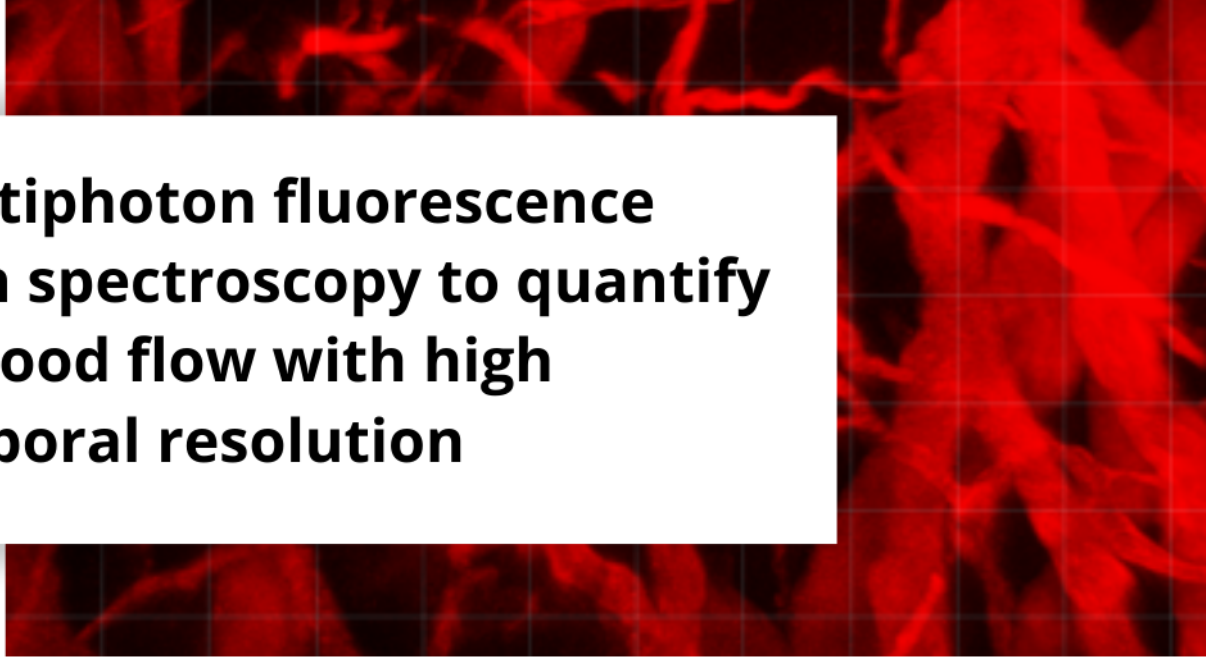

In vivo multiphoton fluorescence correlation spectroscopy to quantify cerebral blood flow with high spatiotemporal resolution

Cerebral blood flow (CBF) measurements provide critical information about physiological and pathological processes within the central nervous system (CNS). The complex microvascular network plays a fundamental role within the CNS, where neuronal activity regulates the flow of nutrients. Understanding blood flow dynamics with high spatial and temporal resolution is essential to understanding the role of vascular dysfunction in a variety of pathological processes. Using multiphoton in vivo fluorescence correlation spectroscopy (FCS), blood flow rates can be determined at individual pixels with sub-micron resolution.

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The explicit/implicit distinction in studies of visuomotor learning: Conceptual and methodological pitfalls

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A ubiquitous problem in science—from a physicist estimating the position of an electron (Heisenberg, 1927) to a social scientist conducting opinion polling (Bishop, 2004)—is that the measurement process can change the measured quantity itself. In addition, variation in measurement methodology may inadvertently favor one component of the measured quantity over another, leading to different results even though the measured quantity has not changed—for example, both gross domestic product and gross national product assess the economic activity of a country, but focus on different components. A recent paper by Maresch, Werner, and Donchin in this issue of the European Journal of Neuroscience (Maresch et al., 2020) brings these issues to bear on one of the most widely studied motor learning paradigms – visuomotor adaptation (Krakauer et al., 2000; Martin et al., 1996).

