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【编者按】在国内的很多临床前研究中,往往容易忽略甚至不知道“临床(前)行为评价”内容,为此,本期丹尼尔结合工作中的一个研究方法——临床(前)研究中的行为评价和自己的体会,论述了“临床(前)行为评价”的重要性。此文有助于读者今后的研究实践。

Topics of interest – 'Bench to Bedside: Bridging the gap between pre-clinical to clinical investigations in neurological research'

Although useful pre-clinical animal models are often used to develop treatment strategies, the translation of these into a clinical benefit remains uncommon. A major contributing factor to this predicament is an inconsistency in the methodological approaches used between pre-clinical and clinical research. There is frequently a lack of consensus in the measures used and definitive experimental endpoints.

The use of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated macaques in the study of Parkinsonian motor symptoms is a primary example, whereby subjective behavioural rating scales have been used in order to determine pharmacological effects of novel treatment therapies[1]. In contrast, evaluation of treatment effects on the motor symptoms in patients with Parkinson's disease (PD) is assessed using patient diaries, where reports of treatment experiences are written on a daily basis[2]. These contrasting methodological approaches highlight the difficulty of translating positive data found at the pre-clinical level into the clinical domain.

To provide a solution to this problem, we have recently employed whole-body kinematic analyses in MPTP-treated macaques[3] to evaluate clinically effective anti-parkinsonian agents in order to validate a novel objective approach for testing therapeutic treatments. Animals were first trained to perform on unconstrained locomotor tasks, specifically to freely walk on simple apparatus, following which pharmacological treatments were tested in the same conditions.

These unbiased quantitative analyses of motor function during unrestricted movement allowed mechanistic identification of clinically effective treatments against parkinsonian motor disabilities (i.e. L-DOPA, pramipexole, ropinirole, amantadine and istradefylline). The high resolution of these analyses dissociates specific clusters of motor control parameters that are improved from those that remain affected. For example, L-DOPA treatment enhanced movement velocity and stride length during walking, but had no effect on stance duration or foot elevation.

These recording methodologies and analytical tools for assessment of motor control capacities are readily transferable to a clinical setting, offering an efficient and reliable avenue for predicting/evaluating therapeutic benefit of novel treatments. This methodological approach, which has been validated in human patients, bridges the gap between preclinical and clinical research. Together, these tools support (i) greater translational efficacy of novel therapeutic interventions and (ii) objective fine-tuning of existing drug treatments used in patients with parkinsonian or other neuro-motor disorders.

References

【1】Ko WK, et al. Mov Disord 2014; 29:772 – 9.
【2】LeWitt PA, et al. Ann Neurol 2008; 63:295 – 302.
【3】Ko et al. Society of Neuroscience 2015. Abstract/poster 2015-S-3976-SfN.

本栏目由李秦博士主持。