Sam Harvey, MSpPath^{a,b}, Miranda L. Rose, PhD^{a,b}, Emily Brogan, PhD^{a,c}, John E. Pierce, PhD^{a,b}, Erin Godecke, PhD^{a,c}, Sonia L.E. Brownsett, PhD^{a,d,e}, Leonid Churilov, PhD^{a,f,g}, David Copland, PhD^{a,d,e}, Michael Walsh Dickey, PhD^{a,h,i}, Jade Dignam, PhD^{a,d,e}, Natasha A. Lannin, PhD^{a,j}, Lyndsey Nickels, PhD^{a,k}, Julie Bernhardt, PhD^{a,f,g}, Kathryn S Hayward, PhD^{a,f,g}

^a Centre of Research Excellence in Aphasia Recovery and Rehabilitation, ^bLa Trobe University, ^c Edith Cowan University, ^d Queensland Aphasia Research Centre, ^e University of Queensland, ^fUniversity of Melbourne, ^g Florey Institute of Neuroscience and Mental Health, ^hUniversity of Pittsburgh, ⁱVA Pittsburgh, ^jMonash University, ^kMacquarie University

This is the Accepted Version of the manuscript reproduced under a CC BY-NC-ND license. Please visit https://doi.org/10.1016/j.apmr.2022.12.002 to access the Publisher's Version of Record.

Abstract

The effect of treatment dose on recovery of post-stroke aphasia is not well understood. Inconsistent conceptualisation, measurement, and reporting of the multiple dimensions of dose hinders efforts to evaluate dose-response relationships in aphasia rehabilitation research. We review the state of dose conceptualisation in aphasia rehabilitation and compare the applicability of three existing dose frameworks to aphasia rehabilitation research - the Frequency, Intensity, Time, and Type principle (FITT), the Cumulative Intervention Intensity (CII) framework, and the Multidimensional Dose Articulation Framework (MDAF). The MDAF specifies dose in greater detail than the CII framework and the FITT principle. On this basis we selected the MDAF to be applied to three diverse examples of aphasia rehabilitation research. We next critically examined applicability of the MDAF to aphasia rehabilitation research and identified the next steps needed to systematically conceptualise, measure, and report the multiple dimensions of dose, which together can progress understanding of the effect of treatment dose on outcomes for people with aphasia following stroke. Further consideration is required to enable application of this framework to aphasia interventions that focus on participation, personal, and environmental interventions and to understand how the construct of episode difficulty applies across therapeutic activities used in aphasia interventions.

Keywords

Aphasia, rehabilitation, treatment, dose

Abbreviations

- CII Cumulative Intervention Intensity
- FITT Frequency, intensity, time, and type
- ICF International Classification of Functioning, Disability and Health
- MDAF Multidimensional Dose Articulation Framework

Funding sources

This work was supported by the NHMRC-funded Centre of Research Excellence in Aphasia Recovery and Rehabilitation (#1153236). NAL supported by Heart Foundation (Australia) fellowship (GNT102055). KSH supported by a NHMRC fellowship (#1088449). SH received an Australian Government Research Training Program scholarship.

Disclosures None

Systematic investigation of treatment dose, that is, how much treatment and in what schedule, is essential for a breakthrough in stroke and aphasia recovery¹. To date, investigations of the effect of treatment dose on aphasia recovery have been exploratory, unsystematic, and hampered by issues relating to dose conceptualisation, measurement, and reporting²⁻⁴. In this paper we examine the complexity of aphasia treatment dose exploration and consider conceptual frameworks to underpin the development of high quality dose-related aphasia rehabilitation research.

Systematic reviews and meta-analyses indicate that treatments for aphasia are, on average, effective⁵⁻⁷. However, aphasia is a heterogeneous condition with highly variable treatment response across individuals and point estimates of effects may conceal important individual differences in response to a given treatment dose⁸. Aphasia heterogeneity stems from differential impacts from stroke on i) diffuse neural networks that underpin language processing, and ii) the complex process of interpersonal communication. Effective communication relies on rapid interactions between multiple linguistic components (e.g., phonology, lexical-semantics, syntax, discourse processing) in multiple modalities (e.g., spoken, written, gestural) that intersect with cognitive functions (e.g., attention, working memory). These are mediated by different context-dependent social norms (e.g., formality, familiarity), degrees of conversational freedom (e.g., shared referents, novel topics), and communicative goals (e.g., everyday functional transactions, group social interactions). Aphasia arises from a breakdown of one or more of the linguistic components, resulting in a variety of patholinguistic phenotypes.

Different aphasia treatments have been developed to address this heterogeneity. Impairment-focused approaches aim to target breakdown in linguistic processes. Functional approaches aim to enhance participation in personally relevant communication-related activities and may include nonverbal communication methods such as drawing, gesture, and the use of communication devices. Psychological treatments aim to address the mental health consequences of communication disability, and environmental approaches target communication partners and communication accessibility. It is common in clinical practice for people with aphasia to undertake treatments using multiple different approaches simultaneously9. Determining the required dose of each different treatment approach to achieve the communication goals of a person with aphasia is of primary clinical and research importance. To achieve this, consistent conceptualisation and systematic measurement and reporting of treatment dose is a necessary precursor.

