Grand challenges in dementia 2010

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Dementia is widely recognized as a major, rapidly escalating, epidemic world-wide challenge to the global health care system. In fact, Alzheimer's Disease International (ADI2009) estimates that there are over 35 million people with dementia today world-wide. Since the numbers of patients with this condition nearly double every 20 years, it is predicted that there will be about 66 million in 2030, and 115 million in 2050. This is true not only in wealthy nations, but ADI estimates that 58% of the people with dementia live in low and middle income countries. As the population in these countries continues to age, as in the rest of the world, it is expected that their proportion of patients will grow to 71% by 2050, whereas the research on conditions causing dementia is overwhelmingly done in high-income countries. Thus, the balance of disease burden is shifting, the burden of research is uneven, and yet, according to the ADI, "…The quality of many studies was relatively poor, although it is steadily improving."

The impact of dementia is staggering regardless of the aspect measured. For example, the annual economic cost of dementia has been estimated at U. S. $315 billion (ADI, 2009). Seventy-two percent of these costs arise from high income countries that have only 38% of the patients. However, the cost for caring that is mostly " indirect" (i. e. informally provided by family members or individuals hired outside the health care system) nowadays, especially in low income countries, but will become increasingly " direct" (i. e placed in the hands of institutions) and thus impact their national budgets increasingly. There is — of course — no unanimously accepted measure of the suffering caused to patients and families, whereas the still imperfect means to make financial estimates of the cost of dementia continue to

improve. These, as well as numerous additional, converging statistics, support ADI's proposal that " The World Health Organization (WHO) should declare dementia a world health priority" (ADI, 2009).

Compounding this staggering challenge, the cause of most of the most common forms of dementia, starting with AD, remains unknown (Jellinger 2009 Kuljiš, 2009a). Furthermore, the leading hypothesis about its pathogenesis — the amyloid hypothesis — has been questioned for many years and is of late under revision due to the failure of several treatments based on this concept (Geerts, 2009). Similar challenges are experienced across the board in the entire field, necessitating a re-thinking of basic conceptual tenets all the way through specific translational applications to diagnosis, treatment and eventual prevention.

Frontiers in Dementia aims at contributing decisively to this challenge by serving an essential, mostly unaddressed role in the global fight against dementia. While there is fortunately an increased awareness of the challenges posed by dementia, and agencies such as ADI have been mobilizing for many years to improve still inadequate governmental and private resources for the care of demented patients and their families, conquering these conditions by applications of modern biomedicine remains hampered by the lack of a unifying scheme for their understanding and treatment (Kuljiš, 2009a). This should not be surprising, since it is only part of the most tangible consequences of the lack of a viable framework for understanding human behavior and cognition as an emergent property of the brain (Kuljiš, 2010). As a result, most attempts to unravel the causes of dementia — and by extension the design of useful treatments and

prevention — depend on a rather simplistic, if still somewhat useful model of the brain as a “ sick machine” that arose in the 18th Century (La Mettrie, 1748), that has been successful by exploring increasingly “ atomizing” reductionist models, in the absence of an equally successful scheme that allows the wealth of molecular-level observations to be integrated through increasingly higher-scale levels of organization all the way up to the individual patient (Kuljiš, 2009a , b , 2010). None of this should stop, however, since the explosion of knowledge on putative molecular mechanisms of dementia has inspired an increasing number of possible avenues for translational applications, that may continue to yield palliative strategies, and possibly prevention, even in the absence of a more coherent conceptual scheme to integrate levels of medical and scientific inquiry spanning from the molecule all the way to the entire organism. Frontiers in Dementia will thus be a forum for the communication and exchange of ideas that continue exploiting the considerable advantages of Molecular Medicine (a “ Bottom Up” approach), at the same time that it fosters the search for avenues in Integrative Neuroscience and the Generative Sciences that seeks to develop a much-needed “ Top Down” model to tackle Dementia together — and in harmony — with the comparatively well developed “ Bottom Up” model.

The search for a viable integrative — theoretical and experimental — model is probably the main, and yet essentially unrecognized, cause of the Innovation Gap that afflicts the entire field of dementia among other challenges in cognition, behavior and consciousness. The Innovation Gap (IG) in Dementia is a complex set of challenges that includes the failure of

models of genetically-caused Alzheimer’s disease (AD) lesions and other models of dementia to prove as useful as hoped in the testing of innovative treatments, the reduction in the number of newly developed medications for Alzheimer’s disease (AD) despite the increasing number of resources spent in their development, and the apparent failure of many recently tested agents for AD (Geerts, 2009 ; Sigurdsson, 2010). While it is clear that the latter are among the more numerous reasons contributing to the IG, it has not been recognized to the same extent that the IG is due mainly to the relatively crude extrapolation of mainly Molecular Level hypotheses — and actual molecular discoveries — in the field of dementia to higher levels such as neuronal networks and the behavior of the organism (Kuljiš, 2009a). In fact, molecular approaches necessitate as much reductionism as possible to achieve the utmost rigurosity, and therefore have tended to neglect key aspects of dementia that include the remarkable selectivity for specific neurons, neuronal networks and even regions of the brain (Kuljiš, 2009b). While this should not be ever interpreted as indicating that the former approaches are not useful, the state of the field clearly indicates a need for true integration and collaboration across disciplinary borders. Since this unmet need is often given merely lip service, we intend Frontiers in Dementia to provide not only a forum, but an increasingly powerful demonstration and incentive for such integration.

In keeping with the goals and philosophy of the Frontiers Organization, we will also promote a wide range of contributions to the field of dementia, ranging from the much-needed array of hypotheses on pathogenesis and pathophysiology (Fernández et al., 2008) to Systems-Level approaches (

Kuljiš, 2009b), passing through molecular, neuropsychological and clinical research levels of inquiry, among many others. Frontiers in Dementia will thus become not only a significant contributor to the most common approaches in the fight against dementia, but will actually help push the boundaries of the field in directions that are both promising but seriously neglected, and that need to be developed urgently in order to conquer Alzheimer's disease and related disorders.

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