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Hope, Thomas M.H. and Friston, Karl J. and Price, Cathy J. and Leff, Alex P. and Rotshtein, Pia and Bowman, Howard (2018) Recovery After Stroke: Not So Proportional After All? *Brain*. ISSN 0006-8950. (In press)

### DOI

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# Recovery after stroke: not so proportional after all?

Thomas M.H. Hope <sup>1</sup> \*, Karl Friston <sup>1</sup>, Cathy J. Price <sup>1</sup>, Alex P. Leff <sup>2,3</sup>,  
Pia Rotshtein <sup>4</sup> & Howard Bowman <sup>4,5</sup>

1. Wellcome Centre for Human Neuroimaging, University College London, UK.
2. Institute of Cognitive Neuroscience, University College London, UK.
3. Dept. of Brain Repair and Rehabilitation, Institute of Neurology, University College London, UK.
4. School of Psychology, University of Birmingham, UK.
5. School of Computing, University of Kent, UK.

\* Corresponding author: Dr Thomas M.H. Hope, Wellcome Centre for Human Neuroimaging, Institute of Neurology, University College London, 12 Queen Square, London, WC1N 3AR, UK. Phone: +44 (0)20 3448 4345. E-mail: t.hope@ucl.ac.uk

**References:** 29

**Words:** (abstract): 196; (body): 3,156

**Keywords:** proportional recovery, stroke, methods, statistics.

23 **ABSTRACT**

24 The proportional recovery rule asserts that most stroke survivors recover a fixed proportion of lost  
25 function. To the extent that this is true, recovery from stroke can be predicted accurately from  
26 baseline measures of acute post-stroke impairment alone. Reports that baseline scores explain more  
27 than 80%, and sometimes more than 90%, of the variance in the patients' recoveries, are rapidly  
28 accumulating. Here, we show that these headline effect sizes are likely inflated.

29 The key effects in this literature are typically expressed as, or reducible to, correlation  
30 coefficients between baseline scores and recovery (outcome scores minus baseline scores). Using  
31 formal analyses and simulations, we show that these correlations will be extreme when outcomes  
32 are less variable than baselines, which they often will be in practice regardless of the real  
33 relationship between outcomes and baselines. We show that these effect sizes are likely to be over-  
34 optimistic in every empirical study that we found, which reported enough information for us to  
35 make the judgement, and argue that the same is likely to be true in other studies as well. The  
36 implication is that recovery after stroke may not be as proportional as recent studies suggest.

37

## 38 1. INTRODUCTION

39 Clinicians and researchers have long known stroke patients' initial symptom severity is related to  
40 their longer term outcomes (Jongbloed, 1986). Recent studies have suggested that this relationship  
41 is stronger than previously thought: that most patients recover a fixed proportion of lost function.  
42 Studies supporting this 'proportional recovery rule' are rapidly accumulating (Stinear, 2017): in five  
43 studies since 2015 (Byblow *et al.*, 2015; Feng *et al.*, 2015; Winters *et al.*, 2015; Buch *et al.*, 2016;  
44 Stinear *et al.*, 2017b), researchers used the Fugl-Meyer scale to assess patients' upper limb motor  
45 impairment within two weeks of stroke onset ('baselines'), and then again either three or six months  
46 post-stroke ('outcomes'). The results were consistent with earlier observations (Prabhakaran *et al.*,  
47 2007; Zarahn *et al.*, 2011) that most patients recovered ~70% of lost function. Taken together, these  
48 studies report highly consistent recovery in over 500 patients, across different countries with  
49 different approaches to rehabilitation, regardless of the patients' ages at stroke onset, stroke type,  
50 sex, or therapy dose (Stinear, 2017). And there is increasing evidence that the rule also captures  
51 recovery from post-stroke impairments of lower limb function (Smith *et al.*, 2017), attention (Marchi  
52 *et al.*, 2017; Winters *et al.*, 2017), and language (Lazar *et al.*, 2010; Marchi *et al.*, 2017), and may  
53 even apply generally across cognitive domains (Ramsey *et al.*, 2017). Even rats appear to recover  
54 proportionally after stroke (Jeffers *et al.*, 2018).

55 Strikingly, many of these studies report that the baseline scores predict 80%-90%, or more,  
56 of the variance in empirical recovery. When predicting behavioural responses in humans, these  
57 effect sizes are unprecedented. Recently, Winters and colleagues (2015) reported that recovery  
58 predicted from baseline scores explained 94% of the variance in the empirical recovery of 146 stroke  
59 patients. Like many related reports (Stinear, 2017), this study also reported a group of (65) 'non-  
60 fitters', who did not make the predicted recovery. But if non-fitters can be distinguished at the acute  
61 stage, as this and other studies suggest (Stinear, 2017), the implication is that we can predict most  
62 patients' recovery near-perfectly, given baseline scores alone. Stroke researchers are used to  
63 thinking of recovery as a complex, multi-factorial process (Nelson *et al.*, 2016). If the proportional  
64 recovery rule is as powerful as it seems, post-stroke recovery is simpler and more consistent than  
65 previously thought.

66 In what follows, we argue that the empirical support for proportional recovery is weaker  
67 than it seems. These results are typically expressed as, or reducible to, correlations between  
68 baselines and recovery (outcomes minus baselines). These analyses pose well-known challenges,  
69 which have been discussed by statisticians for decades (Lord, 1956; Oldham, 1962; Cronbach and  
70 Furby, 1970; Hayes, 1988; Tu *et al.*, 2005). Much of this discussion is focused on problems induced

71 by measurement noise, and measurement noise is also the focus of the only prior application of that  
72 discussion to the proportional recovery rule (Krakauer and Marshall, 2015). Here, we argue that  
73 empirical studies of proportional recovery after stroke are likely confounded entirely regardless of  
74 measurement noise.

75 Our argument is that: (a) correlations between baselines and recovery are spurious when  
76 they are stronger than correlations between baselines and outcomes; (b) this is likely when  
77 outcomes are less variable than baselines; which (c) will often happen in practice, whether or not  
78 recovery is proportional. This argument follows from a formal analysis of correlations between  
79 baselines and recovery, which we introduce in section 2 and illustrate with examples. We then  
80 employ that analysis to re-examining the empirical support for the proportional recovery rule in  
81 section 3.

82

## 83 **2. THE RELATIONSHIPS BETWEEN BASELINES, OUTCOMES, AND RECOVERY**

84 For the sake of brevity, we define ‘baselines’ =  $X$ , ‘outcomes’ =  $Y$ , and ‘change’ (recovery) =  $\Delta$ : i.e.  $Y$   
85 minus  $X$ . The ‘correlation between baselines and outcomes’ is  $r(X,Y)$ , and the ‘correlation between  
86 baselines and change’ is  $r(X,\Delta)$ . Finally, we define the ‘variability ratio’ as the ratio of the standard  
87 deviation ( $\sigma$ ) of  $Y$  to the standard deviation of  $X$ :  $\sigma_Y/\sigma_X$ .

88  $X$  and  $Y$  are construed as lists of scores, with each entry being the performance of a single  
89 patient at the specified time point. We assume that higher scores imply better performance, so  
90  $r(X,\Delta)$  will be negative if recovery is proportional (to lost function). One can equally substitute ‘lost  
91 function’ (e.g. maximum score minus actual score), for ‘baseline score’, but while this makes  $r(X,\Delta)$   
92 positive if recovery is proportional, it is otherwise equivalent.

93

### 94 *2.1. Strong correlations imply the potential for accurate predictions*

95 Strong correlations between any two variables typically imply that we can use either variable to  
96 predict the other. Out-of-sample predictions should tend toward the least-squares line defined by  
97 the original (in-sample) correlation. Some empirical studies employ this logic to derive ‘predicted  
98 recovery’ ( $p\Delta$ ) from the least-squares line for  $r(X,\Delta)$ , reporting  $r(p\Delta,\Delta)$  instead of  $r(X,\Delta)$  (Winters *et*  
99 *al.*, 2015; Marchi *et al.*, 2017). Since the magnitudes of  $r(X,\Delta)$  and  $r(p\Delta,\Delta)$  are the same by definition  
100 (see proposition 8, Appendix A, and Figure 1), the preference for either expression over the other is  
101 arguably cosmetic.