Aims

Following a brief review of the evidence for dose effects in aphasia treatment research, we aim to (1) identify the limitations of current dose conceptualisation, measurement, and reporting in aphasia treatment research, (2) compare and contrast the applicability of existing dose frameworks to aphasia treatment research, (3) apply the most appropriate framework to a range of aphasia rehabilitation studies, and (4) propose steps required to systematically evaluate the effect of dose on treatment outcomes for people with aphasia following stroke.

Evidence for dose effects in aphasia rehabilitation research

Systematic reviews have concluded that higher treatment doses may lead to better aphasia recovery^{3, 5}. The recent network meta-analysis of individual patient data (n=959, 25 trials) by the RELEASE group³ suggested that the greatest language gains measured on standardised aphasia assessment batteries were following doses of 20-50 hours delivered at either 2-4 hours (for functional communication) or 9+ hours (for overall language and comprehension) per week. The 2016 Cochrane review of speech and language therapy in aphasia⁵ likewise found superiority of more treatment hours over fewer for the recovery of functional communication and written expression but found no clear dose-response relationships for other aphasia outcomes.

The critical dose required to demonstrate clinically meaningful and statistically significant recovery of language and communication remains unknown but will likely be specific to aphasia treatment type and phase of recovery. Studies in the acutesubacute phase have found no superiority of relatively higher compared to lower treatment doses^{10, 11}. Husak and colleagues conducted a systematic review of aphasia rehabilitation in the first four months following stroke. Of six studies meeting inclusion criteria, five studies found no significant difference in outcomes between participants provided either a lower or higher number of treatment hours, and one study reported superior findings in outcomes when participants received less treatment in the early recovery period. In contrast, dose-response relationships in the chronic phase of recovery appear to favour higher over lower doses of treatment^{12, 13}. A recent Intensive Comprehensive Aphasia Program delivered 100 hours of treatment over 3 weeks and demonstrated medium to large effect sizes immediately following treatment and at longer term (e.g., 3-month) follow up¹⁴. The dose delivered in this program was much higher than the most frequently prescribed dose of 30 hours as reported in a recent review of dose that examined 112 aphasia treatment research studies². Given these results, it is possible other trials that have published null effects have failed to deliver a sufficient dose to elicit a therapeutic effect5, a phenomenon recognised across the domains of rehabilitation trials1. Therefore, given the heterogeneity of aphasia and uncertainty regarding dose-response relationships, systematic investigation of treatment dose is required to progress this emerging field of research and positively influence language and communication outcomes for people living with aphasia.

Limitations associated with current dose conceptualisation, terminology, and reporting in aphasia rehabilitation research *Dose is under-specified in aphasia rehabilitation research*

Consensus on dose terminology for non-pharmacological treatments has not been established within the stroke rehabilitation literature¹⁵ nor in aphasiology². In aphasia treatment studies, there is inconsistent use of terminology to describe dose dimensions. For example, *dose*, *dosage*, and *intensity* are used interchangeably to refer to divergent concepts including: the number of repetitions within a specific therapy task¹⁶; the number, duration, and frequency of sessions¹⁷; the overall duration of a treatment program in weeks¹⁸; and, the total number of treatment hours provided over the course of an intervention^{5, 19}. This inconsistency creates confusion and confounds attempts to examine dose-response relationships that may underpin treatment effectiveness^{4, 20}.

Aphasia researchers and clinicians most commonly report treatment dose as the amount of time spent in the treatment environment, usually measured in hours⁴. Hours of treatment are easy to calculate, aid comparison between studies, and can be easily interpreted by healthcare providers, recipients, policy makers, and funding bodies. However, measuring dose only in hours may be inadequate due to an inaccurate assumption that all hours of treatment are equal. Clinically, each hour of treatment may comprise a variety of different tasks, targeting different goals, each requiring the provision of a different number and combination of therapeutic tasks that might be punctuated by periods of rest or inactivity²¹. In research reports, especially large trials, it is not always clear how often different therapeutic activities are performed within a given period of time unless treatment details are accurately defined, measured and reported²².

A recurring limitation in examinations of dose effects in aphasia rehabilitation is the inconsistent measurement and reporting of treatment dose^{4, 5, 11, 19}. For example, previous reviews have been constrained by a lack of comprehensive data collection in clinical trials^{4, 5, 19} and have suggested that improved quality of trial reporting "will further contribute to transparency, replication of findings, and subsequent meta-analyses."⁵ Although clear reporting of intervention duration, dose, intensity, and mode of delivery is vital for interpretation of results and study replication, Hoffman et

al.²³ argue these features are frequently omitted from rehabilitation reports. A review of 96 published aphasia rehabilitation studies highlighted underspecification of dose reporting, particularly in early-stage research in which questions of dose were examined before scaling up to definitive trials²⁴. In contrast, a meta-analysis of 67 aphasia treatment data sets with at least 10 participants per study²⁵ found consistent reporting of details of treatment intensity (defined as hours per week; 89.6% of studies), frequency (number of therapy days per week; 98.5%), and dose (total number of therapy hours; 92.5%) at the group level. This highlights that there is variability in reporting of dose along the aphasia research pipeline.

