

From bench to bedside: the importance for neurodegenerative disorders of crosstalk between basic and clinical research

Dear Reader,

A serious limitation of modern medical sciences is the frequent failure to translate the wealth of information provided by preclinical research into commensurate gains in new treatments, diagnostics and prevention. This gap – sometimes called the ‘valley of death’ – is particularly evident in the field of neurodegeneration.

Alzheimer’s disease (AD) and Parkinson’s disease (PD) are the two most frequent neurodegenerative disorders in the general population. For both, age is the main risk factor and the prevalence and social costs of these diseases are therefore bound to increase progressively and dramatically with growing life expectancy. Despite the urgency to find new therapies capable of modifying AD or PD progression, research efforts have not been conclusive.

In contrast to the unsuccessful search for new and effective therapies, understanding of the pathogenic mechanisms underlying AD and PD has progressed considerably. Major advances and new insights concern, for example, the mechanisms governing the pathological aggregation of key proteins (β -amyloid, tau, α -synuclein), the nature and processes of neuronal damage associated with these aggregate formations, and the role of neuroinflammation in fueling the neurodegenerative process. Yet, this knowledge has only marginally enriched the therapeutic armamentarium of clinical neurologists. As new aspects of the mechanisms of neurodegeneration are pinpointed, novel therapeutic agents designed to correct the biochemical or molecular defect are tested in animal models. Results are often encouraging, but more often than not enthusiasm fades when the new strategy is tested in the clinical setting – especially in large controlled clinical trials.

Various explanations for the frustrating gap separating basic from clinical research have been offered, but one general element clearly stands out: inadequate communication between these two research spheres. Basic scientists and clinical researchers or clinicians do not communicate enough and often find it hard to understand each other. As a result, basic and clinical neurosciences tend to diverge. This gap goes some way towards explaining the difficulty of using experimental models for testing new therapies. Animal models used in preclinical studies prove extremely useful for dissecting pathogenic mechanisms; however, the same models have clear limitations when they are used to test treatments intended to be transferred to patients. This could be due, at least in part, to the use of evaluation parameters different from those used in clinical settings. In AD, for example, β -amyloid imaging and cerebrospinal fluid measurement of A β and tau have become valuable disease biomarkers in patients; however, these markers are rarely used when testing new treatments in mouse models of AD. Similar issues emerge in PD research, where an even wider panel of experimental models is available.

Close and orchestrated crosstalk between basic scientists and clinical researchers must therefore be encouraged. This would favor the adoption of shared solutions to the problems faced by translational neuroscience. Research should proceed from bench to bed and back to bench, with basic neuroscientists taking advantage of the different perspectives that clinical researchers are able to offer. This, for neurodegenerative diseases, may provide an effective way of increasing chances of bridging the “valley of death”.

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