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The multifinger force deficit: A protocol to detect incipient cognitive decline

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INTRODUCTION

Clear prospective associations exist between grip strength and multiple indices of health and well-being, including frailty, morbidity, and mortality. The usual explanation is that low grip strength arises from loss of muscle function, indicative of a more general decline in physical health.[1] However, the relationship that also exists between grip strength and preservation of cognitive capacity[2,3]—when cognitive and muscle function are not linked,[4] suggests that this account is incomplete. Beyond middle age, individual variations in grip strength may predominantly be a marker of brain health, rather than physical status.[5] Application of grip force demands sophisticated neuromuscular coordination and control. Advances in brain imaging make clear that neural degeneration is an orderly and sequential process[6] affecting networks that mediate functionally related processes such as cognition and motor control.[7] From this perspective, the proximate cause of the relationship between grip strength and cognitive decline is weakening of the functional integrity of brain networks. The distal cause is the dysregulation of multiple physiological systems, which ultimately also becomes manifested in the associations of grip strength (and cognitive function) with frailty, morbidity, and mortality.

POTENTIAL AND IMPEDIMENTS

In light of its power to predict health outcomes that may only become evident several decades later, it has been proposed that grip strength be used as a biomarker of aging[8]—a "vital sign" for middle-aged and older adults.[9] But there are obstacles to be overcome. The first arises from the fact that *changes* in grip strength are more revealing with respect to cognition[10] than any one-off measurement. Although declines in grip strength can be registered over periods as short as 6 months,[11] to provide a biomarker, repeated observations must be made. Reliability of measurement thus becomes paramount. Obfuscating variation can arise for reasons as mundane as a failure to recalibrate dynamometers, changes in testing personnel, and from what might appear minor alterations in the assessment procedure.[12] The reading will depend on the time of day at which it was obtained,[13] and can be influenced by small changes in posture, such as the angle of the elbow or wrist.[5] These factors conspire to increase the level of noise relative to the signal and reduce the sensitivity with which grip strength can act as a biomarker for cognitive dysfunction. The more insidious problem is that a *decline*

[Correction added on 11 May 2022, after first online publication: Projekt IReL funding statement has been added.]

in grip strength cannot be detected instantaneously. A period of time must elapse between measurements before the determination can be made.

Efforts have therefore been made to establish whether one-off assessments can make good on the promise of prognosis offered by the associations seen in cohort studies. Large normative samples have been used to generate cut-off points for low grip strength. The aim has been to identify those at risk of developing a variety of disorders, including frailty, sarcopenia, metabolic syndrome, and cardiovascular disease. In practice, the performance of these cut-off points varies by population, with age, ethnicity, and in the presence of comorbid conditions.[14] The clinical exploitation of cut-off points is also handicapped by the use of different testing methods and dynamometers, and by the need to account for a wide range of mediating variables including height, body-mass, body-mass index (BMI) and hand dimensions. As the impact of these variables highlights, morphometric factors contribute to individual differences in grip strength, independently of the neurodegenerative processes that account for the associations between grip strength and cognition. As a consequence, a one-off measurement of maximum grip strength may not identify individuals at risk of cognitive decline. A novel way of applying hand-grip dynamometry may permit the physiological factors that give rise to population level relationships between grip strength and cognitive function, to be assessed in individuals by means of a single test.

THE MULTI-FINGER FORCE DEFICIT

In conventional grip strength testing, a dynamometer is held in one hand, with the index, middle, ring, and little fingers flexed around a handle instrumented to record force. The individual being tested is asked to apply as much force as possible to the handle over a period of several seconds. The highest level achieved during this interval is recorded. This value reflects the net force generated by the four fingers acting in concert. With a suitably configured device, it is also possible to register independently the force generated by each finger, either when in isolation, or in combination with the other fingers. Perhaps unexpectedly, the maximum force that can be produced by each finger decreases in proportion to the number of other fingers that are engaged simultaneously.[15] When all four fingers are engaged together, the force applied by each finger is typically about half that which can be applied when it is used in isolation. This is referred to as the "multi-finger force deficit."

The level of neural drive received by the muscles that generate grip force is also inversely related to the number of fingers engaged.[15] In other words, a requirement to activate maximally all of the muscles that flex the fingers presents the CNS with a significant challenge. Individuals vary in the degree to which they can meet this challenge. The diminution of the force applied by each digit in a four-finger grip is larger in older persons than in the young.[16–18] It is also greater in those who have incurred damage to their brain networks, for example as a consequence of stroke.[19] Unlike conventional grip strength testing, the multi-finger force deficit (MFFD) tells us about the brain and not the brawn.

Is it practical to use this method instead of conventional grip strength testing? As it is challenging to support and stabilize a conventional dynamometer when a single digit is used to apply force, in most MFFD protocols a separate transducer is dedicated to each finger (Figure 1). The transducer may be in the style of a "button" placed on a flat surface, on which downward pressure is applied,[16] or it may be attached to a loop placed around the finger, to record the tension generated by flexion of the metacarpophalangeal and interphalangeal joints.[15] In most cases,[16–18] three trials of 2 s duration (in random order) are undertaken for each of five combinations (digits II to V separately, and digits II to V in concert). The largest force generated in each set of three trials is recorded—usually by means of a computer or microprocessor. The magnitude of the MFFD is calculated by expressing the sum of the largest values recorded for the four individual digits in the multifinger condition, as a proportion of the sum of the values recorded for each digit used in isolation. Estimation of the MFFD takes about 5 min longer than the Southampton protocol[20] (≅6 min) which is adopted widely[21] for conventional grip strength testing. It is possible that in some circumstances this may exceed the time available for a clinical assessment.