To determine what requires measurement, we must consider the dose of 'active' ingredients²⁶. These are the procedures presumed to teach or enhance new learning and behaviour. For example, in Semantic Feature Analysis, repeatedly pairing the spoken label of a noun with its semantic features is considered an active ingredient (Boyle et al., 2021). Closer examination of the quantity and quality of active ingredients may enhance our understanding of the mechanisms that transform therapy received into improved health and wellbeing^{27, 28}. Conceptualising, measuring, and reporting dose as provision of active ingredients should allow more refined interrogation of dose-response relationships for a given treatment²⁰, ²⁹. Once identified, optimizing delivery of active ingredients has the potential to increase treatment efficiency and effectiveness. *Dose specification in reporting guidelines*

The Template for Intervention Description and Replication (TIDieR)²³ and the Consolidated Standards of Reporting Trials (CONSORT)³⁰ guide standardised reporting of intervention research, but both lack specificity regarding dose reporting. For example, reporting item 8 of the TIDieR²³ requires description of "when" and "how much" treatment has been provided. This includes the "number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose", but these terms are not defined precisely. Reporting Item 4a of the CONSORT Statement extension for reporting non-pharmacological interventions³¹ suggests authors "describe the number of sessions, timing of each session, duration of each session, duration of each main component of each session, and overall duration of the intervention". While this offers greater characterisation of treatment dose, these reporting items provide no guidance regarding what constitutes or how to identify the main components of a session.

The Rehabilitation Treatment Specification System²⁷ was developed with the goal of achieving consistent terminology use and reporting across disciplines, and to support the development of rehabilitation treatments. This system focuses on targets (the behaviour that is expected to change as a result of treatment), ingredients (what a clinician does to effect change), and mechanism(s) of action (why a given treatment works). It has been applied to three broad aphasia intervention approaches: neurobiological32, cognitive-linguistic³³, and functional approaches³⁴. In each case, conceptualising and reporting "ingredients" remained a challenge because there was insufficient prescription within the Rehabilitation Treatment Specification System to guide dose reporting and no other universally agreed upon guidelines for the reporting of dose in aphasia rehabilitation.

To undertake a systematic investigation of dose, the field of aphasia research needs a conceptual framework with common terminology to guide dose articulation that can be implemented across research studies. Consistency is vital to accurately frame research questions, design studies, investigate treatment fidelity, compare across and replicate studies, and improve communication amongst all stakeholders^{23, 25, 28}. Although there are several wellaccepted frameworks and guidelines to support sophisticated study conceptualisation and high-quality reporting of complex behavioural treatment studies^{23, 30, 35}, existing frameworks used in aphasia research underspecify the multidimensional nature of dose in aphasia rehabilitation. An ideal dose framework would provide a comprehensive and granular characterisation of the amount of treatment provided across all types of aphasia treatment. To our knowledge, there are three dose-specific frameworks for nonpharmacological rehabilitation interventions, the Frequency, Intensity, Time, and Type principle (FITT)³⁶ which is commonly applied in physical exercise programs, the Cumulative Intervention Intensity (CII) framework²⁶, and the Multidimensional Dose Articulation Framework (MDAF)¹⁵. We now review the applicability of each framework to aphasia treatment research.

Comparison of the applicability of existing dose frameworks to aphasia rehabilitation research

Frequency, Intensity, Time, and Type principle (FITT)

The American College of Sports Medicine's Guidelines for Exercise Testing and Prescription recommend practitioners use the FITT principle – frequency (how often), intensity (how hard), time (duration or how long), and type (mode or what kind) of exercise – when designing and prescribing individualised physical exercise programs³⁶. Additional components such as volume (total amount of exercise) and progression (exercise advancement) can also be considered³⁶. The FITT principle has been applied, though not routinely, in post-stroke exercise research³⁷, and has recently been used as a framework to quantify the dose of swallowing rehabilitation exercises provided in an inpatient rehabilitation setting³⁸. It has not, to our knowledge, been applied to aphasia rehabilitation research.

Cumulative Intervention Intensity framework (CII)

Warren and colleagues' CII framework²⁶ asserts that the amount of treatment provided or received is a product of the number of times the active ingredients of treatment are applied per session and the number of sessions provided over the treatment duration. The active ingredients are the actions performed by either the treatment provider or recipient that are theoretically linked to the underlying mechanisms of that treatment²⁷. Figure 1 depicts the relationship between dose form, dose, session duration, session frequency, total intervention duration, and cumulative intervention intensity with an adaptation to the original CII framework²⁶ separating dose and session duration because these two parameters can be manipulated independently (e.g., dose of 50 or 100 trials in a 30-minute session, dose of 100 trials in a 30- or 60-minute session)²⁹. First developed to characterise treatments in the field of developmental disabilities, this framework has been used to report treatment dose in a small number of aphasia studies^{16, 39} and other speech-language pathology areas such as apraxia of speech⁴⁰ and paediatric language⁴¹. For example, in a study comparing the effect of intensive versus distributed treatment, Dignam and colleagues used the CII to demonstrate non-significant differences in the average number of therapeutic inputs provided throughout treatment between groups³⁹.



