, the exemplary DS would model some simple feature of emotion theory, which could then be bridged to some feature of neurobiology. Nothing close to this is given in the article. Instead of demonstrating with an example, the author has spent his effort, and pages, attempting to convince others of the workability of his idea. This may be convincing to readers with a strong neuropsychological background, but practitioners of DS would be, like us, mathematically oriented and would find a quantitative example much more convincing.

Although we are willing to believe that it may be possible to use DS to bridge emotion theory and neurobiology, until a specific DS is proposed and is validated as at least somewhat workable by comparison with observations in the real world, there is no assurance that the proposed theory is useful. See Perlovsky (2002) for an example of a step in this direction.

Anything can be modeled by the use of mathematics. Mathematics is arguably nothing more than the use and manipulation of symbols to test ideas and hypotheses. This target article proposes a hypothesis. Any hypothesis could be tested or demonstrated by mathematics. What is needed is demonstration and verification of the hypothesis by comparison with observation.

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On the relationship between rhythmic firing in the supramammillary nucleus and limbic theta rhythm

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Abstract: Lewis emphasizes the role of theta oscillations in emergent coupling among neural subsystems during emotionally relevant tasks or situations. Here I present some recent data on the relationship of rhythmic neuronal discharge in the supramammillary nucleus and the large-scale theta oscillations in the limbic system which provide support to many of his ideas regarding vertical integration in dynamic systems.

There are two structures in the posterior hypothalamus which exhibit theta rhythmic neuronal discharge. The mammillary body nuclei, which only receive descending input from the hippocampal formation, have been characterized in detail in Lewis's target article. I will add some recent observations regarding the other, the theta-generating diencephalic structure, which has direct bidirectional connections with the septohippocampal system. As mentioned in the target article, in rats anesthetized with urethane the majority of neurons in the supramammillary nucleus (SUM) fire rhythmically in synchrony with hippocampal theta rhythm (Kirk & McNaughton 1991; Kocsis & Vertes 1994). As these neurons project to the septum and hippocampus it is generally assumed that their role is to mediate ascending activation leading to hippocampal theta rhythm. The connections between SUM and the septohippocampal system are reciprocal, however, and there is strong evidence that both septum and SUM are capable of generating theta rhythmic activity. It has been shown that theta rhythm may persist in the septum-hippocampus after large lesions in the posterior hypothalamus (Thinschmidt et al. 1995), as well as in the SUM after pharmacological suppression of the septal generator (Kirk et al. 1996).

Activation (electrical or pharmacological stimulation) of the SUM always results in hippocampal synchronization, but SUM neurons may also be synchronized with hippocampal theta when the rhythm does not originate from the SUM. Few data exist regarding the natural behaviors in which SUM activation significantly contributes to limbic theta rhythm. Pan and McNaughton (2002) used a variety of experimental paradigms to study the effect of partial lesions of the SUM on different behaviors in defensive and learning tasks, and tested whether these effects can be related to the known role of SUM in frequency modulation of the theta rhythm (Kirk & McNaughton 1993). They found that SUM lesion and the resulting small decrease in theta frequency did not change the performance of rats in a spatial learning task (water maze), as hippocampal damage would, but the pattern of changes in motivated-emotional behavior (hyperactivity in defensive and operant tasks) appeared, in general, to be similar to those after hippocampal lesions (Pan & McNaughton 2002). This indicates that although SUM discharge may be generally synchronized with hippocampal oscillations during all theta states, including, for example, moving around in the water maze, its functional contribution to limbic theta is limited to emotional behaviors.

