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Introduction and Methods

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Abstract

The SREBR was designed to be an up-to-date review of the current evidence in stroke rehabilitation, related to the effectiveness of both pharmacological and non-pharmacological interventions. In this first chapter, we describe the origins of the SREBR and detail the methodology including the literature search strategy, data abstraction process, scoring the methodological quality of individual studies and the process that was used to formulate the levels of evidence which form the basis of the review.

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1.1 Introduction

The Heart and Stroke Foundation of Canada (2003) estimates that there are approximately 50,000 new strokes in Canada each year, although precise estimates are difficult to obtain. Every ten minutes someone in Canada suffers from a stroke. The economic and human costs associated with stroke are considerable, particularly when the impact of stroke-related disability is considered. With the ageing of the population these numbers are expected to rise despite the best efforts of stroke prevention and acute care interventions (Teasell et al., 2014).

Stroke rehabilitation can help to significantly reduce disabilities and handicaps arising from stroke, allowing stroke survivors to regain their independence.

The SREBR was conceived when the Heart and Stroke Foundation of Ontario (HSFO), in consultation with the Ontario Ministry of Health and Long-Term Care (MoHLTC), established a Consensus Panel on Stroke Rehabilitation in 1999. *The Stroke Rehabilitation Consensus Panel Report* was subsequently submitted to the HSFO in May 2000. That report came up with 15 recommendations. The 12th recommendation stated *"The Ministry of Health and Long-Term Care and the Heart and Stroke Foundation of Ontario jointly support an ongoing program to review and summarize the current state of stroke rehabilitation research, with the purpose of maintaining timely and accurate information on effective stroke rehabilitation, identifying ideas for further research, supporting continuous peer-review and encouraging improved evidence-based practice."* The Stroke Rehabilitation Evidence-Based Review (SREBR) was intended to help fulfill that recommendation and continues to do so 18 years and 18 editions later.

The SREBR was designed to be an up-to-date review of the current evidence in stroke rehabilitation, related to the effectiveness of both pharmacological and non-pharmacological interventions. We continue to update the review annually, with the aim of providing a comprehensive, easily accessible review, which will help to facilitate a best-practice approach to stroke rehabilitation. A number of factors make such a review increasingly critical: 1) The limitations of acute and preventative measures in stroke care; 2) Increasingly aging populations in a number of countries with a growing number of stroke survivors; 3) An impressive and growing evidence base for the efficacy of stroke rehabilitation; 4) The complex interdisciplinary nature of stroke rehabilitation; 5) An increasing emphasis on evidence-based practice and guideline adherence in improving stroke rehabilitation outcomes. What nobody anticipated was that there would be so many new studies, a number approaching almost 3,000 RCTs at the time of this writing.

1.2 Chapter Structure and Format

Due to the increasing number of studies included with each new EBRSR edition, the length of the chapters will continue to increase in size, making it more difficult to access the information of interest. For this reason, the 18th edition of the EBRSR divides each chapter with the exception of 1 through to 5 and Chapter 20 in two documents to ease the access to the core information discussed in the review. Each chapter will consist of the primary review document and a supplementary document containing tables summarizing key aspects of the studies included in the review document. All tables in the supplementary document are numbered to correspond to the respective sections/subsections in primary review.

1.2.1 Primary Review Document Format

Each chapter with the exception of 20, follows a standard format. A title page and abstract introduces every chapter, followed by the key points of the chapter which are conveniently provided at the beginning and throughout the document where the appropriate topic is being discussed. A table of contents is also provided for pagination purposes. The content of the chapter is further formatted such that each section consists of an introduction, often followed by various tables which are analyzed in the discussion section that follows. Based on the data presented in the discussion, levels of evidence are formulated and conclusions are drawn (refer to section 1.4.1 below for information regarding the levels of evidence). Deviations from this presentation format occurs in the cases where there is a lack of literature hence a descriptive review of the data is provided. As with the key points, the levels of evidence are provided throughout the chapter and compiled at the end of the chapter prior to the references.