Figure 1 Cumulative Intervention Intensity framework, as adapted by Baker³⁰ (copyright Wiley, reproduced with permission)



Figure 2 Multidimensional Dose Articulation Framework¹⁵ (copyright Wolters Kluwer Health, Inc. reproduced with permission

Multidimensional Dose Articulation Framework (MDAF)

A group of multidisciplinary stroke researchers with expertise spanning upper limb, mobilisation, motor speech, and cognitive functions proposed the MDAF¹⁵ (Figure 2). It was developed to guide the specification of non-pharmacological therapeutic dose, conceptualise the multidimensional nature of, and links between, dose dimensions, and provide consistent terminology across the stroke recovery and rehabilitation fields¹⁵. As Figure 2 shows, an intervention is provided over a duration (e.g., weeks, months, or years). Within that time, treatment occurs on one or more days which can vary in number and spacing (e.g., daily or weekly treatment). On any given treatment day, there will be one or more sessions which can be defined by their length in time. Sessions contain episodes of variable length that are either active (i.e., time spent on a task) or inactive (i.e., pauses or breaks). The ratio of active to inactive time in a given session renders the session density. Active episodes comprise tasks of different intensity (Figure 2 height of episode) and difficulty (colour of episode). Taken together, these multiple dimensions of dose constitute the overall amount of treatment provided or received. The MDAF emphasizes it can be used to conceptually plan (methods) and actually report what dose is delivered (results). Due to the recency of publication of this framework, there are no published examples of its application in the literature.

Table 1 provides a comparison of dose dimensions and terms defined by the FITT principle, the CII framework, and the MDAF including reference to commonly used terms in the aphasia literature. There is some overlap between these conceptual frameworks but also some important structural differences. The MDAF clearly provides a more comprehensive characterisation of dose than the CII framework and the FITT principle (Table 1). In particular, the MDAF specifies more detailed temporal parameters (days, number and spacing of days and sessions) and episode-level characteristics (length, difficulty, and intensity) than the CII framework and the FITT principle. Neither the CII framework nor the FITT principle include dose dimensions that are not captured in the MDAF. The CII framework and the FITT principle include specification of the content of treatment (labelled dose form and type, respectively) whereas the MDAF does not include specification of treatment content; the MDAF was developed to examine constructs of dose irrespective of treatment type and is intended to be used in conjunction with treatment specification tools (e.g., TIDieR). Although treatment type and treatment dose are interrelated and require consideration when designing a research protocol or clinical intervention program, the current investigation is primarily concerned with dose conceptualization, not treatment specification.

Given uncertainty regarding which dose parameters are important for recovery, greater specification may be advantageous

Conceptual descriptor (terminology used in aphasia literature)	FITT	СП	MDAF
Task being performed (task, activity)	Туре	Dose form	Detailed using treatment specification tool (e.g., TIDieR)
Overall amount of treatment provided or received (dose, dosage)	Volume	Cumulative intervention intensity	Defined in relation to all dimensions listed below
Overall length of the intervention (total duration, intervention/treatment period/phase)		Total intervention duration	Duration
Number of days of intervention			Days (number)
The distribution of days, number of days per week			Days (spacing)
Number of sessions		Product of total intervention duration x session frequency	Sessions (number)
The distribution of sessions, number of sessions per week (<i>frequency</i> , <i>intensity</i> *)	Frequency	Session frequency	Sessions (spacing)
Timed duration of session(s)	Time	Session duration	Session length
Amount of time spent actively engaged in therapy activities [#] (time-on-task)			Sum of length of active episodes
Proportion of time spent actively engaged in therapy activities			Session density (i.e., sum of length of active episodes / session length)
Basic unit of treatment which contains the active ingredient(s) of a treatment		Teaching episode	Episode
Number of episodes administered during a session		Dose	Sum of episodes
How long the task is performed for, in units of time [#]			Episode length
How hard the task is to perform [#] (task difficulty, task hierarchy)			Episode difficulty
How much of the task is performed per episode or unit of time [#] (<i>dose rate</i> ¹⁶)	Intensity		Episode intensity

Table 1 Dose descriptors and common terms used in aphasia literature that are covered by the FITT principle³⁶, CII framework²⁶, and MDAF¹⁵

* Commonly defined as the number of hours per week. # Descriptors used by Hayward and colleagues¹⁵.

