



Diabetic neuropathy: are we still barking up the wrong tree and is change finally in sight?

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To the Editor: I read with interest the review article by Callaghan et al on diabetic neuropathy that was recently published in *Diabetologia* [1]. One seemingly relentless problem with this elusive diabetes complication is that recommended diagnostic methods [2] are much more applicable to research rather than to everyday clinical practice. As a result, diagnostic guidelines for diabetic neuropathy within diabetes clinic settings remain widely variable. Its heterogeneous presentation and insidious natural history render diabetic neuropathy research equally problematic. Clinical trials investigating a therapeutic role for protein kinase C β (PKC β) inhibition, nerve growth factor (NGF) and aldose reductase inhibition [3] in established neuropathy using robust diagnostic criteria have been largely disappointing, and effective licensed treatments are still unavailable. The role of metabolic factors, such as lipids and sphingolipids, in the aetiology of neuropathy is discussed in some detail in the review by Callaghan and colleagues [1]. Although of novel scientific interest, further research in this area is realistically unlikely to influence clinical practice. Despite observed associations between dyslipidaemia and neuropathy, the limited outcome studies on lipid-lowering therapies in diabetic neuropathy are both unconvincing and conflicting [4]. The interventional research studies targeting obesity that are proposed by Callaghan et al [1] may show an interesting positive effect on neural function but, in the real world, weight loss and lifestyle modification remain a key strategic measure in diabetes irrespective of their effect on neuropathy. As prediabetes (impaired fasting glucose and impaired glucose tolerance), which is often related to obesity, is related to early complications, including neuropathy [5], investment in diabetes

prevention programmes would seem a much safer direction. After all, the past has taught us with some conviction that prevention of neuropathy (as shown by the DCCT and, to a lesser extent, by the UK Prospective Diabetes Study [UKPDS]), is a much more reliable option than treatment.

Unsurprisingly, patients' understanding of neuropathy remains nebulous when compared with that of the other microvascular complications of diabetes, particularly in those who are asymptomatic. And in those with symptoms, particularly those troubled with severe neuropathic pain, therapeutic options also remain disappointing, as is well highlighted by Callaghan and colleagues [1]. However, the importance of a specialist team in managing painful neuropathy needs to be emphasised, as, in our experience, patient education and psychological support are invaluable in complementing otherwise suboptimal pharmacotherapies [6]. Whilst we should certainly not underestimate the wealth of scientific research in the last two decades, clinically relevant outcomes have been lacking. With the increasing worldwide prevalence of diabetes, and of diabetic neuropathy, there is a need for quicker, more intuitive diagnostic devices. Smart artificial-intelligence systems are making good headway in diabetes research and provide a new platform for a long-awaited 'one-language' approach to diagnosing and managing diabetic neuropathy [7]. Our own ongoing research in this area, utilising simple standard clinical variables, is certainly very encouraging [8]. As recent events related to coronavirus disease-2019 (COVID-19) continue to unfold, changes in clinical practice are inevitable [9] and practical, low- or non-contact techniques provided by medical artificial-intelligence systems will almost certainly become the way of the 'new-normal' future.

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