102 Nevertheless, the correlation between predicted and empirical data is a common measure  
103 of predictive accuracy: the stronger the correlation, the better the predictions. Very strong  
104 correlations are unusual when predicting behavioural performance in humans – both because  
105 behaviour itself is complex, and because of measurement noise in behavioural assessment. Once  
106  $r(p\Delta, \Delta) > \sim 0.95$ , for example (Winters *et al.*, 2015), this prognostic problem has seemingly been  
107 ‘solved’ more accurately than many might have thought possible.

108

### 109 2.2. $r(X, \Delta)$ is spurious when stronger than $r(X, Y)$

110 Recovery is precisely the difference between baselines and outcomes. When  $r(X, \Delta)$  is strong,  
111 implying that we can predict recovery accurately given baselines, it is tempting to assume that we  
112 can also predict outcomes equally accurately, by simply adding predicted recovery to baselines.  
113 More formally, the assumption is that  $r(X+p\Delta, Y) \approx r(p\Delta, \Delta)$ . This assumption is wrong.

114 In fact,  $r(X+p\Delta, Y) \approx r(X, Y)$  (see appendix A, proposition 8, and Figure 1). When recovery is  
115 predicted from baselines, the correlation between ‘baselines plus predicted recovery’ and outcomes,  
116 is never stronger than the correlation between baselines and outcomes. When  $r(X, \Delta)$  is stronger  
117 than  $r(X, Y)$ ,  $r(X, \Delta)$  is *spurious*, because it encourages an over-optimistic impression of how  
118 predictable outcomes are, given baselines.

119

### 120 2.3. The canonical example of spurious $r(X, \Delta)$

121 The canonical example of spurious  $r(X, \Delta)$  is when X and Y are independent random variables with the  
122 same variance:  $\sigma_Y/\sigma_X \approx 1$  and  $r(X, Y) \approx 0$ , but  $r(X, \Delta) \approx -0.71$  (Oldham, 1962). This  $r(X, \Delta)$  suggests that  
123 we can predict recovery relatively well, but we cannot use ‘predicted recovery’ to predict outcomes  
124 equally well (see Figure 1).

125

126 --Figure 1--

127

128 Krakauer and Marshall (2015) recently argued that this scenario has little relevance to (most)  
129 empirical studies of recovery after stroke. This is because: (a) spurious  $r(X, \Delta)$  only emerge here when  
130  $r(X, Y)$  is weak; and (b) empirical  $r(X, Y)$  are usually strong, because X and Y are dependent, repeated  
131 measurements from the same patients. If spurious  $r(X, \Delta)$  only or mainly emerged when  $\sigma_Y/\sigma_X \approx 1$  and

132  $r(X,Y) \approx 0$ , they might indeed be irrelevant in practice. Unfortunately, spurious  $r(X,\Delta)$  also emerge in  
133 another scenario, which is very common in studies of recovery after stroke.

134

#### 135 2.4. Spurious $r(X,\Delta)$ are likely when $\sigma_Y/\sigma_X$ is small

136 For any X and Y, it can be shown that:

$$137 \quad r(X, \Delta) = \frac{\sigma_Y \cdot r(X, Y) - \sigma_X}{\sqrt{\sigma_Y^2 + \sigma_X^2 - 2 \cdot \sigma_X \cdot \sigma_Y \cdot r(X, Y)}} \quad (\text{Equation 1})$$

138 A formal proof of Equation 1 is provided in Appendix A (proposition 4 and theorem 1; also  
139 see (Oldham, 1962)); its consequence is that  $r(X,\Delta)$  is a function of  $r(X,Y)$  and  $\sigma_Y/\sigma_X$ . To illustrate that  
140 function, we performed a series of simulations (see Appendix B) in which  $r(X,Y)$  and  $\sigma_Y/\sigma_X$  were  
141 varied independently. Figure 1 illustrates the results: a surface relating  $r(X,\Delta)$  to  $r(X,Y)$  and  $\sigma_Y/\sigma_X$ .  
142 Figure 2 illustrates example recovery data at six points of interest on that surface.

143

144 --Insert Figures 2 and 3 and Table 1--

145

146 Point A corresponds to the canonical example of spurious  $r(X,\Delta)$ , introduced in the last  
147 section: i.e.,  $\sigma_Y/\sigma_X \approx 1$  and  $r(X,Y) \approx 0$ , but  $r(X,\Delta) \approx -0.71$  (see Figure 3a). At point B,  $\sigma_Y/\sigma_X \approx 1$  and  $r(X,Y)$   
148 is strong, so recovery is approximately constant (Figure 3b) and  $r(X,\Delta) \approx 0$ , consistent with the view  
149 that strong  $r(X,Y)$  curtail spurious  $r(X,\Delta)$  (Krakauer and Marshall, 2015). However the situation is  
150 more complex when  $\sigma_Y/\sigma_X$  is more skewed.

151 When  $\sigma_Y/\sigma_X$  is large, Y contributes more variance to  $\Delta$ , and  $r(X, \Delta) \approx r(X,Y)$ ; this is Regime 1.  
152 Points C and D illustrate the convergence (Figure 3c-d). Data like this might suggest recovery  
153 proportional to *spared* function. By contrast, when  $\sigma_Y/\sigma_X$  is small, X contributes more variance to  $Y-X$ ,  
154 and  $r(X,\Delta) \approx r(X,-X)$ : i.e. -1 (see appendix A, theorem 2); this is Regime 2, where the confound  
155 emerges. Point E corresponds to data predicted by the proportional recovery rule: all patients  
156 recover exactly 70% of lost function (Figure 2e). Here,  $\sigma_Y/\sigma_X$  is already small enough (0.3) to be  
157 dangerous: after randomly shuffling Y,  $r(X,Y) \approx 0$ , but  $r(X,\Delta)$  is almost unaffected (Point F, and Figure  
158 3f). Even if patients do recover proportionally, in other words, empirical data may enter territory, on  
159 the surface in Figure 2, where spurious  $r(X,\Delta)$  are likely.

160

161 2.5.  $\sigma_Y/\sigma_X$  will often be small, whether or not recovery is proportional

162 Proportional recovery implies small  $\sigma_Y/\sigma_X$ , but small  $\sigma_Y/\sigma_X$  does not imply proportional recovery; for  
163 example, constant recovery with ceiling effects will produce the same effect. To illustrate this, we  
164 ran 1,000 simulations in which: (i) 1,000 baseline scores are drawn randomly with uniform  
165 probability from the range 0-65 (i.e. impaired on the 66-point Fugl-Meyer upper-extremity scale); (ii)  
166 outcome scores were calculated as the baseline scores plus half the scale's range (33); and (iii)  
167 outcome scores greater than 66 were set to 66 (i.e. a hard ceiling). Mean  $r(X,Y)$  and  $r(X,\Delta)$  were  
168 calculated both before and after shuffling the outcomes data for each simulation. After shuffling,  
169  $r(X,Y) \approx 0$  and  $r(X,\Delta) = -0.88$ : ceiling effects make  $\sigma_Y/\sigma_X$  small enough to encourage spurious  $r(X,\Delta)$ .  
170 And just as importantly, before shuffling,  $r(X,Y) = 0.89$  and  $r(X,\Delta) = -0.90$ : even when  $r(X,\Delta)$  is *not*  
171 spurious (because  $r(X,Y)$  is similarly strong), we cannot conclude that recovery is really proportional.

172

### 173 3. RE-EXAMINING THE EMPIRICAL LITERATURE ON PROPORTIONAL RECOVERY

174 The relationships between  $r(X,Y)$ ,  $r(X,\Delta)$  and  $\sigma_Y/\sigma_X$ , merit a re-examination of the empirical support  
175 for the proportional recovery rule. In the only study we found, which reports individuals' behavioural  
176 data, Zarahn and colleagues (2011) consider 30 patients' recoveries from hemiparesis after stroke.  
177 Across the whole sample,  $r(X,Y) = 0.80$  and  $r(X,\Delta) = -0.49$ ; after removing 7 non-fitters:  $r(X,Y) = 0.75$   
178 and  $r(X,\Delta) = -0.95$ . Removing the non-fitters increases the apparent predictability of recovery but  
179 reduces the predictability of outcomes (and reduces  $\sigma_Y/\sigma_X$  from 0.88 to 0.36). Notably, the residuals  
180 for both correlations are identical (see Figure 4), and in fact this is always true (see Appendix A,  
181 proposition 10).  $r(X,\Delta)$  has the same errors as  $r(X,Y)$ , but a larger effect size:  $r(X,\Delta)$  is over-optimistic.