Г

Study		Harnish et al., 2014 ¹⁶	Rose et al., 2022 ⁴²	Attard et al., 2018 ⁴³
Treatment description including		Individual cued picture naming treatment. Each	Group-based treatment. Participants received either	Group-based treatment. Multiple treatment
tasks performed		episode, one picture was presented followed by a	Constraint-Induced Aphasia Therapy-Plus or	approaches including communication therapy,
		fixed sequence of eight cues (confrontation,	Multi-Modality Aphasia Therapy44 and	conversation activity, social interaction, peer
		orthographic, repetition, delayed recall,	participated in naming, phrase and sentence	support, psychological support, stroke and aphasia
		semantic, phonological, repetition, delayed	production, requesting and clarification of speech	education, and participation in art, music, and yoga
		recall) with one naming opportunity per cue.	acts within six different communication games.	activities.
e dimension	Duration	2 weeks	2 weeks	12 weeks
	Days (number)	8 days	10 days	12 days
	Days (spacing)	4 days per week	Daily	1 day per week
	Sessions (number)	8 sessions	30 sessions	12 sessions
	Sessions (spacing)	1 per day	3 per day	1 per day
	Session length	60 minutes	60 minutes	120 minutes
	Session density	Not reported	Not reported	Not reported
	(proportion of time spent	Session density estimated to be 1 (60 minutes	Participants in groups of 3 take turns to lead the	
	active compared to	time on task, 0 time off task)	task. Each participant therefore leads on	
	inactive)		approximately 20 minutes per session and follows	
			on 40 minutes per session.	
dos	Episode length	Approximately 1 minute	Variable depending on task and participant factors	Not reported
ц			(e.g., aphasia severity)	
DA	Episode difficulty	Not reported	The task and targets are selected based on	Not reported
Z			participant performance using a prespecified rubric	
			based on linguistic difficulty.	
	Episode intensity	8 naming opportunities per episode	Variable depending on task and participant factors	Not reported
			(e.g., aphasia severity).	
	Additional dose	400 naming opportunities per session, 6.67	15-minute daily home practice	Spouses involved in a parallel program: some
	dimensions	naming opportunities per minute	Participant self-rating of fatigue and distress was	sessions joint with person with aphasia and some
			measured on 100mm visual analogue scale at start	sessions separate for spouses.
			and end of every day.	

Table 2 Application of the MDAF to the published reports of three selected intervention studies

when evaluating dose-response relationships. Therefore, the MDAF is the most likely candidate of these three frameworks to progress understanding of dose-response relationships in poststroke aphasia rehabilitation research. We will now apply the MDAF to three diverse aphasia treatments and demonstrate its potential utility.

Applications of the MDAF to aphasia rehabilitation research

Table 2 demonstrates application of the MDAF to intervention studies that we selected to cover the breadth of aphasia treatment approaches including an individual lexical-retrieval treatment¹⁶, a group-based combined lexical retrieval and syntax treatment⁴², and an interdisciplinary group-based intervention that targets multiple areas of the International Classification of Functioning, Disability and Health (ICF)⁴³. Each column in Table 2 represents the overall amount of treatment provided in each study. The values in Table 2 are the doses planned to have been delivered, as reported in each study. In this study, we retrospectively applied the MDAF to published reports however, the MDAF is intended to be used prospectively to describe both the planned and actual doses delivered in a trial¹⁵. While the dimensions of duration, days, session length, and density were consistently reported, data concerning the dimensions of episode length, difficulty, and intensity were not always available. Multidimensional dose specification was comprehensive for the individual and groupbased impairment-focused treatments^{16, 42}; all dose dimensions were reported in these studies with the exception of episode difficulty in the individual therapy¹⁶. Dose specification as per the MDAF was only partially achieved in the group-based intervention targeting multiple ICF areas⁴³ with only overall duration, number of treatment days, number of treatment sessions, and session length reported.

A key strength of the MDAF is that it provides a systematic approach for specifying and reporting dose that can be applied to a range of aphasia treatments. Lack of reporting of some dose dimensions in published studies may reflect limited attention to these dimensions in the intervention design phase. Indeed, the MDAF may be an especially useful tool in early-phase research when questions regarding dose-relationships should be addressed before scaling up to large scale definitive trials¹⁵. We will now outline challenges associated with describing and quantifying dose dimensions in complex behavioural interventions.

Challenges applying the MDAF to aphasia rehabilitation research

Aphasia treatments range in scope across the dimensions of the ICF including those focused on participation (e.g., community aphasia groups⁴³), personal factors (e.g., $mood^{45}$), and the environment (e.g., Communication Partner Training⁴⁶). Table 2 demonstrates that isolating episodes within interventions focused on reducing linguistic impairment, such as naming or syntax therapies, is reasonably straightforward¹⁶ but is more complicated in groupbased treatments targeting multiple areas of the ICF43. Interventions focused on participation, personal, or environmental factors are generally multifaceted in design and application, and frequently involve dyads or groups of people. Defining, isolating, and counting episodes in these multicomponent interventions requires further research. For example, within a complex group-level communication intervention that uses art making as a therapeutic activity and social interaction as the target⁴³, what is the episode and what is episode difficulty? Can these treatment approaches be reduced to discrete episodes or do they require a less granular, more global framework that allows for flexibility and iterative adaptation as therapies develop over the course of intervention? Aphasia rehabilitation is not alone in utilising multicomponent approaches that span the entire ICF, with social work another example where alternative frameworks for conceptualising dose and ensuring treatment fidelity have been applied⁴⁷. For example, Washington and colleagues47 demonstrated stronger fidelity when using a composite dose measure compared to a measure of the sum of individual elements in their study of a complex multicomponent social work intervention.