1.2.2 Supplementary Document Format

In the previous EBRSR versions, summary tables of the studies included for review were often provided in one document incorporated with the content of the chapter. Starting from the 17th edition, the summary tables were removed from the primary review document and provided in a supplementary document. Furthermore, the new summary tables varied slightly in format from the previous version to include additional information such as the time post-stroke (TPS) and demographic data, and to delineate more clearly the key concepts extracted from each study under the headings described below:

1. **Study:** Includes the primary author name, the year of publication, country of publication, study design, PEDro score (where applicable), time post-stroke (TPS) as a mean value for the population sample in question, and the sample size.
2. **Methods:** Divided in 3 sections:
    a. **Population**: Includes demographic information concerning the study sample.
    b. **Intervention**: Provides information regarding the interventions being studied and their prescription, along with the timeline of the study.
    c. **Outcomes**: Includes information pertaining to the outcomes measured in the study.
3. **Results**: Includes the major results of the study.

As with the primary review document, a title page, the table of contents, and a reference list is provided.

1.3 Article Assessment

1.3.1 Literature Search Strategy

For the first edition of the SREBR a literature search using multiple databases (MEDLINE, EBASE, MANTIS, PASCAL and Sci Search) was conducted to identify all potential trials published from 1970-2001, regardless of study design. The search was restricted to the English language and excluded animal studies. Search terms included, but were not restricted to: *"stroke", "cerebrovascular accident", "cerebrovascular disorder", "rehabilitation", "physiotherapy", "occupational therapy", "speech therapy", "recreation therapy"*. From 2001 onwards, the authors of each of the chapters have conducted their own searches. Databases used include EMBASE, CINAHL, PubMED, ProQuest, PsycINFO, AMED, and Scopus. Key terms were tailored to identify potential trials within each subsection of every chapter. Depending on the breadth of the current evidence, searches may have been restricted to randomized

controlled trials, since they are given the greatest emphasis when formulating conclusions. This review was restricted to published works. Although it was not confined to the results from randomized controlled trials (RCT), these articles received priority when formulating conclusions. Systematic reviews and meta-analyses were also incorporated in the content of the chapters.

1.3.2 Data Abstraction and Quality Assessment Tool

Methodological quality of individual RCTs was assessed using the Physiotherapy Evidence Database (PEDro) tool. PEDro (which can be found at: http://www.pedro.fhs.usyd.edu.au/scale_item.html) was developed for the purpose of accessing bibliographic details and abstracts of randomized-controlled trials (RCT), quasi-randomized studies and systematic reviews in physiotherapy. Studies included in this review using a non-experimental or uncontrolled design (non-randomized comparative trials, cohort studies or retrospective studies) could not be assigned a PEDro score and were given a "No Score" designation.

The PEDro Scale consists of 10 quality ratings each receiving either a yes or no score. The scale and the authors' interpretation and implementation of the scoring system is detailed in Table 1. In many cases, the criteria detailed by PEDro were easily applied and have been reproduced here almost verbatim. However, there was a discrepancy in the scoring of adequacy of follow-up (#7).

Table 1. The PEDro Scale

1. ***"Subjects were randomly allocated to groups."*** (in a crossover study, subjects were randomly allocated an order in which treatments were received). A point for random allocation was awarded if random allocation of patients was stated in its methods. The precise method of randomization need not be specified. Procedures such as coin-tossing and dice-rolling were considered random. Quasi-randomization allocation procedures such as allocation by bed availability did not satisfy this criterion.

2. ***"Allocation was concealed."*** A point was awarded for concealed allocation if this was explicitly stated in the methods section or if there was reference that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was "off-site."

3. ***"The groups were similar at baseline regarding the most important prognostic indicators."*** A trial was awarded a point for baseline comparability if at least one key outcome measure at baseline was reported for the study and control groups. This criterion was satisfied even if only baseline data of study completed-only subjects were presented.