182

183 --Insert Figure 3--

184

185 We can also use Equation 1 to reinterpret studies that do not report individual patient data.  
186 One example is the first study to report proportional recovery from aphasia after stroke (Lazar *et al.*,  
187 2010). Here,  $r(X,\Delta) \approx -0.9$  and  $\sigma_Y/\sigma_X \approx 0.48$ ; Equation 1 implies that  $r(X,Y)$  was either  $\sim 0.78$  or zero.  
188 Similarly, in the recent study of proportional recovery in rats (Jeffers *et al.*, 2018),  $\sigma_Y/\sigma_X \approx 0.8$ , and  
189  $r(X,\Delta) \approx -0.71$ ; Equation 1 implies that  $r(X,Y)$  was either much stronger ( $>0.95$ ) or considerably  
190 weaker ( $\sim 0.29$ ) than  $r(X,\Delta)$ . In both cases,  $r(X,\Delta)$  tells us less than expected about how predictable  
191 outcomes really were, given baseline scores.



192 Many recent studies report inter-quartile ranges (IQRs), rather than standard deviations, for  
193 the baselines and outcomes of patients deemed to recover proportionally. Accepting some room for  
194 error, we can also estimate  $\sigma_Y/\sigma_X$  from those IQRs. In one case (Winters *et al.*, 2015),  $r(X,\Delta) = -0.97$   
195 and  $\sigma_Y/\sigma_X = 0.158$ , while in another (Veerbeek *et al.*, 2018),  $\sigma_Y/\sigma_X = 0.438$  and  $r(X,\Delta) \approx -0.88$ . In both  
196 cases, Equation 1 implies that  $r(X,\Delta)$  would be at least that strong as that reported, regardless of  
197  $r(X,Y)$ : here again, the headline effect sizes do not tell us how predictable outcomes actually are,  
198 given baseline scores.

199 Many studies in this literature only relate baselines to recovery through multivariable  
200 models (Buch *et al.*, 2016; Marchi *et al.*, 2017; Winters *et al.*, 2017); in these studies, we cannot  
201 demonstrate confounds directly with Equation 1. Nevertheless, these studies are also probably  
202 confounded, because any inflation in one variable's effect size will inflate the multivariable model's  
203 effect size as well. As discussed in section 2.5, empirical studies of recovery after stroke should tend  
204 to encourage small  $\sigma_Y/\sigma_X$ , whether or not recovery is really proportional. Consequently, the null  
205 hypothesis will rarely be that  $r(X,\Delta) \approx 0$ . For example, in the only multivariable modelling study,  
206 which reports IQRs for its fitter-patients' baselines and outcomes (Stinear *et al.*, 2017c),  $\sigma_Y/\sigma_X \approx 0.48$ ,  
207 which implies that the weakest  $r(X,\Delta)$  was  $-0.88$ , for any positive value of  $r(X,Y)$ .

208 Finally, while  $r(X,\Delta)$  can be misleading if it is extreme relative to  $r(X,Y)$ , the reverse is also  
209 true. One study in this literature which employs outcomes as the dependent variable, rather than  
210 recovery (Feng *et al.*, 2015), reports that  $r(X,Y) \approx 0.8$  and  $\sigma_Y/\sigma_X = 1.2$  in their 'combined' group of 76  
211 patients. By Equation 1,  $r(X,\Delta) = -0.05$ : i.e. recovery was uncorrelated with baseline scores. These  
212 authors only report proportional recovery in a sub-sample of their patients (but not the information  
213 we need to re-examine that claim), but their full sample seems better described by constant  
214 recovery (as in Figure 3b).

215

#### 216 4. Discussion

217 The proportional recovery rule is striking because it implies that recovery is simple and consistent  
218 across patients (non-fitters notwithstanding), and because that implication appears to be justified by  
219 strong empirical results (Stinear, 2017). We contend that the empirical support for the rule is weaker  
220 than it seems.

221 In summary, our argument is that  $r(X,\Delta)$  is spurious when stronger than  $r(X,Y)$ , and that the  
222 conditions which encourage spurious  $r(X,\Delta)$  will be common in empirical studies of recovery after  
223 stroke, whether or not recovery is really proportional. Many empirical  $r(X, \Delta)$  in this literature appear

224 to be spurious in this sense. And in any case, strong  $r(X,\Delta)$  are insufficient evidence for proportional  
225 recovery if they are *not* spurious (because they are accompanied by similarly strong  $r(X,Y)$ ).

226 The only previous discussion of the risk of spurious  $r(X,\Delta)$ , in analyses of recovery after stroke,  
227 (Krakauer and Marshall, 2015), concluded that this risk is small provided the tools used to measure  
228 post-stroke impairment are reliable: i.e. so long as measurement noise is minimal. Crucially, our  
229 analysis applies entirely regardless of measurement noise. We contend that the risk of spurious  $r(X,\Delta)$   
230 is significant, if there are ceiling effects on the scale used to measure post-stroke impairment, and if  
231 most patients improve between baseline and subsequent assessments. The criteria will usually be met  
232 in practice, because every practical measurement of post-stroke impairment employs a finite scale,  
233 and because non-fitters, who do not make the predicted recovery, are removed prior to calculating  
234  $r(X,\Delta)$ .

235 We are not suggesting that there is anything wrong with the practice of distinguishing fitters  
236 from non-fitters. Indeed, our results prove that this work may be valid regardless of our other  
237 concerns. Non-fitters do not recover as predicted; by definition, they contribute the largest, negative  
238 residuals to  $r(X,\Delta)$ . In Figure 4 and appendix A (proposition 9), we show that the residuals for  $r(X,Y)$   
239 and  $r(X,\Delta)$  are exactly the same, so the same patients will be placed in the same sub-groups regardless  
240 of which correlation is used, and biomarkers which distinguish those sub-groups at the acute stage  
241 (Stinear, 2017), will be equally accurate regardless of which correlation is used. Nevertheless, extreme  
242  $r(X,\Delta)$  for patients classified as fitters, will naturally encourage the assumption that those fitters'  
243 outcomes are largely determined by initial symptom severity. If this assumption is true, therapeutic  
244 interventions must be largely ineffective (or at least redundant) for these patients. Our analysis  
245 suggests that this assumption is wrong.

246 Nevertheless, we are not claiming that the proportional recovery rule is wrong. Our analysis  
247 suggests that empirical studies to date do not demonstrate that the rule holds, or how well, but we  
248 could only confirm that  $r(X,\Delta)$  was actually over-optimistic in one study, which reported individual  
249 patient data. And while we have also shown that extreme  $r(X,\Delta)$  and  $r(X,Y)$  can result from non-  
250 proportional (constant) recovery, this is simply a plausible alternative hypothesis about how patients  
251 really recover.

252 Quite how to interpret empirical recovery with confidence in this domain, remains an open  
253 question: we have articulated a problem here, hoping that recognition of the problem will motivate  
254 work to solve it. Nevertheless, we can make some recommendations for future studies in the field.

255 First, these studies should report  $r(X,\Delta)$ ,  $r(X,Y)$ , and  $\sigma_Y/\sigma_X$ , for those patients deemed to  
256 recover proportionally. Despite our concerns about  $r(X,\Delta)$ , we do learn something when  $r(X,Y)$  is  
257 strong, but  $r(X,\Delta)$  is weak, as in Feng and colleagues' (2015) results in section 3, which appeared to be  
258 better explained by constant recovery than by proportional recovery.

259 Second, future studies should consider explicitly testing the hypothesis that recovery depends  
260 on baseline scores (Oldham, 1962; Hayes, 1988; Tu *et al.*, 2005; Tu and Gilthorpe, 2007; Chiolero *et*  
261 *al.*, 2013). These tests sensibly acknowledge that the null hypothesis is rarely  $r(X,\Delta) \approx 0$  in these  
262 analyses. However, they do not address the proper measurement and interpretation of effect sizes,  
263 which is our primary concern here; somewhat paradoxically, this means that they may be less useful  
264 in larger samples than in smaller samples (Friston, 2012; Lorca-Puls *et al.*, 2018).