The MDAF includes episode difficulty as a static quality intrinsic to the task being performed. Although the role of perceived task difficulty in aphasia treatment is being evaluated⁴⁸, neither perceived nor intrinsic task difficulty have been linked to dose despite the clinical relevance. In aphasia treatments, difficulty may be operationalised in relation to choice of targets and their lexical properties, cognitive load, linguistic level, communicative context, presence or absence of distractors or cues, or speed of response. For example, in word retrieval treatment, a task requiring retrieval of an abstract, low frequency target word (e.g., justice) will be intrinsically more difficult than retrieval of a concrete, high frequency word (e.g., man)⁴⁹. Using those words in sentences may be experienced as a more challenging task for individuals with syntactic processing deficits than those without. Importantly, this perceived difficulty may reduce with treatment while the intrinsic difficulty of the task remains unchanged. Clinicians may aim to pitch a given task at an appropriate challenge point by manipulating the rate that word and sentence production tasks need to be completed and the complexity of the communication environment where the task(s) take place (e.g., with the therapist in a quiet clinic room; in a group conversation; in a busy shopping centre). While reliable measurement of task difficulty within and across different therapeutic tasks is still to be established, its identification as a distinct dose parameter that is intrinsic to the tasks and could be experimentally manipulated is a necessary precursor step.

In summary, the MDAF appears well suited to dose description for treatments in which episodes are discrete and countable but more work is required to determine how best to articulate and quantify dose in complex multi-faceted aphasia treatments. Further work will be required to understand the dimension of episode difficulty across therapeutic activities used in aphasia interventions.

Box 1 Next steps to progress systematic dose conceptualisation, measurement, and reporting in aphasia rehabilitation

- Aphasia researchers could attempt to capture the multiple dimensions of dose in treatment studies
- Aphasia researchers could use the MDAF to systematically specify dose in early-phase research protocols and reporting
- Aphasia researchers could aim to delineate and define episodes within treatments that target discourse, participation, personal factors, and the communication environment
- Aphasia researchers could conduct research that aims to understand episode difficulty within and across different therapeutic tasks. This may require development of reliable measurement tools for episode difficulty.
- Aphasia clinicians could use the MDAF to systematically capture clinical dose data

Summary

Dose is an important factor in stroke and aphasia rehabilitation. Personalised treatment prescription should consist not only of the type but also the dose of treatment required to promote long term positive change for a specific individual with aphasia. Given the heterogeneity of people with aphasia and the large variability in aphasia treatment targets and approaches, treatment doses will likely require personal calibration to a range of biological, aphasia, and psychosocial recovery factors with consideration of personal relevance, motivation, and reward. To get closer to this objective, we need to document all dose dimensions for a given treatment⁵⁰. Moreover, investigation of dose prompts deep thinking into the theory behind why and how a treatment works. While the issue of what comprises a clinically practical dose to deliver is relevant, it is distinct from the question of the dose required to drive recovery. The priority for researchers is to use treatment theory and systematic investigation to determine personalised dose targets in order that aphasia outcomes can be improved for individuals. Once gold-standard treatment regimens are established, the discussion of what is feasible, practical, and economical will follow. A multidimensional dose framework is required to guide the development, implementation, and evaluation of dose-finding studies designed to determine the range of safe and tolerable doses of an intervention and dose-response relationships. Such a

framework would enable synthesis of data across studies and theoretical exploration of what drives treatment response in aphasia treatments, inform the extension of reporting guidelines, aid clinical decision-making, and guide health policy makers. We propose the Multidimensional Dose Articulation Framework¹⁵ is a first step towards this purpose and suggest further research to refine this framework to support application to aphasia interventions focused on participation, personal, and environmental intervention approaches. Aphasia researchers are urged to consider using the MDAF to describe dose prescription in research protocols and to frame the reporting of dose parameters in aphasia treatment research.