Motor adaptation refers to the phenomenon by which the motor system changes its output—motor commands—in response to error (Krakauer et al., 2019; Shadmehr et al., 2010). Over the last decade, studies have converged on the idea that there are two distinct components to the adaptation process: an *implicit* component, which is an involuntary response to sensory prediction error (and proceeds even when it elicits increases in performance error (Mazzoni & Krakauer, 2006)) and an *explicit* component, which is a deliberative adjustment of aiming direction in response to performance error (Taylor et al., 2014).

Accurately assigning adaptive changes to these two components is important to the study of motor learning both for correct identification of neural mechanisms and for the design of interventions in the case of disease-related adaptation deficits. The existence of different methodologies for identification of explicit and implicit components means that ambiguities can arise across studies: differing results may relate either to true differences in underlying components of learning or just differences in what each method of measurement detects.

To describe existing methods, it is useful to consider a paradigm commonly used in the visuomotor adaptation literature, that of visuomotor rotation (VMR) (Krakauer et al., 2000; Mazzoni & Krakauer, 2006; Morehead et al., 2015; Taylor & Ivry, 2011). In a typical VMR experiment, a participant makes planar reaches with direct vision of their hand occluded and replaced with cursor feedback. During training, cursor feedback is rotated by a certain amount (e.g. 30°) relative to hand motion. To compensate, the hand will end up moving 30° (or some fraction thereof) in the opposite direction, with the presumption that this is accomplished through a combination of implicit and explicit components. A variety of ways to distinguish implicit from explicit adaptation have been proposed for VMR experiments. Earlier studies employed post-study interviews or questionnaires, which contained questions about participant awareness for the perturbation and about use of explicit strategies to counter it (Benson et al., 2011; Neville & Cressman, 2018). Such self-reporting methods, however, are limited by either the ability of participants to accurately recall what was happening during the experiment itself or the unavoidable ambiguities inherent in how questions are interpreted (a problem well known to political pollsters).

More recently, two other methods have been introduced: *verbal reports*, whereby participants directly report their aiming angle on a trial-by-trial basis (Taylor & Ivry, 2011; Taylor et al., 2014), and *exclusion*, whereby participants disengage their strategy and aim directly to the target because of direct instruction to do so or from cues indicating that the rotation is off on that trial (Benson et al., 2011; Heuer & Hegele, 2015; Morehead et al., 2015; Neville & Cressman, 2018; Taylor et al., 2014) (Figure 1).

Notably, studies that used both the verbal report and exclusion methods have yielded contradictory results, with some studies showing relatively close agreement (Taylor et al., 2014) and others showing clear differences, with exclusion measures typically yielding lower estimates of the implicit component (Bond & Taylor, 2015; Bromberg et al., 2019; Leow et al., 2017) (although showing better congruence when the trained rotation is small in magnitude (Bond & Taylor, 2015)). Moreover, estimates of implicit adaptation through exclusion seem to display much lower inter-individual variability compared to estimates using reporting, for the same participants (Wilterson & Taylor, 2019). This unsatisfactory state of affairs underscores the need for a single study that carefully and directly compares these two measurement approaches. Here, Maresch and colleagues (Maresch et al., 2020) sought to do exactly this. In a series of experiments, they used both verbal report and exclusion methods to assess implicit and explicit adaptation both during and immediately following VMR training.

One result from Maresch and colleagues is clear: methods matter. For example, when participants had to provide verbal reports on every training trial (consistent-report group), explicit adaptation was increased compared to when they only had to do so intermittently. This finding suggests that the balance between the implicit and explicit processes can be changed by the frequency of the measurement—an example of the measurement process altering the measured quantity itself. An even more surprising observation was that verbal reports and exclusion can yield very different assessments of explicit adaptation during training even when the frequency of probe trials is the same—which may be an example of each type of measurement preferentially accessing different components of the quantity they are trying to measure. Puzzlingly, estimates were more congruent in the post-learning, aftereffect, phase.

Several explanations could be offered for the effect of measurement frequency on the degree of explicit adaptation. Asking the participant to report their aiming direction on every trial lengthens the inter-trial interval, potentially allowing for decay of implicit adaptation; alternatively, the higher frequency of reports might help the participant more quickly converge on the correct strategy. In either case, the result would be an increase in the explicit component. It is a bit harder to explain why the report versus exclusion methods would yield different results even within the same group.

