Measuring Neuroplasticity Associated with Cerebral Palsy Rehabilitation

An MRI based Power Analysis

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Researchers are increasingly looking to quantify brain changes in clinical trials of motor rehabilitation in order to better understand how behavioural training invokes clinical improvements, and/or to index subtle brain changes. Power analyses are relied on to plan clinical-trial enrolment numbers, but basing these on expected behavioural improvements may underpower neuroimaging measures of brain change. We provide analyses that allow researchers to adequately power MRI studies of neuroplasticity.

Aim

Determine required participant counts for a longitudinal rehabilitative study of children with unilateral cerebral palsy (UCP) considering changes in cortical thickness of the impaired sensorimotor cortex, and fractional anisotropy (FA) of the more-affected corticomotor tract.

Methods

Power analyses were calculated using R. Two sources of variance were accounted for: response to therapy and measurement error. Response to therapy was approximated to have a standard deviation of 15%. Measurement error was calculated by applying identical analyses to MRI datasets from five children with UCP, who were imaged 20 weeks apart without any intervention in-between. Examples of cortical thickness [1], ROI-seeded tractography, and surface fMRI driven tractography [2] are presented in Figure 1 (left). The range of effect sizes investigated (Table 1) were based on published literature. A standard alpha of 0.05 was used.

Table 1: Effect size ranges investigated and justifications.

CHANGE	LOWER EFFECT SIZE	UPPER EFFECT SIZE
ROI-Seeded Tractography	1% FA Increase. Optimistic for very effective therapy. Demonstrated in healthy adults learning a motor task.	3% FA Increase. Unrealistic for current therapies; used to match surface-fMRI tractography method range.
Surface fMRI Driven Tractography	1% FA Increase. Realistic estimate for current therapies.	3% FA Increase. Heavily Optimistic. Demonstrated in healthy adults learning a motor task.
Cortical Thickness	6% increase. Realistic estimate for current therapies.	12% Heavily Optimistic estimate. Degree of life-long developmental adaptation in teenagers with CP.

Results

At the lowest tested effect sizes (Table 1), after accounting for expected data loss due to behavioural and image-processing issues, estimated required participant numbers were 101, 128 and 42 for cortical thickness, region-of-interest-based tractography, and fMRI-seeded tractography, respectively. Participant numbers fell to 21 for fMRI-seeded tractography when a more data-driven FA change of 1.5% was assumed, but this sample size may be too small to adequately represent the highly heterogeneous UCP population. All values were sensitive to the probability of achieving a successful scan (Figure 1, right). These numbers do not take into account general study attrition.

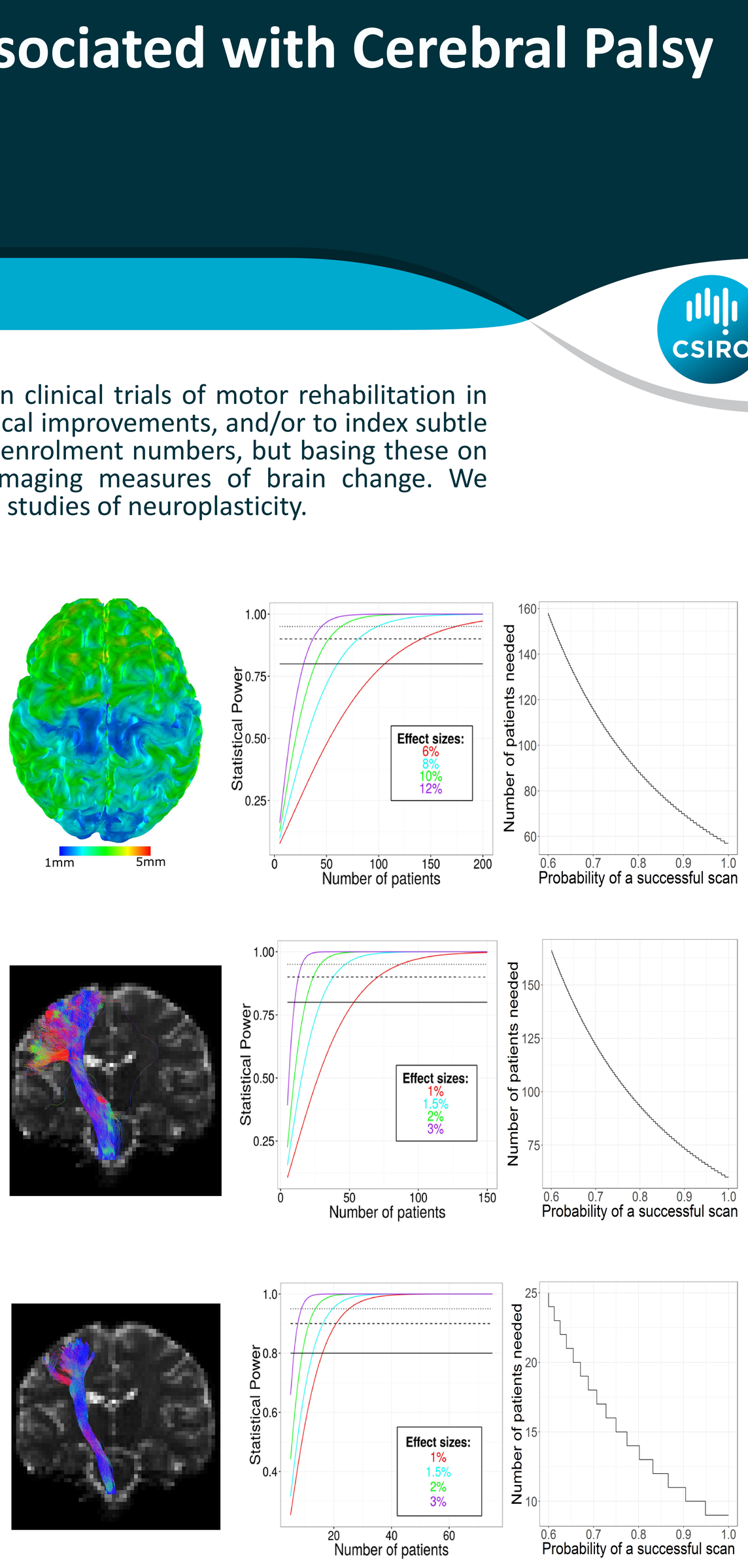

Figure 1: Example of cortical thickness (top), projected onto the pial surface; ROI-seeded diffusion tractography (middle); and surface-fMRI seeded tractography (bottom) in a single participant with UCP. Note the higher anatomical specificity of the surface-fMRI seeded method, relative to the ROI-seeded method. Middle Column: Statistical power for each method at a range of effect sizes, assuming no patient attrition. Three power thresholds are illustrated, 80% (full line), 90% (dashed line) and 95% (dotted line). Right Column: The number of children required to be scanned at both time points taking into account a variety of success rates of scanning and image processing. Displayed are changes of 8%, 1%, and 1.5% in cortical thickness (top), ROI-seeded tractography (middle) and surface-fMRI-seeded tractography (bottom), respectively.

Conclusions

This study provides a number of hints to future rehabilitation trials utilising neuroimaging:

- Cortical thickness analyses and standard ROI-driven tractography require large scale trials to achieve meaningful statistical power
- Small and medium trials should consider harmonising scanning protocols to allow the pooling of data
- For tractography, the specific method used strongly dictates trial power
- For surface fMRI driven tractography, cohort homogeneity is likely to be a more influential factor in interpretation than statistical power
- Improving successful-scan rates can drastically reduce required enrolee numbers

References

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FOR FURTHER INFORMATION

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