References

- Dalton EJ, Churilov L, Lannin NA, Corbett D, Hayward KS. Dose articulation in preclinical and clinical stroke recovery: Refining a discovery research pipeline and presenting a scoping review protocol. *Frontiers in neurology*. 2019;10:1148
- Harvey SR, Carragher M, Dickey MW, Pierce JE, Rose ML. Treatment dose in post-stroke aphasia: A systematic scoping review. *Neuropsychological rehabilitation*. 2021;31:1629-1660
- REhabilitation and Recovery of peopLE with Aphasia after StrokE (RELEASE) Collaborators. Dosage, intensity, and frequency of language therapy for aphasia: A systematic review–based, individual participant data network metaanalysis. *Stroke*. 2022;29:956-967
- Harvey S, Carragher M, Dickey MW, Pierce JE, Rose ML. Dose effects in behavioural treatment of post-stroke aphasia: A systematic review and meta-analysis. *Disability and rehabilitation*. 2022;44:2548-2559
- Brady MC, Kelly H, Godwin J, Enderby P, Campbell P. Speech and language therapy for aphasia following stroke. *Cochrane database of systematic reviews*. 2016
- Pierce JE, O'Halloran R, Menahemi-Falkov M, Togher L, Rose ML. Comparing higher and lower weekly treatment intensity for chronic aphasia: A systematic review and meta-analysis. *Neuropsychological rehabilitation*. 2021;31:1289-1313
- Robey RR. A meta-analysis of clinical outcomes in the treatment of aphasia. *Journal speech, language, hearing reseach.* 1998;41:172-187
- Menahemi-Falkov M, Breitenstein C, Pierce JE, Hill AJ, O'Halloran R, Rose ML. A systematic review of maintenance following intensive therapy programs in chronic post-stroke aphasia: Importance of individual response analysis. *Disability* and rehabilitation. 2021:1-16
- Rose M, Ferguson A, Power E, Togher L, Worrall L. Aphasia rehabilitation in australia: Current practices, challenges and future directions. *International journal of speech-language pathology*. 2014;16:169-180
- Godecke E, Armstrong E, Rai T, Ciccone N, Rose ML, Middleton S, et al. A randomized control trial of intensive aphasia therapy after acute stroke: The Very Early Rehabilitation for Speech (VERSE) study. *International journal of stroke*. 2021;16:556-572
- 11. Husak RS, Wallace SE, Marshall RC, Visch-Brink EG. A systematic review of aphasia therapy provided in the early period of post-stroke recovery. *Aphasiology*. 2021:1-34
- 12. Breitenstein C, Grewe T, Floel A, Ziegler W, Springer L, Martus P, et al. Intensive speech and language therapy in patients with chronic aphasia after stroke: A randomised, openlabel, blinded-endpoint, controlled trial in a health-care setting. *The Lancet*. 2017;389:1528-1538
- Stahl B, Mohr B, Buscher V, Dreyer FR, Lucchese G, Pulvermuller F. Efficacy of intensive aphasia therapy in patients with chronic stroke: A randomised controlled trial. *Journal of neurology, neurosurgery and psychiatry.* 2018;89:586-592
- 14. Leff AP, Nightingale S, Gooding B, Rutter J, Craven N, Peart M, et al. Clinical effectiveness of the queen square intensive comprehensive aphasia service for patients with poststroke aphasia. *Stroke*. 2021;52:e594-e598

- Hayward KS, Churilov L, Dalton EJ, Brodtmann A, Campbell BCV, Copland D, et al. Advancing stroke recovery through improved articulation of nonpharmacological intervention dose. *Stroke*. 2021;52:761-769
- Harnish SM, Morgan J, Lundine JP, Bauer A, Singletary F, Benjamin ML, et al. Dosing of a cued picture-naming treatment for anomia. *American journal of speech-language pathology*. 2013;23:S285-299
- 17. Marshall RC, Tompkins CA, Phillips DS. Improvement in treated aphasia: Examination of selected prognostic factors. *Folia phoniatrica et logopaedica*. 1982;34:305-315
- Kurland J, Anna L, Stokes P. Effects of a tablet-based home practice program with telepractice on treatment outcomes in chronic aphasia. *Journal of speech, language & hearing research.* 2018;61:1140-1156
- Brady MC, Ali M, VandenBerg K, Williams LJ, Williams LR, Abo M, et al. Dosage, intensity, and frequency of language therapy for aphasia: A systematic review–based, individual participant data network meta-analysis. *Stroke*. 2021;29:956-967
- 20. Brogan E, Ciccone N, Godecke E. An exploration of aphasia therapy dosage in the first six months of stroke recovery. *Neuropsychological Rehabilitation*. 2021;31:1254-1288
- 21. Brogan E, Godecke E, Ciccone N. Behind the therapy door: What is "usual care" aphasia therapy in acute stroke management? *Aphasiology*. 2020;34:1291-1313
- 22. Behn N, Harrison M, Brady MC, Breitenstein C, Carragher M, Fridriksson J, et al. Developing, monitoring, and reporting of fidelity in aphasia trials: Core recommendations from the collaboration of aphasia trialists (cats) trials for aphasia panel. *Aphasiology*. 2022:1-23
- Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: Template for intervention description and replication (tidier) checklist and guide. *Bmj.* 2014;348:g1687
- 24. Dipper LT, Franklin S, De Aguiar V, Baumgaertner A, Brady M, Best W, et al. An umbrella review of aphasia intervention description in research: The aspire project. *Aphasiology*. 2021:1-26
- 25. Collaboration R. Communicating simply, but not too simply: Reporting of participants and speech and language interventions for aphasia after stroke. *International journal of speech-language pathology*. 2020;22:302-312
- 26. Warren SF, Fey ME, Yoder PJ. Differential treatment intensity research: A missing link to creating optimally effective communication interventions. *Mental retardation and developmental disabilities research reviews*. 2007;13:70-77
- 27. Van Stan JH, Dijkers MP, Whyte J, Hart T, Turkstra LS, Zanca JM, et al. The rehabilitation treatment specification system: Implications for improvements in research design, reporting, replication, and synthesis. *Archives of physical medicine and rehabilitation*. 2019;100:146-155
- 28. Fridriksson J, Basilakos A, Boyle M, Cherney LR, DeDe G, Gordon JK, et al. Demystifying the complexity of aphasia treatment: Application of the rehabilitation treatment specification systemx. *Archives of physical medicine and rehabilitation*. 2022;103:574-580
- 29. Baker E. Optimal intervention intensity. *International journal* of speech-language pathology. 2012;14:401-409
- Schulz KF, Altman DG, Moher D. Consort 2010 statement: Updated guidelines for reporting parallel group randomised trials. *Trials*. 2010;11:1-8
- Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, Group* C. Extending the consort statement to randomized trials of nonpharmacologic treatment: Explanation and elaboration. *Annals of internal medicine*. 2008;148:295-309
- 32. Basilakos A, Hula WD, Johnson LP, Kiran S, Walker GM, Fridriksson J. Defining the neurobiological mechanisms of action in aphasia therapies: Applying the rehabilitation treatment specification system framework to research and practice in aphasia. *Archives of physical medicine and rehabilitation*. 2022;103:581-589