4. ***"There was blinding of all subjects."*** The person in question (subject, therapist or assessor) was considered blinded if he/she did not know which group the subject had been allocated to. In addition, subjects and therapists were only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In drug therapy trials, the administrator of the drug was considered the therapist and was considered blinded if he/she did not prepare the drug and was unaware of the drug being administered.

5. ***"There was blinding of all therapists who administered the therapy."*** (refer to criteria 4.)

6. ***"There was blinding of all assessors who measured at least one key outcome"*** (refer to criteria 4).

7. ***"Adequacy of follow-up."*** For the purposes of this review, follow-up was considered adequate if all or 85% of

subjects that had been originally randomized could be accounted for at the end of the study.

8. ***"Intention to treat."*** All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat". For purpose of the present evidence-based review, a trial was awarded a point for intention-to-treat if the trial explicitly stated that an intention-to-treat analysis was performed or if all of the subjects received the intervention.

9. ***"The results of between-group statistical comparisons are reported for at least one key outcome."*** Scoring of this criterion was design dependent. As such, between groups comparison may have involved comparison of two or more treatments, or comparison of treatment with a control condition. The analysis was considered a between-group analysis if either a simple comparison of outcomes measured after the treatment was administered was made, or a comparison of the change in one group with the change in another was made. The comparison may be in the form of hypothesis testing (e.g. p-value) or in the form of an estimate (e.g. the mean, median difference, difference in proportion, number needed to treat, relative risk or hazard ratio) and its confidence interval. A trial was awarded a point for this criterion if between-group comparison on at least one outcome measure was made and its analysis of comparison was provided.

10. ***"The study provides both point measures and measures of variability for at least one key outcome."*** A point measure was referred as to the measure of the size of the treatment effect. The treatment effect was described as being either a difference in group outcomes, or as the outcome in (each of) all groups. Measures of variability included standard deviations, standard errors, confidence intervals, interquartile ranges (or other quartile ranges), and ranges. Point measures and/or measures of variability that were provided graphically (for example, SDs may be given as error bars in a Figure) were awarded a point as long as it was clear what was being graphed (e.g. whether error bars represent SDs or SEs). For those outcomes that were categorical, this criterion was considered to have been met if the number of subjects in each category was given for each group.

(Although the identification of eligibility criteria is also considered under the PEDro scoring system, it was not used to calculate PEDro scores for this review. Subject selection influences the external validity, not the internal or statistical validity of a study).

The maximum score a study could receive was 10. Two independent raters reviewed each article. Scoring discrepancies were resolved through discussion.

Studies scoring 9-10 were considered methodologically to be of "excellent" quality. Studies with PEDro scores ranging from 6-8 were considered to be of "good" quality, while studies scoring 4-5 were of "fair" quality. Studies that scored below 4 were felt to be of "poor" quality. The authors arrived at these descriptive terms of quality assessment arbitrarily in an effort to simplify the interpretation of results. PEDro scores were included as a guide to help readers interpret the methodological quality. Trials of low quality were not excluded from the review. Non-RCTs could not be assigned a PEDro score and received a "No Score" designation. They were used to formulate conclusions only in the absence of RCTs.

1.4 Determining Levels of Evidence

1.4.1 Assigning Levels of Evidence and Formulating Conclusions

There are many systems currently available to summarize a body of knowledge and to establish levels of evidence. Some of these are increasingly complex, requiring a specialized body of knowledge for correct

interpretation. With our focus on ease and accessibility, we intentionally chose a system that was simple and straight-forward. The levels of evidence used to summarize the findings are based on the levels of evidence developed by Sackett et al. (2000). For the purpose of this review, a simplified version of the categories used by Sackett et al. (2000) was adopted. Instead of the original 10 scoring categories, we developed a scoring system ranging from a level 1 evidence to a level 5 evidence,and added descriptions to each category to help designate the appropriate level of evidence based on the type of research design. In the Version 4.0 of this grading scheme used in this review, the evidence level of 1 category is further divided into 2 subcategories to distinguish between a single RCT with a PEDro score ≥ 6 (Level 1b), and 2 or more RCTs with PEDro scores ≥ 6 (Level 1a) (see Table 2).