265 These hypothesis tests will also all be confounded by ceiling effects. We recommend that  
266 future studies should measure the impact of such effects, perhaps by reporting the shapes of the  
267 distributions of X and Y (greater asymmetry implying more prominent ceiling effects). Future studies  
268 should also attempt to minimise ceiling effects. One approach might be to remove patients whose  
269 outcomes are at ceiling: though certainly inefficient, this does at least remove the spurious  $r(X,\Delta)$  in  
270 our simulations of constant recovery (section 2.5). However, it may be difficult to determine which  
271 patients to remove in practice; the Fugl-Meyer scale, for example, imposes item-level ceiling effects,  
272 which could distort  $\sigma_Y/\sigma_X$  well below the maximum score. A better, though also more complex  
273 alternative, may be to employ assessment tools expressly designed to minimise ceiling effects, or to  
274 add such tools to those currently in use.

275 More generally, we may need to replace correlations with alternative methods, which can  
276 provide less ambiguous evidence for the proportional recovery rule. One principled alternative might  
277 employ Bayesian model comparison to adjudicate between different forward or generative models of  
278 the data at hand: i.e. using the empirical data to quantify evidence for or against competing  
279 hypotheses about the nature of recovery, which may or may not be conserved across patients. We  
280 hope that our analysis here will encourage work to develop such methods, delivering better evidence  
281 for (or against) the proportional recovery rule.

282

## 283 **ACKNOWLEDGMENTS**

284 This study was supported by the Medical Research Council (MR/M023672/1, MR/K022563/1),  
285 Wellcome (091593/Z/10/Z), and the Stroke Association (TSA PDF 2017/02). The funders had no

286 participation in the design and results of this study. We would also like to thank the (anonymous)  
287 reviewers, whose constructive comments helped us to improve the paper.

288

289

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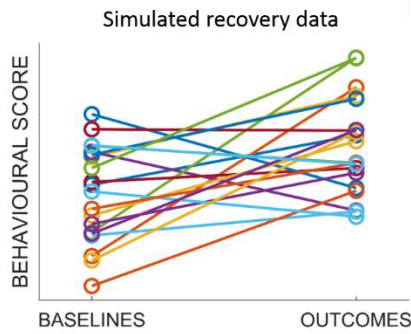
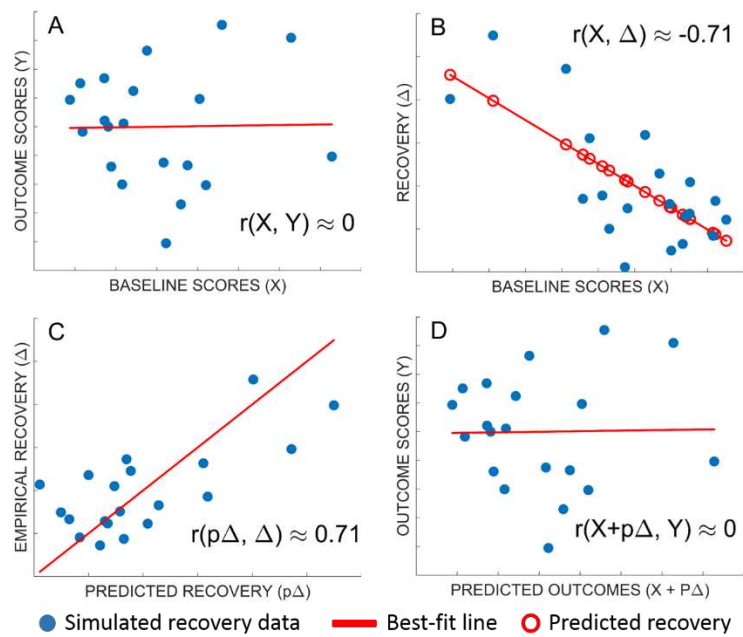


Figure 1



360

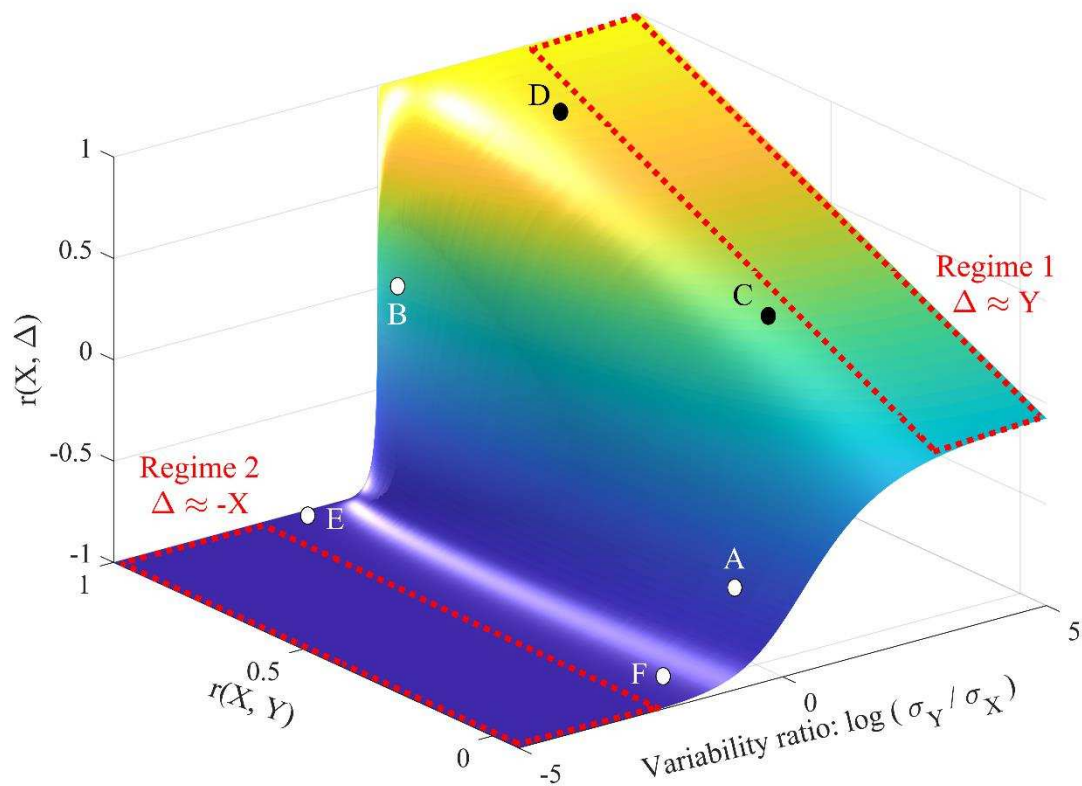
361 **Figure 1: A canonical example of spurious  $r(X, \Delta)$ .** Baselines scores are uncorrelated with outcomes  
362 (A), but baseline scores appear to be strongly correlated with recovery (B). That correlation can be  
363 used to derive predicted recovery, which is strongly correlated with empirical recovery (C) – but  
364 predicted outcomes, derived from that predicted recovery, are still uncorrelated with empirical  
365 outcomes (D).