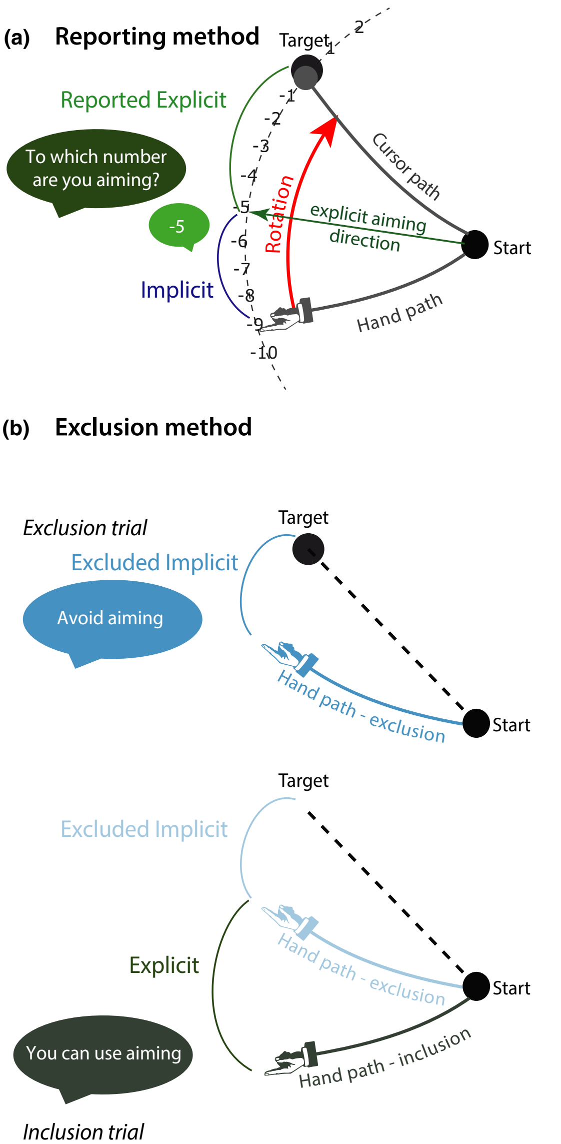

FIGURE 1 Report-based versus Exclusion-based measures of implicit and explicit adaptation. Here, a visuomotor rotation (red arrow) introduces a dissociation between hand and cursor movement direction. (a) Under the Report method, the difference between the participants' reported aiming direction and the target provides an estimate of the explicit component (green); the difference between the reported aiming direction and the actual hand movement direction provides an estimate of the implicit component (blue). (b) Under the Exclusion method, on some trials, typically without visual feedback, participants may be instructed to disengage any strategy (exclusion trials, light blue), providing an estimate of the implicit component; this can be compared to trials where they are allowed to use strategy (inclusion trials), with the difference in movement direction between these two trial types providing an estimate of the explicit component. Figure adapted from Maresch et al. (2020)

In their discussion, the authors propose a different explanation for both the increased adaptation in the consistent-report group, and measurement differences between report-based and exclusion-based measurements within the same group. Their explanation is based on the idea that explicit adaptation itself is not a monolithic process, but consists of two sub-components: an aiming direction that is either remembered target by target (and subsequently cached), or is instead recalculated parametrically for each target (McDougle & Taylor, 2019), with the former component expressible at low reaction times but the latter requiring high reaction times. First, the discrepancies between report and exclusion measures even within the same group may arise due to each measure preferentially accessing one or other of the sub-components. Specifically, the authors hypothesize that exclusion measures weigh the computed component more heavily, compared to aiming reports, whereas continuous reporting might promote the computed, high-reaction-time component. They base this on the longer time between target appearance and movement in the consistent-reporting group, which could indicate a longer reaction time associated with the computed component. Second, the higher explicit adaptation in the consistent-reporting group compared to the intermittent-reporting groups may arise from each method differentially favoring sub-components. These are interesting speculations, although testing them may pose methodological challenges: how can we both ask a participant their aiming direction, and measure their reaction time on the same trial? And, even if this challenge was overcome, should an identified low-reaction-time component still be termed explicit (Huberdeau et al., 2019), when the low reaction time is unlikely to allow for deliberation?