- 33. Boyle M, Gordon JK, Harnish SM, Kiran S, Martin N, Rose ML, et al. Evaluating cognitive-linguistic approaches to interventions for aphasia within the rehabilitation treatment specification system. *Archives of physical medicine and rehabilitation*. 2022;103:590-598
- 34. Cherney LR, DeDe G, Hoover EL, Murray L, Obermeyer J, Pompon RH. Applying the rehabilitation treatment specification system to functional communication treatment approaches for aphasia. *Archives of physical medicine and rehabilitation*. 2022;103:599-609
- 35. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. Spirit 2013 statement: Defining standard protocol items for clinical trials. *Annals of internal medicine*. 2013;158:200-207
- American College of Sports M. Acsm's guidelines for exercise testing and prescription. Lippincott williams & wilkins; 2013.
- 37. Billinger SA, Boyne P, Coughenour E, Dunning K, Mattlage A. Does aerobic exercise and the fitt principle fit into stroke recovery? *Current neurology and neuroscience reports*. 2015;15:1-8
- Choy J, Pourkazemi F, Anderson C, Bogaardt H. Dosages of swallowing exercises prescribed in stroke rehabilitation: A medical record audit. *Dysphagia*. 2022:1-14
- 39. Dignam J, Copland D, McKinnon E, Burfein P, O'Brien K, Farrell A, et al. Intensive versus distributed aphasia therapy: A nonrandomized, parallel-group, dosage-controlled study. *Stroke*. 2015;46:2206-2211
- Mozeiko J, Abolafia V, Garneau A, Coelho C. Intensive sound production treatment for severe, chronic apraxia of speech. *Aphasiology*. 2020;34:1164-1181
- Justice LM. Conceptualising "dose" in paediatric language interventions: Current findings and future directions. *International journal of speech-language pathology*. 2018;20:318-323
- 42. Rose ML, Nickels L, Copland D, Togher L, Godecke E, Meinzer M, et al. Results of the compare trial of constraintinduced or multimodality aphasia therapy compared with usual care in chronic post-stroke aphasia. *Journal of neurology, neurosurgery & psychiatry.* 2022;93:573-581
- Attard MC, Loupis Y, Togher L, Rose ML. The efficacy of an inter-disciplinary community aphasia group for living well with aphasia. *Aphasiology*. 2018;32:105-138
- 44. Rose ML, Attard MC, Mok Z, Lanyon LE, Foster AM. Multimodality aphasia therapy is as efficacious as a constraintinduced aphasia therapy for chronic aphasia: A phase 1 study. *Aphasiology*. 2013;27:938-971
- Baker C, Worrall L, Rose M, Ryan B. 'It was really dark': The experiences and preferences of people with aphasia to manage mood changes and depression. *Aphasiology*. 2020;34:19-46
- 46. Simmons-Mackie N, Raymer A, Cherney LR. Communication partner training in aphasia: An updated systematic review. *Archives of physical medicine and rehabilitation*. 2016;97:2202-2221
- 47. Washington T, Zimmerman S, Cagle J, Reed D, Cohen L, Beeber AS, et al. Fidelity decision making in social and behavioral research: Alternative measures of dose and other considerations. *Social work research*. 2014;38:154-162
- Bruehl S, Willmes K, Binkofski F. Interfered-naming therapy for aphasia (inta): Behavioural and computational effects of a novel linguistic-executive approach. *Aphasiology*. 2021:1-22
- Nickels L. Therapy for naming disorders: Revisiting, revising, and reviewing. *Aphasiology*. 2002;16:935-979
- 50. Keith RA. Treatment strength in rehabilitation. Archives of physical medicine and rehabilitation. 1997;78:1298-1304