366

367

368

Figure 2

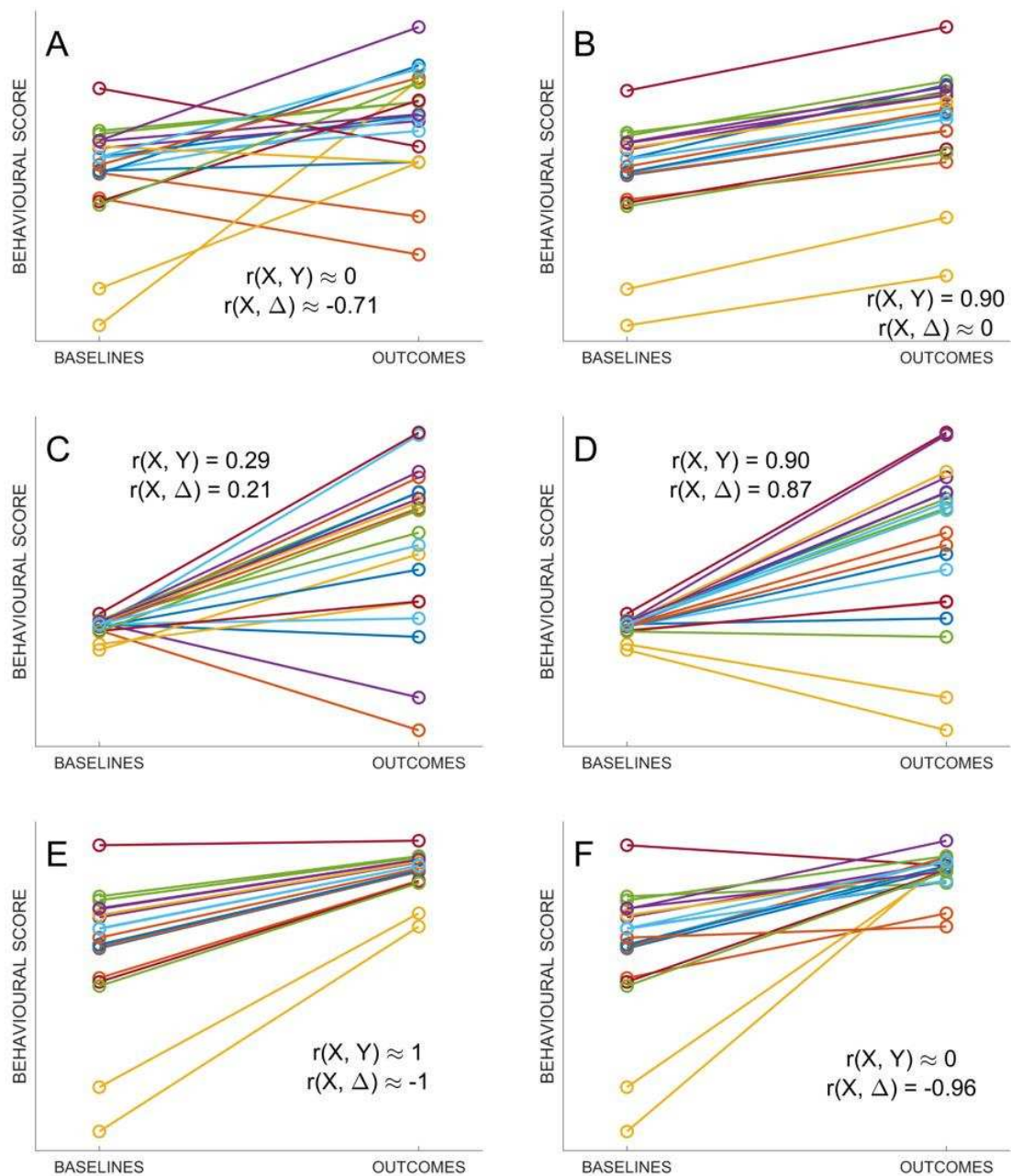


369

370 **Figure 2: The relationship between  $r(X, Y)$ ,  $r(X, \Delta)$  and  $\sigma_Y / \sigma_X$ .** Note that the x-axis is log-transformed to  
 371 ensure symmetry around 1; when X and Y are equally variable,  $\log(\sigma_Y / \sigma_X) = 0$ . Proposition 7 in Appendix  
 372 A provides a justification for unambiguously using a ratio of standard deviations in this figure, rather  
 373 than  $\sigma_Y$  and  $\sigma_X$  as separate axes. The two major regimes of Equation 1 are also marked in red. In Regime  
 374 1, Y is more variable than X, so contributes more variance to  $\Delta$ , and  $r(X, \Delta) \approx r(X, Y)$ . In Regime 2, X is  
 375 more variable than Y, so X contributes more variance to  $\Delta$ , and  $r(X, \Delta) \approx r(X, -X)$  (i.e. -1). The transition  
 376 between the two regimes, when the variability ratio is not dramatically skewed either way, also allows  
 377 for spurious  $r(X, \Delta)$ . For the purposes of illustration, the figure also highlights 6 points of interest  
 378 on the surface, marked A-F; examples of simulated recovery data corresponding to these points are  
 379 provided in Figure 3.

380

381



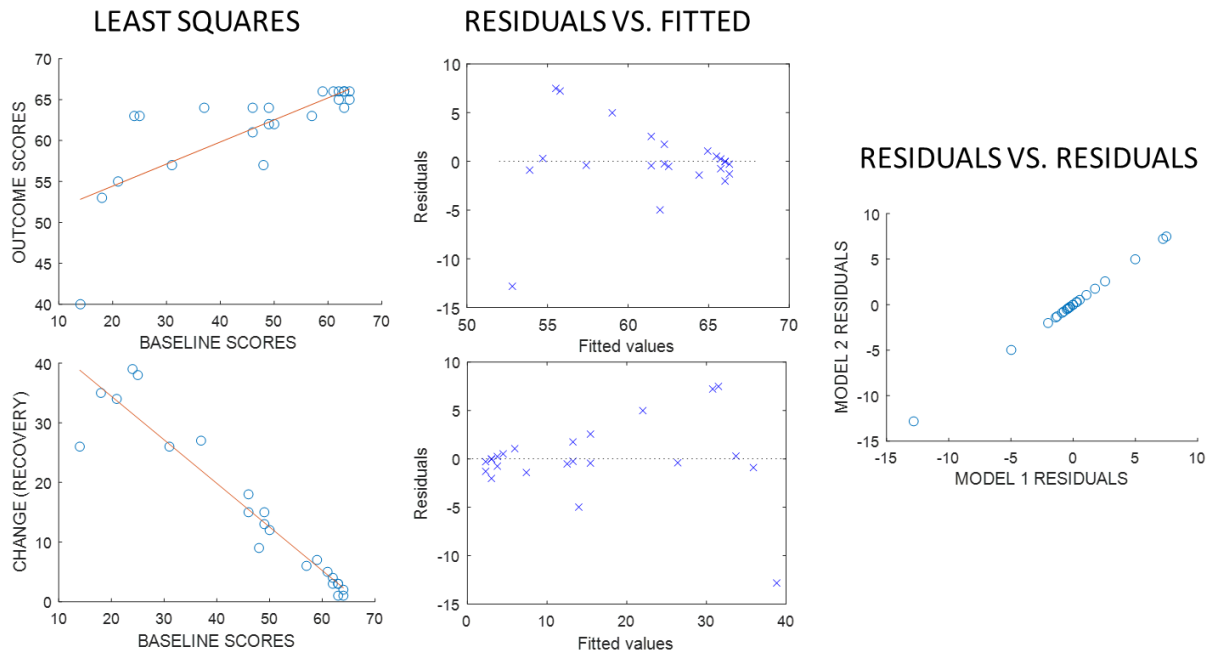
383

384 **Figure 3: Exemplar points on the surface in Figure 2.** Simulated recovery data, corresponding to the  
 385 points A-F marked on the surface in Figure 1. (A) Baselines and outcomes are entirely independent  
 386 ( $r(X, Y) = 0$ ), yet  $r(X, \Delta)$  is relatively strong; this is the canonical example of mathematical coupling, first  
 387 introduced by Oldham (1962); (B) Recovery is constant with minimal noise, so baselines and  
 388 outcomes are equally variable ( $\sigma_Y/\sigma_X \approx 1$ ) and recovery is unrelated to baseline scores ( $r(X, \Delta) \approx 0$ );  
 389 (C-D) Outcomes are more variable than baselines ( $\sigma_Y/\sigma_X \approx 5$ ), and  $r(X, \Delta)$  converges to  $r(X, Y)$ ; (E)  
 390 Recovery is 70% of lost function, so outcomes are less variable than baselines ( $\sigma_Y/\sigma_X \approx 0.3$ ); even  
 391 with shuffled outcomes data (F) baselines and recovery still appear to be strongly correlated.



392

Figure 4



393

394 **Figure 4:** (Left) Least squares linear fits for analyses relating baselines to (upper) outcomes and  
395 (lower) recovery, using the fitters' data reported by Zarahn and colleagues (Zarahn *et al.*, 2011).  
396 (Middle) Plots of residuals relative to each least squares line, against the fitted values in each case.  
397 (Right) A scatter plot of the residuals from the model relating baselines to change, against the  
398 residuals from the model relating baselines to outcomes: the two sets of residuals are the same.

399

400

Table 1

REGIME	VARIABILITY OF Y ( $\sigma_Y$ )	VARIABILITY OF X ( $\sigma_X$ )	$\Delta$ [= Y-X]	$r(X,\Delta)$ [=r(X,Y-X)]
1	Smaller	Larger	$Y-X \approx -X$	$r(X,Y-X) \approx r(X,-X) = -1$
2	Larger	Smaller	$Y-X \approx Y$	$r(X,Y-X) \approx r(X,Y)$

401

## 402 **Supplementary Appendix A: formal relationships between the correlations**

403 We present a simple, general and self-contained formulation of the proportional recovery concept.  
404 We have derived all of the key results from first principles, while acknowledging previous  
405 presentations of these results when they can be found in the literature.