The explicit versus implicit dichotomy might be ill-posed

A deeper issue needs to be raised which extends beyond mere methodological concerns: is labeling component processes as explicit versus implicit conceptually misleading? In other words, are the component processes *themselves* fundamentally explicit or implicit, or are they instead differentially available to awareness? These are not the same thing but can be unintentionally conflated. As Wittgenstein pointed out, just because you cannot verbally articulate what a clarinet sounds like does not mean you do not have explicit knowledge of how it sounds (Wittgenstein, 2009). Conversely, if study participants are able to provide a *post hoc* verbal report that something just happened, this does *not* mean the process was controlled explicitly. A person can report after a hiccup that it occurred but that does not mean they were in explicit control of it. In an example from the motor learning literature, in the serial reaction time task (SRTT), it is assumed that if subjects verbally report afterwards that they were not aware of the full sequence then they must have learned it entirely implicitly. As Shanks and colleagues have convincingly argued (Shanks, 2005), however, this is fallacious. Indeed, it has been shown that learning in the SRTT can be almost entirely attributed to explicit awareness of fragments even if they are not assembled into full sequence awareness (Moisello et al., 2009).

Explicit adaptation was contrasted against implicit adaptation in our original 2006 paper (Mazzoni & Krakauer, 2006). There, participants were *given* an explicit instruction, that they could aim to a different target and, thus, eliminate target error. Importantly, this explicit aiming was set up in opposition to another process—driven by sensory prediction error—that was deemed implicit precisely because it countered task success: it is logically contradictory to posit two *explicit* processes at war with each other in order to fail at the task! Such a contradiction would be akin to someone overtly turning the bath tap on and pulling the plug at the same time. All papers since ours, however, have been based on the assumption that something available to post-trial verbal report implies explicit self-instruction during the trial and thereby excludes an implicit process. The error here is to go from the correct conclusion that these instruments reveal more than a single process to giving these processes the names of the instruments. Exclusion trials are not immune to this error either: if the participant becomes explicitly aware of the action they were taking to counter the rotation, and is able to explicitly disengage that action, it does not necessarily follow that they learned that action through an explicit process.

An alternative approach has been to eschew instruction or report altogether. Haith and colleagues (Haith et al., 2015) used manipulation of the reaction time to dissect adaptation into its components, a dissection which does not require use of the terms implicit and explicit per se. That said, there have been attempts to map processes that are differentially reaction time sensitive onto the implicit/explicit distinction based on the assumption that longer reaction times imply the need for deliberation before a movement is made (Leow et al., 2017). However, assuming a one-to-one equivalence between low- and high-reaction-time components on the one hand, and implicit and explicit components on the other, may also be problematic: recent work suggests that initially explicit components can become expressible at low reaction times with prolonged practice (Huberdeau et al., 2019). Moreover, these low-reaction-time adaptation components can be substantially greater in magnitude than implicit adaptation estimated through aftereffects (Huberdeau et al., 2019; McDougle & Taylor, 2019). Again, a distinction should be made between showing that adaptation is comprised of dissociable components versus inferring the nature of the component processes, for example, that one process is overtly strategic just because it was revealed by verbal report, or that one process was always implicit because it later became expressible at low reaction times.

Conclusion

The important findings reported by Maresch and colleagues (Maresch et al., 2020) illustrate that there is no gold standard for decomposing adaptation into implicit and explicit components. It is to be hoped that their results will lead to more caution when interpreting and comparing the results of future studies that use different methodologies to identify implicit and explicit components of adaptation. However, we need to be aware that it might not be sufficient to just nail down methodological differences. This is because the implicit/explicit distinction has likely been imposed more by our experimental methods, especially those requiring some kind of verbal report, than by the underlying biological reality. It is almost certain that the cognitive-motor processes operating in visuomotor adaptation tasks are more graded and granular than the simplistic explicit/implicit dichotomy currently dominating discussion. Methodological pitfalls can obscure deeper conceptual ones.

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No new data were gathered for this commentary.

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