The dynamics of coupling between rhythmic discharge in the SUM and the "global" theta rhythm represented by hippocampal field potentials was further examined in urethane anesthetized rats by comparing the direction of influence during theta states occurring spontaneously and evoked by sensory stimulation (Kaminski & Kocsis 2003). The direction of the theta drive between the two structures and its temporal dynamics was analyzed using the method of directed transfer function (DTF). This measure is derived from short-time spectral estimates based on an autoregressive model (Kaminski & Blinowska 1991) and it provides information about the direction of propagation of neuronal activity and its spectral content. It makes use of the asymmetry of the transfer matrix which describes connections between channels. A larger DTF between two signals in one direction as compared with that for the opposite direction indicates an influence of one structure on the other. We found that DTF values were consistently higher for the descending than the ascending direction in the majority of SUM neurons. Significant SUM-to-hippocampus DTF at theta frequency only appeared for short periods, on the background of a dominant descending drive. Only in a few experiments was the ascending SUM-to-hippocampus theta drive found to dominate the relationship between the two structures, but the asymmetry in these cases was also limited to episodes of sensory stimulation (i.e., tail pinch).

During theta states the oscillations in the two structures are coupled so that each SUM neuron fires at a certain phase relative to the hippocampal rhythm. The phase is different for different SUM neurons but when single cells are recorded over several theta episodes their phase is always the same (Kocsis & Vertes 1997). Thus, every time the two oscillators get engaged – that is, switch from non-coherent activity to coherent rhythm – they do so at a certain phase even if the frequency of theta shows significant variations (between 3.7 and 5.6 Hz in our experiments). But what happens if a change in frequency occurs when the two structures are already connected? We examined this question using segments of recordings in which theta rhythmic activity was elicited in anesthetized rats by tail pinch but in which the rhythm persisted after cessation of the sensory stimulus (Kocsis 2000). It is important to note that during such episodes the frequency of theta decreased without an intervening non-theta state. We found that the firing of many SUM neurons followed the hippocampal theta waves with a constant delay (rather than a constant phase), suggesting that during deceleration associated with a shift from sensory elicited theta to spontaneous theta, this group of neurons was driven by a descending input, most likely from the medial septum.

These findings indicate that SUM is only driving field oscillations in the hippocampus during epochs of sensory elicited theta rhythm, under urethane anesthesia, whereas spontaneous theta in SUM is controlled by descending input from the septohippocampal system. This suggests that although during certain states the rhythmically firing SUM neurons work to accelerate the septal theta oscillator, thereby adding to "global" synchronization of the limbic system, in other states (such as after cessation of the stimulus in these experiments) they surrender to the driving of the slower rhythm of septal origin and assume positions entrained by the superordinate oscillatory network.

Emotional-cognitive integration, the self, and cortical midline structures

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Abstract: Lewis discusses the dynamic mechanisms of emotional-cognitive integration. I argue that he neglects the self and its neural correlate. The self can be characterized as an emotional-cognitive unity, which may be accounted for by the interplay between anterior and posterior medial cortical regions. I propose that these regions form an anatomical, physiological, and psychological unity, the cortical midline structures (CMSs).

Lewis discusses the dynamic mechanisms of emotional-cognitive integration and relates them nicely to various neural networks. These include the orbitomedial prefrontal cortex (OMPFC), the anterior cingulate (AC), the dorsolateral prefrontal cortex (DLPFC), and various subcortical regions (hippocampus, amygdala, nucleus accumbens, brain stem/basal forebrain, ventral tegmental area, ventral pallidum). Though quite exhaustive, his overview neglects two important points. First, he neglects what results from emotional-cognitive integration. I argue that the self as emotional-cognitive unity results from the integration between emotional and cognitive function. Second, Lewis almost entirely neglects posterior and medial cortical structures. He includes the OMPFC and DLPFC, but he does not consider the posterior cingulate (PC) or the medial parietal cortex (MPC). I argue that the interplay between anterior and posterior medial cortical regions generates a functional unit, the cortical midline structures (CMSs). The CMSs are suggested to account for emotional-cognitive unity, the self.