406 We assume two variables  $X'$  and  $Y'$  corresponding to performance at initial test ( $X'$ ) and at second  
407 test ( $Y'$ ). These will be represented as column vectors, with each entry being the performance of a  
408 single patient and vector lengths being  $N \in \mathbb{N}$ . Performance improves as numbers get bigger, up to a  
409 maximum, denoted  $Max$ , which corresponds to no discernible deficit. Severity is measured as  
410 difference from maximum, i.e.  $Max - X'$ .

411 The two variables ( $X'$  and  $Y'$ ) could be specialised to more detailed formulations: e.g., true score  
412 theory or with an explicit modelling of measurement or state error. However, this would not impact  
413 any of the derivations or inferences that follow. Indeed, the results that we present would hold even  
414 in the complete absence of measurement noise, which has been considered the main concern for  
415 the validity of quantifications of proportional recovery.

416

### 417 **Demeaning**

418 Without loss of generality, we work with demeaned variables. That is, where over-lining denotes  
419 mean, we define new variables as,

$$420 \quad X = X' - \overline{X'}$$

$$421 \quad Y = Y' - \overline{Y'}$$

422 This also means that recovery, i.e.  $Y - X$ , will be demeaned, since, using proposition 1, the following  
423 holds.

$$424 \quad Y - X = (Y' - \overline{Y'}) - (X' - \overline{X'}) = (Y' - X') - (\overline{Y'} - \overline{X'}) = (Y' - X') - \overline{(Y' - X')}$$

### 425 **Proposition 1**

426 Let  $V$  and  $W$  be vectors of the same length, denoted  $N$ . Then, the following holds,

$$427 \quad \overline{V + W} = \overline{V} + \overline{W}$$

428 with  $\overline{V - W} = \overline{V} - \overline{W}$  as a trivial consequence.

### 429 **Proof**

430 By distributivity of multiplication through addition and associativity of addition, the following holds.

$$431 \quad \overline{V + W} = \left( \frac{1}{N} \sum_{i=1}^N V_i \right) + \left( \frac{1}{N} \sum_{i=1}^N W_i \right) = \frac{1}{N} \left( \sum_{i=1}^N V_i + \sum_{i=1}^N W_i \right) = \frac{1}{N} \left( \sum_{i=1}^N (V_i + W_i) \right) = \overline{(V + W)}$$

432 QED

### 433 **Correlations**

434 There are two basic correlations we are interested in, (1) the correlation between initial  
435 performance and performance at second test, i.e.  $r(X, Y)$ , and (2) the correlation between initial  
436 performance and recovery, i.e.  $r(X, Y - X) = r(X, \Delta)$ . The latter of these is the key relationship, and

437 we would expect this to be a negative correlation; that is, as initial performance is smaller (i.e.  
 438 further from  $Max$ ), the larger is recovery. (One could also formulate the correlation as  $r((Max -$   
 439  $X), Y - X)$ , which would flip the correlation to positive, but the two approaches are equivalent).

440 Our main correlations are defined as follows,

$$441 \quad r(X, Y) = \frac{\sum_{i=1}^N X_i \cdot Y_i}{(N - 1) \cdot \sigma_X \cdot \sigma_Y}$$

$$442 \quad r(X, (Y - X)) = \frac{\sum_{i=1}^N (X_i \cdot (Y_i - X_i))}{(N - 1) \cdot \sigma_X \cdot \sigma_{(Y-X)}}$$

### 443 **Standard Deviation of a Difference**

444 We need a straightforward result on the standard deviation of a difference.

#### 445 **Proposition 2**

$$446 \quad \sigma_{(A-B)} = \sqrt{\sigma_A^2 + \sigma_B^2 - 2 \cdot cov(A, B)}$$

#### 447 **Proof**

448 The result is a direct consequence of the following standard result from probability theory, e.g. see  
 449 Ross, S. M. (2014). *Introduction to probability and statistics for engineers and scientists*. Academic  
 450 Press.,

$$451 \quad \sigma_{(A-B)}^2 = \sigma_A^2 + \sigma_B^2 - 2 \cdot cov(A, B)$$

452

### 453 **Key Results**

454 The following proposition enables us to express the key correlation,  $r(X, (Y - X))$ , in terms of  
 455 covariance of its constituent variables.

#### 456 **Proposition 3**

$$457 \quad r(X, (Y - X)) = \frac{cov(X, Y) - cov(X, X)}{\sigma_X \cdot \sqrt{\sigma_Y^2 + \sigma_X^2 - 2 \cdot cov(X, Y)}}$$

#### 458 **Proof**

459 Using distributivity of multiplication through addition, associativity of addition, the definition of  
 460 covariance and proposition 2, we can reason as follows.

$$461 \quad r(X, (Y - X)) = \frac{\sum_{i=1}^N (X_i \cdot (Y_i - X_i))}{(N - 1) \cdot \sigma_X \cdot \sigma_{(Y-X)}} = \frac{\sum_{i=1}^N (X_i Y_i - X_i X_i)}{(N - 1) \cdot \sigma_X \cdot \sigma_{(Y-X)}} = \frac{\sum_{i=1}^N (X_i Y_i) - \sum_{i=1}^N (X_i X_i)}{(N - 1) \cdot \sigma_X \cdot \sigma_{(Y-X)}}$$

$$462 \quad = \frac{cov(X, Y) - cov(X, X)}{\sigma_X \cdot \sigma_{(Y-X)}} = \frac{cov(X, Y) - cov(X, X)}{\sigma_X \cdot \sqrt{\sigma_Y^2 + \sigma_X^2 - 2 \cdot cov(X, Y)}}$$

463 QED

464 It is straightforward to adapt proposition 3 to be fully in terms of correlations.

465 **Proposition 4**

466 
$$r(X, (Y - X)) = \frac{\sigma_Y \cdot r(X, Y) - \sigma_X \cdot r(X, X)}{\sqrt{\sigma_Y^2 + \sigma_X^2 - 2 \cdot \sigma_X \cdot \sigma_Y \cdot r(X, Y)}}$$

467 **Proof**

468 Straightforward from proposition 3 and definition of correlations, which gives the relationship  
 469  $cov(A, B) = \sigma_A \cdot \sigma_B \cdot r(A, B)$ . QED

470 **Scale Invariance**

471 The next set of propositions justifies working with a standardised  $X$  variable.

472 **Lemma 1**

473 
$$\forall c \in \mathbb{R} \cdot |c| \cdot \sigma_A = \sigma_{(c.A)}$$

474 **Proof**

475 Using distributivity of a multiplicative constant through averaging,  $\sqrt{d^2} = |d|$  and distributivity of  
 476 square root through multiplication, we can reason as follows.

477 
$$\sigma_{(c.A)} = \sqrt{\frac{\sum_{i=1}^N (c \cdot A_i - \overline{c \cdot A})^2}{N - 1}} = \sqrt{\frac{\sum_{i=1}^N (c \cdot A_i - c \cdot \bar{A})^2}{N - 1}} = |c| \cdot \sqrt{\frac{\sum_{i=1}^N (A_i - \bar{A})^2}{N - 1}} = |c| \cdot \sigma_A$$

478 QED

479 **Proposition 5 (Invariance to scaling)**

480 The absolute magnitude of a correlation is not changed by scaling either variable by a constant, i.e.

481 
$$\forall c \in \mathbb{R} \cdot r(A, B) = \text{sign}(c) \cdot r(c.A, B) = \text{sign}(c) \cdot r(A, c.B)$$

482 where  $\text{sign}(d) = \text{if } (d < 0) \text{ then } -1 \text{ else } +1$ .