THE HYPOTHESIS

Identifying the magnitude of the MFFD as a sensitive measure of the functional integrity of brain networks is a substantial jump in thinking. This also leads naturally to a new hypothesis—the magnitude of the MFFD will provide a marker of incipient cognitive decline.

Beyond inviting reassessment of the associations between grip strength and indices of health and well-being, what does this hypothesis offer clinical practice? The answer is that multi-finger dynamometry overcomes the major obstacles that have prevented the relationships between grip strength and cognitive function witnessed in longitudinal studies, from being exploited for individual prognosis. Since the non-neurologic (e.g., morphometric) factors remain constant across all assessments (the same muscles serve as actuators both when a finger is engaged in

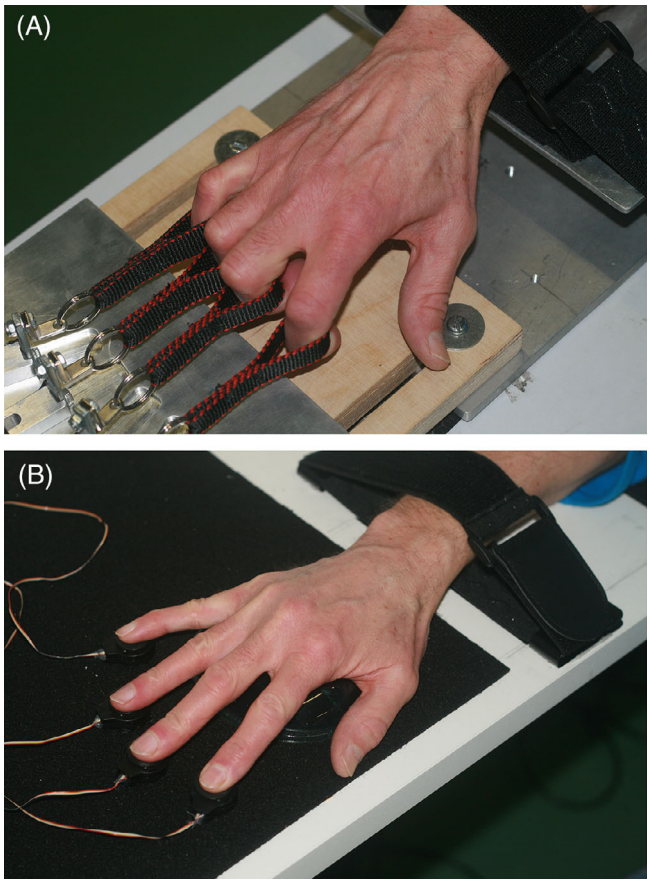

FIGURE 1 Multifinger dynamometry may be implemented by (A) recording the tension generated by flexion of the metacarpophalangeal and interphalangeal joints, via loops placed around the fingers which are fixed to (e.g., s-beam style) force sensors, or (B) by using force transducers in the style of a "button," placed on a flat surface, on which downward pressure is applied

isolation and when used in combination with other fingers), they do not contribute to differences between individuals. The MFFD thus provides a bona fide measure of neural sufficiency. As the force decrement (when all fingers are used) is defined in relation to the overall capacity of the individual at that moment in time, its magnitude is also amenable to direct interpretation. Critically, it is therefore not necessary that multiple measurements have been obtained previously in order for the potential clinical significance of a single reading to be determined.

HOW MIGHT THIS HYPOTHESIS BE TESTED?

The hypothesis can be tested by determining the validity of the MFFD as a marker of brain health and cognitive dysfunction. Its construct validity may be established through associations with neural imaging derived indices of brain integrity/connectivity/pathology. Standardized test batteries are employed to operationalize elements of cognition such as executive function, memory, attention and processing speed, and determine the degree to which they are subject to change. The content validity of the MFFD can be verified through its analytical mapping onto these constructs. In determining criterion validity, it is helpful to distinguish between concurrent and predictive. In respect of concurrent validity, cross-sectional studies can delineate associations between the MFFD and both global and composite measure of cognitive function. The degree to which the MFFD can distinguish among frailty phenotypes differentiated by the contribution of cognitive dysfunction[22] will provide a further means of testing the hypothesis. Perhaps most critically in terms of the prospects for individual prognosis offered by this measure, its addition to existing longitudinal studies can serve to establish predictive validity and generate normative values for the MFFD which can be applied subsequently to screen for incipient cognitive decline.

CONCLUSION

While it has been clear for some time that handgrip strength is associated with cognitive function, it has not thus far been feasible to utilize this knowledge for individual prognosis. The present hypothesis is that the MFFD - a sensitive index of neural sufficiency, is a proxy measure of functional brain integrity which can provide a biomarker to identify those at risk of future cognitive impairment.

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CONFLICT OF INTEREST
The author declares that there are no conflicts of interest.

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