Lewis focuses on the mechanisms of integration rather than on their result. Based on my own review of various emotional and cognitive imaging studies (Northoff & Bermpohl 2004), I argue that the self is what results from emotional-cognitive integration. What is called the self has been associated with the following functions: The feeling of being causally involved in an action has been referred as to as "agency" (Farrer et al. 2003; Frith 2002). Moreover, the own self and its body can be located in space resulting in spatial perspectivity (Ruby & Decety 2001). Another process related to the self is called "ownership." This concerns the experience that one's own body and environment are perceived as personal and closely related to one's own self (Damasio 1999). A further function of the self concerns recognition of the own person and particularly of one's own face, which is called self-awareness or self-recognition (Keenan et al. 2000; 2001). The self is also closely related to its own memories, that is, to autobiographical memories that can be encoded and retrieved (Northoff & Bermpohl 2004).

What is the emotional-cognitive thread linking these processes associated with the self? Damasio (1999) speaks of a "core self," which he describes by the continuous conjunction of intero- and exteroceptive stimuli leading to the experience of the self as a unit. I argue that this unit of the self is an emotional-cognitive unity.

I believe that this emotional-cognitive unity is the processing of self-referential stimuli as distinguished from non-self-referential stimuli. Self-referential stimuli are stimuli that are experienced as strongly related to one's own person. They have also been described as "self-related" or "self-relevant" (Craik 1999; Kelley et al. 2002; Northoff & Bermpohl 2004). The self-relevance of a stimulus is not intrinsic to the stimulus, but rather is determined by the individual and personal context in which it is perceived. I suppose that this is accounted for by linking the stimulus to emotions. The more emotional involvement, the more relevant that particular stimulus is for the person, that is, for its self. Cognitive function then allows for distinguishing these emotionally loaded stimuli from non-emotional ones. Such emotional-cognitive integration leads to the distinction between self-referential and non-self-referential stimuli and ultimately to a self as being distinct from other selves.

Lewis's second neglect concerns posterior and medial cortical regions, the PC and MPC. I argue that the neural correlate of the self as emotional-cognitive unity consists in the collaboration between anterior and posterior cortical midline regions (see also Northoff & Bermpohl 2004). These regions form an anatomical, physiological, and psychological unit which I call cortical midline structures (CMS). CMS include the OMPFC, the AC, the dorsomedial prefrontal cortex (DMPFC), the medial parietal cortex (MPC), and the PC.

Anatomically, the various regions within the CMS maintain strong and reciprocal projections among each other. Furthermore, they show a similar pattern of connectivity to other cortical and subcortical brain regions. These mostly include the regions Lewis discusses, the DLPFC, hippocampus, amygdala, nucleus accumbens, brain stem/basal forebrain, ventral tegmental area, and ventral pallidum (Ongur & Price 2000). The subcortical connections may account for top-down modulation of subcortical regions by CMS (see, e.g., Nagai et al. 2004; Northoff 2002).

Physiologically, the CMS exhibit a high level of neural activity during so-called resting conditions such as fixation task (Raichle et al. 2001). They show the highest level of neural activity during the resting state among all brain regions; this has been characterized as "physiological baseline" or "default mode" (Gusnard & Raichle 2001; Raichle et al. 2001). The CMS are involved in various emotional and cognitive processes, all involved in the processing of self-referential stimuli (see Northoff & Bermpohl 2004). The high resting level of neural activity in the CMS may thus be reflected in continuous emotional-cognitive integration, reflecting self-referential processing, and ultimately in ongoing experience of a self as "psychological baseline."

Functionally, the question for the mechanisms of how the different CMS regions are integrated into a functional unit remains. Among others, Lewis mentions effective connectivity and pattern of activation and deactivation as potential mechanisms of integration. Interestingly, both mechanisms have been described in CMS. A recent study (Greicius et al. 2003) observed increased effective connectivity between OMPFC and PC only in the resting state, whereas during cognitive processing it decreased. Some studies have demonstrated coactivation of anterior and posterior