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To: jeevacation@gmail.com

Subject: Greetings Jeff - from Rama

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Attachments: A_proposal_to_advance_our_understanding_of_The_Human_Brain_in_Health_and_Disease.doc

Greetings Jeff!

I am glad that Al Seckel put us back in touch and we had the opportunity to talk about neuroscience and other matters. It was almost as though we were simply resuming our conversation from where we left off 12 years ago. I am pleasantly surprised you remembered our conversations not just about brains but also about muses (Yes I agree the muse represents one of the fundamental constants of the universe!).

I am also pleased to hear that one of your current missions is to fund unconventional approaches to neuroscience research. You asked what I thought the major breakthroughs were in the last decade. I am taking the liberty of attaching an informal grant proposal. Last year, the center received "seed money" of \$300,000 from a private source, which provides a starting point for expansion of work in our area. Our long-term goal is to attract funds up to \$5 million; this would allow the CBC to become financially self-sustaining.

While the pace of progress has been exhilarating, we still do not understand many of the basic functions of the brain, such as how we recognize faces, why we dream, sleep, laugh, and how we read and remember. Additionally, although our own interest is mainly theoretical, people who have sustained damage to the nervous system through either disease or injury feel a particular urgency to advance our understanding of how to recover lost function and live without pain.

The CBC has three overlapping agendas:

1. Basic research – understanding how the activity of neurons gives rise to all the richness of our mental life and the whole spectrum of abilities we call human nature. Not just lofty aspects of our minds like morality and judgment but such "elementary" functions as recognizing a face or seeing depth effortlessly in natural scenes.
2. Evolutionary origin of traits that make us uniquely human and the brain structures corresponding to these traits. For as Theodocius Dobzhanski famously said nothing in biology makes any sense except when viewed in the light of evolution.
3. Applied research—using this knowledge to develop new therapies for problems rooted in the brain and nervous system, such as paralysis and other disabilities from stroke, chronic pain, and developmental disorders such as autism and dyslexia.

We are currently focusing our research on the mirror neuron system (MNS). For example,

How “clever” is the MNS? Do intentions need to be imputed to the actions of the model being observed? If you watch a crude hand-manipulated puppet on strings reach for a peanut will the MNS fire? What if you watch someone reach out for something while you are under hypnosis? Or reach for it halfway and suddenly change trajectory?

Temporal sequencing of the MNS: Despite a multitude of studies on the mirror neuron system, researchers have not reached consensus about its primary function in the human brain. Analyzing the temporal structure of the MNS response to observed action may yield new insights into its function. For example, if the MNS is engaged in action prediction (predicting what someone will do next based on what he is doing right now), then we would expect higher MNS activation at the beginning of an action sequence, while prediction is necessary, and lower activation later in the sequence when the purpose of the action is evident.

Morality and the MNS: The right IPL and SPL (in the parietal lobe) are rich in mirror neurons that evolved to enable you to adopt another's SPATIAL vantage point (a small lesion here leads to neglecting the left half of the world) but we suggested in our Reith lectures (2003 BBC) the same system may have evolved to see something from another's CONCEPTUAL view-point ; a necessary pre-requisite for both "theory of mind" (seeing others as intentional beings) and for morality. Our theory predicts, therefore, that patients with damage to the right IPL and SPL should have difficulty in making moral judgments (and confronting moral dilemmas) but have no problems with other abstract questions that are equally difficult. This would be an exciting result because morality has traditionally been considered to be mediated by frontal structures in the brain, rather than embodied in ones spatial understanding of one's body in the world.

Implications for autism: Patient groups exhibiting deficits in mirror neuron system functioning should be studied with two goals in mind: first, to better understand the normal functioning of the mirror system by observing the effects of its dysfunction in autism, and second, to better understand how deficits in mirror neuron functioning may underlie specific impairments found in disorders like autism (and develop treatments). If individuals on the autism spectrum have mirror neuron system deficits, we would predict they would have a particular difficulty discriminating whether movement patterns belong to self or other, as they would have difficulty mapping the visual cues onto their own motor system. Our current research explores whether individuals with autism have a deficit in recognizing visual cartoons (Johansson figures) of their own movement and tell them apart from those of others. Normal people can do this effortlessly.

Mirror visual feedback and virtual reality therapies: Mirror visual feedback, developed in our center a decade ago have been found to be

effective (in controlled trials by a number of other groups) in decreasing phantom pain, complex regional pain syndrome and accelerating recovery from post – stroke paralysis. (The technique is now widely used throughout the world). However, we believe this is only the beginning. Empirical studies of motor simulation and sensory referral are needed to better characterize sensorimotor implications of the mirror neuron system and optimize treatment. In addition, the use of virtual reality technologies presents new opportunities to present carefully tailored visual feedback to a variety of patient populations. Studies of mirror visual feedback could be extended to other groups of patients such as those with chronic pain conditions like fibromyalgia.

Obviously the CBC is involved in a number of other projects besides mirror neurons but this summary of MNS research should give you a picture of our overall strategy.

If any of these lines of research interest you let me know.

Cheers,

Rama

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