483 **Proof**

484 For any  $c \in \mathbb{R}$ , using distributivity of multiplication through mean and addition, and lemma 1, the  
 485 following holds,

486 
$$r(c.A, B) = \frac{\sum_{i=1}^N (c \cdot A_i - \overline{c \cdot A})(B_i - \bar{B})}{(N - 1) \cdot \sigma_{(c.A)} \sigma_B} = \frac{\sum_{i=1}^N (c \cdot A_i - c \cdot \bar{A})(B_i - \bar{B})}{(N - 1) \cdot \sigma_{(c.A)} \sigma_B}$$

487 
$$= \frac{c \cdot \sum_{i=1}^N (A_i - \bar{A})(B_i - \bar{B})}{(N - 1) \cdot |c| \cdot \sigma_A \cdot \sigma_B} = \frac{\text{sign}(c) \cdot \sum_{i=1}^N (A_i - \bar{A})(B_i - \bar{B})}{(N - 1) \cdot \sigma_A \cdot \sigma_B} = \text{sign}(c) \cdot r(A, B)$$

488 Then, one can multiply both sides by  $\text{sign}(c)$  to obtain  $r(A, B) = \text{sign}(c) \cdot r(c.A, B)$ . Additionally,  
 489 as correlations are symmetric,  $\text{sign}(c) \cdot r(c.B, A) = \text{sign}(c) \cdot r(A, c.B)$ , and the full result follows.

490 QED

491 **Corollary 1**

492 
$$\forall c \in \mathbb{R} \cdot r(A, B) = r(c.A, c.B)$$

493 **Proof**

494 Follows from twice applying proposition 5, and that  $sign(c)^2 = +1$ . QED

495 **Proposition 6**

496 
$$\forall c \in \mathbb{R} \cdot r(X, (Y - X)) = r(c.X, (c.Y - c.X))$$

497 **Proof**

498 We can use distributivity of multiplication through subtraction and corollary 1 to give us the  
499 following.

500 
$$r(c.X, (c.Y - c.X)) = r(c.X, c.(Y - X)) = r(X, (Y - X))$$

501 QED

502 It follows from proposition 6 that we can work with a standardised  $X$  variable, since,

503 
$$r(X/\sigma_X, (Y/\sigma_X - X/\sigma_X)) = r(X, (Y - X))$$

504 **Proposition 7 (Sufficiency of variability ratio)**

505 Assume two pairs of variables:  $X_1, Y_1$  and  $X_2, Y_2$ , such that,  $r(X_1, Y_1) = r(X_2, Y_2)$ , then,

506 
$$\frac{\sigma_{Y_1}}{\sigma_{X_1}} = \frac{\sigma_{Y_2}}{\sigma_{X_2}} \implies r(X_1, (Y_1 - X_1)) = r(X_2, (Y_2 - X_2))$$

507 **Proof**

508 The proof has two parts.

509 1) We consider the implications of equality of ratio of standard deviations. Firstly, we note that,

510 
$$\frac{\sigma_{Y_1}}{\sigma_{X_1}} = \frac{\sigma_{Y_2}}{\sigma_{X_2}} \iff \frac{\sigma_{X_2}}{\sigma_{X_1}} = \frac{\sigma_{Y_2}}{\sigma_{Y_1}} \quad (\text{eqn ratios})$$

511 Secondly, using eqn ratios, we can argue as follows,

512 
$$\frac{\sigma_{Y_1}}{\sigma_{X_1}} = \frac{\sigma_{Y_2}}{\sigma_{X_2}} \iff \left( \sigma_{Y_2} = \frac{\sigma_{X_2}}{\sigma_{X_1}} \sigma_{Y_1} \wedge \sigma_{X_2} = \frac{\sigma_{Y_2}}{\sigma_{Y_1}} \sigma_{X_1} \right) \iff \left( \sigma_{Y_2} = \frac{\sigma_{X_2}}{\sigma_{X_1}} \sigma_{Y_1} \wedge \sigma_{X_2} = \frac{\sigma_{X_2}}{\sigma_{X_1}} \sigma_{X_1} \right)$$
  
513 
$$\implies (\exists d \in \mathbb{R} \cdot \sigma_{Y_2} = d \cdot \sigma_{Y_1} \wedge \sigma_{X_2} = d \cdot \sigma_{X_1})$$

514 2) Using 4, the fact that  $r(X_1, Y_1) = r(X_2, Y_2)$ , the property just derived in part 1), with  $d = \frac{\sigma_{X_2}}{\sigma_{X_1}}$  and  
515 rules of square roots, we can reason as follows,

516 
$$r(X_2, (Y_2 - X_2)) = \frac{\sigma_{Y_2} \cdot r(X_2, Y_2) - \sigma_{X_2} \cdot r(X_2, X_2)}{\sqrt{\sigma_{Y_2}^2 + \sigma_{X_2}^2 - 2 \cdot \sigma_{X_2} \cdot \sigma_{Y_2} \cdot r(X_2, Y_2)}} = \frac{\sigma_{Y_2} \cdot r(X_1, Y_1) - \sigma_{X_2} \cdot r(X_1, X_1)}{\sqrt{\sigma_{Y_2}^2 + \sigma_{X_2}^2 - 2 \cdot \sigma_{X_2} \cdot \sigma_{Y_2} \cdot r(X_1, Y_1)}}$$
  
517 
$$= \frac{d \cdot \sigma_{Y_1} \cdot r(X_1, Y_1) - d \cdot \sigma_{X_1} \cdot r(X_1, X_1)}{\sqrt{d^2 \cdot \sigma_{Y_1}^2 + d^2 \cdot \sigma_{X_1}^2 - 2 \cdot d \cdot \sigma_{X_1} \cdot d \cdot \sigma_{Y_1} \cdot r(X_1, Y_1)}} = \frac{d \cdot (\sigma_{Y_1} \cdot r(X_1, Y_1) - \sigma_{X_1} \cdot r(X_1, X_1))}{d \cdot \sqrt{\sigma_{Y_1}^2 + \sigma_{X_1}^2 - 2 \cdot \sigma_{X_1} \cdot \sigma_{Y_1} \cdot r(X_1, Y_1)}}$$
  
518 
$$= r(X_1, (Y_1 - X_1)).$$

519 QED

520 **Proposition 8**

521 If  $\Delta = Y - X$  and  $p\Delta = X \cdot \beta$ , where  $\beta \in \mathbb{R}$ , then,

522 1)  $r(p\Delta, \Delta) = \text{sign}(\beta) \cdot r(X, \Delta)$ ; and

523 2)  $r(X + p\Delta, Y) = \text{sign}(1 + \beta) \cdot r(X, Y)$ .

524 **Proof**

525 Both results are easy consequences of proposition 5.

526 1)  $r(p\Delta, \Delta) = r(X \cdot \beta, \Delta) = \text{sign}(\beta) \cdot r(X, \Delta)$ .

527 2)  $r(X + p\Delta, Y) = r((X + (X \cdot \beta)), Y) = r((X \cdot (1 + \beta)), Y) = \text{sign}(1 + \beta) \cdot r(X, Y) = r(X, Y)$ .

528 QED

529 **Main Findings**

530 **Theorem 1:**

531 Since  $X$  will be standardised, we can adapt the finding in proposition 4, to give us the key  
532 relationship we need,

533 
$$r(X, (Y - X)) = \frac{\sigma_Y \cdot r(X, Y) - \sigma_X}{\sqrt{\sigma_Y^2 + 1 - 2 \cdot \sigma_Y \cdot r(X, Y)}} \quad (\text{eqn Imprint})$$

534 Note, this equation can be found in (Oldham, 1962), and also in (Tu *et al.*, 2005).

535 **Proof**

536 Immediate from proposition 4. QED

537 Theorem 1 shows clearly that  $r(X, (Y - X))$  is fully defined by the correlations  $r(X, Y)$  and  $r(X, X)$ ,  
538 along with the variability of  $Y$ . The correlation of  $X$  with itself, i.e.  $r(X, X)$ , is a prominent aspect of  
539 this equation, which drives its oddities.  $r(X, X)$  reflects the coupling in the equation that arises  
540 because  $X$  appears in both the terms being correlated in  $r(X, (Y - X))$ .  $r(X, X)$  is of course a  
541 constant, i.e. 1 for any  $X$ , so in fact,  $\sigma_Y$  and  $r(X, Y)$ , are the only variables; accordingly, their size  
542 determines the extent to which the imprint of  $X$  in  $Y - X$  drives  $r(X, (Y - X))$ .

543 This leads to the key observation that, as  $\sigma_Y$  gets smaller,  $r(X, (Y - X))$  tends towards  $-r(X, X)$ ,  
544 which equals  $-1$ . In other words, as the variability of  $Y$  decreases, the imprint of  $X$  becomes  
545 increasingly prominent. This is shown in the next theorem.