Table 2. Modified Sackett Scale Version 4.0.

Level	Research Design	Description
Level 1a	Randomized Controlled Trial (RCT)	More than 1 Higher RCT: Randomized Controlled Trial, PEDro score ≥ 6. Includes within subjects comparison with randomized conditions and cross-over designs.
Level 1b	RCT	1 Higher Randomized Controlled Trial, PEDro score ≥ 6.
Level 2	RCT	Lower RCT, PEDro score < 6
	Prospective Controlled Trial (PCT)	Prospective Controlled Trial (not randomized).
	Cohort	Prospective Longitudinal study using at least 2 similar groups with one exposed to a particular condition.
Level 3	Case Control	A retrospective study comparing conditions, including historical cohorts.
Level 4	Pre-Post	A prospective trial with a baseline measure, intervention, and a post-test using a single group of subjects.
	Post-test	A prospective post-test with two or more groups (intervention followed by post-test and no re-test or baseline measurement) using a single group of subjects.
	Case Series	A retrospective study usually collecting variables from a chart review.
Level 5	Observational	Study using cross-sectional analysis to interpret relations.
	Clinical Consensus	Expert opinion without explicit critical appraisal, or based on physiology, biomechanics or "first

		principles".
	Case Report	Pre-post or case series involving one subject.

Using this system, conclusions were easily arrived at when the results of multiple studies were in agreement. However, interpretation became difficult when the study results conflicted. In cases where RCTs also differed in terms of methodological quality, the results of the study (or studies) with the higher PEDro score(s) and statistical power (i.e. large sample size) were more heavily weighted to arrive at the final conclusions. However, there were still some instances where interpretation remained problematic. For instance, the authors needed to make a judgement when the results of a single study of higher quality conflicted with those of several studies of inferior quality. In these cases, we attempted to provide a rationale for our decision and to make the process as transparent as possible.

In the end, the reader is encouraged to be a "critical consumer" of all of the material presented.

1.4.2 Meta-Analysis

Where feasible, we have started the process of creating forest plots to summarize the treatment effect associated with specific interventions, using the results from individual RCTs. Forest plots have now been created using Review Manager version 4.2.8 and have been incorporated into several of the sections. The results of this process are presented as either a common odds ratio for dichotomous outcomes or as a weighted mean difference for continuous variables. Where there was statistically significant heterogeneity among studies, a random effects model was used; otherwise a fixed effects model was used.

Unfortunately, pooled analyses are not consistently possible and were limited by the availability of data contained in the original report and also due to differences between studies in either the intervention provided, or the outcome assessed. Sometimes it is simply not appropriate to try to combine the results from studies; to do so could lead to misleading results. So far, we have used meta-analysis to formulate conclusions for chapters 5, 8, 15, 16, 17 and 18. In these chapters, the results obtained by meta-analysis prevailed and constituted Level 1a evidence. It is our intention to continue to incorporate this process in future editions of the review, wherever possible.

1.5 The SREBR 18th Edition

Since its original publication in April 2002, the SREBR continues to be updated regularly and now includes articles published up to December 2016. To date, we have included over 2,300 randomized controlled trials (RCTs). There are 22 chapters including a detailed review of outcome measures most commonly used in stroke rehabilitation. The Stroke Rehabilitation Clinician's Handbook has been included and was designed to be a quick reference and study guide for students and residents. It is also available online.

References

Teasell, R., Rice, D., Richardson, M., Campbell, N., Madady, M., Hussein, N., Murie-Fernandez, M., & Page, S. (2014). The next revolution in stroke care. *Expert Rev Neurother, 14*(11), 1307-1314.