546 **Theorem 2**

547 
$$r(X, (Y - X)) \rightarrow -r(X, X) = -1, \quad \text{as } \sigma_Y \rightarrow 0$$

548 **Proof**

549 The right hand side of equation *Imprint*, has five constituent terms, two in the numerator and three  
550 in the denominator. Of these five, three are products with the standard deviation of  $Y$ , i.e.  $\sigma_Y$ .  
551 Assuming all else is constant, as  $\sigma_Y$  reduces, the absolute value of each of these three terms reduces  
552 towards zero. The rate of reduction is different amongst the three, but they will all decrease.  
553 Accordingly, as  $\sigma_Y$  decreases,  $r(X, (Y - X))$  becomes increasingly determined by the two terms not

554 involving  $\sigma_Y$ , and thus, it tends towards  $-\frac{r(X,X)}{\sqrt{+1}} = -r(X,X) = -1$ .

555 QED

556

### 557 Equality of Residuals

558 An important finding of section 5 of the main text, is that the residuals resulting from regressing  $Y$   
559 onto  $X$  are the same as regressing  $Y-X$  onto  $X$ . We show in this section, that this equality of residuals  
560 is necessarily the case.

561 We focus on the following two equations,

562 Eqn 1)  $Y = \tilde{X} \cdot \beta_1 + \varepsilon_1$

563 Eqn 2)  $Y - X = \tilde{X} \cdot \beta_2 + \varepsilon_2$

564 where  $\tilde{X}$  is the  $N \times 2$  matrix, with first column being  $X$  and second being the  $N \times 1$  vector of ones  
565 (which provides the intercept term);  $\beta_1$  and  $\beta_2$  are  $2 \times 1$  vectors of parameters and  $Y, X, \varepsilon_1$  and  $\varepsilon_2$   
566 are  $N \times 1$  vectors. As in the rest of this document,  $Y$  and  $X$  are our (demeaned) initial and outcome  
567 variables, while  $\varepsilon_1$  and  $\varepsilon_2$  are our residual error terms.

### 568 Proposition 9

569 If we assume that  $\beta_1$  and  $\beta_2$  are fit with ordinary least squares, with  $\varepsilon_1$  and  $\varepsilon_2$  the associated  
570 residuals, then,  $\varepsilon_1 = \varepsilon_2$ .

### 571 Proof

572 Under ordinary least squares, the parameters are set as follows.

573 
$$\beta_1 = (\tilde{X}^T \tilde{X})^{-1} \tilde{X}^T Y \quad (\text{Eqn 3})$$

574 
$$\beta_2 = (\tilde{X}^T \tilde{X})^{-1} \tilde{X}^T (Y - X) \quad (\text{Eqn 4})$$

575 We start with the second of these, and using left distributivity of matrices, and then substituting Eqn  
576 3, we obtain the following.

577 
$$\beta_2 = (\tilde{X}^T \tilde{X})^{-1} \tilde{X}^T (Y - X) = (\tilde{X}^T \tilde{X})^{-1} \tilde{X}^T Y - (\tilde{X}^T \tilde{X})^{-1} \tilde{X}^T X = \beta_1 - (\tilde{X}^T \tilde{X})^{-1} \tilde{X}^T X$$

578 Using the fact that the variable  $X$  is demeaned, we can now evaluate the main term here as follows,

579 
$$\beta_2 = \beta_1 - (\tilde{X}^T \tilde{X})^{-1} \tilde{X}^T X = \beta_1 - \begin{pmatrix} X^2 & \Sigma X \\ \Sigma X & N \end{pmatrix}^{-1} \begin{pmatrix} X^2 \\ \Sigma X \end{pmatrix} = \beta_1 - \frac{1}{A} \begin{pmatrix} N & -\Sigma X \\ -\Sigma X & X^2 \end{pmatrix} \begin{pmatrix} X^2 \\ \Sigma X \end{pmatrix}$$

580 where  $X^2$  is the dot product of  $X$  with itself,  $\Sigma X$  is the sum of the vector  $X$ , and  $A = NX^2 - \Sigma X \Sigma X$  is  
581 the determinant of the matrix being inverted. From here we can derive the following,

582 
$$\beta_2 = \beta_1 - \frac{1}{A} \begin{pmatrix} NX^2 - \Sigma X \Sigma X \\ -\Sigma X \cdot X^2 + X^2 \cdot \Sigma X \end{pmatrix} = \beta_1 - \frac{1}{A} \begin{pmatrix} A \\ 0 \end{pmatrix} = \beta_1 - \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

583 We can then substitute this equality for  $\beta_2$  in eqn 2 and re-arrange to obtain,

584 
$$Y - X = \tilde{X} \beta_2 + \varepsilon_2 = \tilde{X} \left( \beta_1 - \begin{pmatrix} 1 \\ 0 \end{pmatrix} \right) + \varepsilon_2 = \tilde{X} \beta_1 - X + \varepsilon_2$$

585 It follows straightforwardly from here that,



586

$$Y - \bar{X}\beta_1 = \varepsilon_2$$

587 i.e.  $\varepsilon_1 = \varepsilon_2$ , as required.

QED

588 Proposition 9 shows that the residuals resulting from fitting equations 1 and 2 will be the same. A  
589 consequence of this is that the error variability will be the same. As a result of this, the factor that  
590 determines whether more variance is explained when regressing  $Y$  onto  $X$  or when regressing  $Y - X$   
591 onto  $X$ , is the variance available to explain. That is, the relative variance of  $Y$  and  $Y - X$  drive the  $R^2$   
592 values of these two regressions. This then implicates the variance of  $Y$  and  $X$  and in fact their  
593 covariance (which impacts the variance of  $Y - X$ ).

594 More precisely, we can state the following.

595 1) If  $\sigma_{(Y-X)}^2$  is big relative to  $\sigma_Y^2$ , then regressing  $Y - X$  onto  $X$  will explain more variability than  
596 regressing  $Y$  onto  $X$ .

597 2) If  $\sigma_{(Y-X)}^2$  is small relative to  $\sigma_Y^2$ , then regressing  $Y - X$  onto  $X$  will explain less variability than  
598 regressing  $Y$  onto  $X$ .

599

600

601

602 **Supplementary Appendix B: illustrating the relationship between the correlations**

603

```

604 % This function illustrates the relationship
605 function [r_XY,std_Y,r2,r3] = CheckEqn1()
606
607 noise = [0.01:0.01:1,2:100]; % controls r(X,Y)
608 scale = [0.01:0.01:1,2:100]; % controls sigma_Y/sigma_X
609 X = single(randn(1000,1));
610 for j=1:length(noise)
611     Y = X + single(randn(1000,1).*noise(j)); %Y is X plus noise
612     Y = zscore(Y); % then scale to X so the actual scaling is consistent
613     for k=1:length(scale)
614         Y1 = Y.*scale(k); % rescale to control the variability ratio
615         r_XY(j,k) = corr(X,Y); % calculate the correlation with outcomes
616
617         r2(j,k) = corr(X,Y1-X); % calculate the correlation with change
618         std_Y(j,k) = std(Y1)./std(X); % record the variability ratio
619         r3(j,k) = eqn_r_X_XminusY(r_XY(j),std_Y(j,k)); % check Equation 1
620     end
621 end
622
623 % display the resulting surface (Figure 1)
624 figure,surf(log(std_Y),r_XY,r3,'edgecolor','none')
625 lighting flat
626 l = light('Position',[50 100 100]);
627 l = light('Position',[50 100 -50]);
628 l = light('Position',[50 -100 -50]);
629 l = light('Position',[-50 -15 29]);
630 l = light('Position',[-50 -15 -29]);
631 l = light('Position',[-50 15 -29]);
632 l = light('Position',[50 15 -29]);
633 l = light('Position',[50 15 -50]);
634 shading interp
635 xlabel('log ( sigmaY / sigmaX )')
636 ylabel('r(X,Y)')
637 zlabel('r(X,Y-X)')
638
639 % confirm that equation 1 does actually match 'empirical' r(X,Y-X)
640 figure,scatter(r2(:),r3(:))
641 xlabel('Empirical coefficients')
642 ylabel('Derived coefficients')
643
644 end
645
646 % This function implements Equation 1
647 function res = eqn_r_X_XminusY(r_XY,std_Y)
648
649 res = (((r_XY.*std_Y) - 1) ./ sqrt(1 + (std_Y).^2 - (2*(r_XY.*std_Y))));
650
651 end
652
653

```