

Clinically Important Changes in Progressive Supranuclear Palsy: CGI-C Worsening & Effects on PSPRS, SEADL & RBANS

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AIMS

The PSPRS, RBANS and SEADL are widely-used scales as key endpoints in progressive supranuclear palsy (psp) in clinical trials; however, the magnitude of change required in these measures for a clinically meaningful effect is unclear. A sensitive approach would be to determine what degree of change on a specific rating scale would be considered clinically meaningful for the physician who treats the patient. Using data from two global multinational studies with psp subjects, we sought to identify the mean score change in PSPRS, RBANS and SEADL when the CGI-C rating indicates clinical worsening.

METHODS

We investigated clinically important changes on the PSPRS, RBANS and SEADL when subjects were identified as minimal and moderately worsening using the CGI-C. Clinically important changes were defined as mean change of PSPRS, RBANS and SEADL in subjects rated for the first time as “minimally worse” or “moderately worse” on CGI-C at 6 and 12 months since baseline. Data from these scales was analyzed for baseline, 6 and 12 months for 863 subjects with psp enrolled in two multinational double-blind, placebo-controlled clinical trials.

RESULTS

The mean changes for minimal worsening in PSPRS, SEADL and RBANS for CGI-C of were respectively: 5.93 ± 12.66 ($d=0.51$), -11.04 ± 20.75 ($d=-0.53$) and -2.49 ± 14.29 ($d= -0.18$). The mean changes for moderately worsening in PSRS, SEADL and RBANS for CGI-C of 6 were respectively: 9.34 ± 11.22 ($d=0.90$), -17.28 ± 18.82 ($d= -0.86$) and -2.04 ± 13.49 ($d= -0.16$).

Figure 1: PSPRS, SEADL and RBANS mean changes and graphical representation when minimal worsening is rated

Scale	Visit	Mean	Mean Change	SD	N	Min	Max
CGI-C	CGI5	5.00	N/A	0.00	479	5	5
PSPRS	Baseline	35.92	N/A	10.53	478	9	68
PSPRS	CGI5	41.85	5.93	12.66	472	10	84
RBANS	Baseline	74.37	N/A	13.49	440	43	121
RBANS	CGI5	71.88	-2.49	14.29	410	41	122
SEADL	Baseline	58.13	N/A	21.03	476	10	90
SEADL	CGI5	47.09	-11.04	20.75	474	1	90

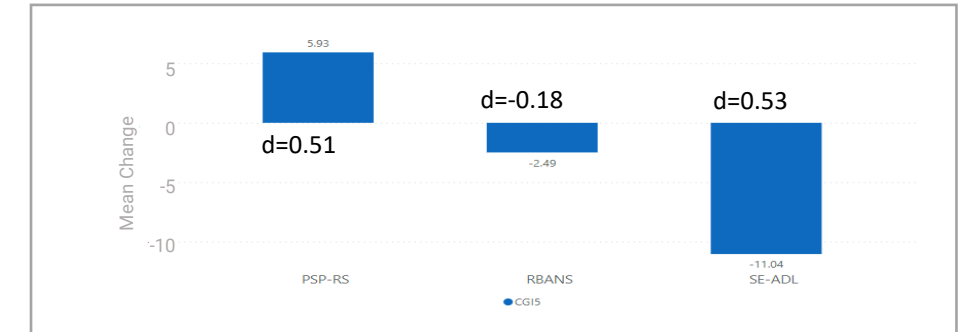
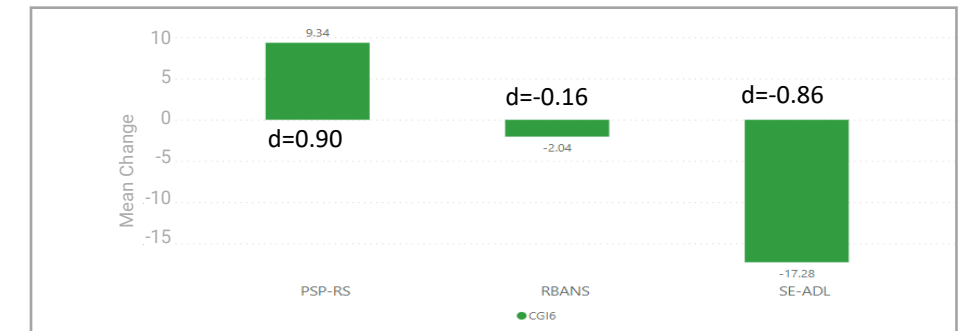


Figure 2: PSPRS, SEADL and RBANS mean changes and graphical representation when moderately worsening is rated.

Scale	Visit	Mean	Mean Change	SD	N	Min	Max
CGI-C	CGI6	6.00	N/A	0.00	261	6	6
PSPRS	Baseline	39.71	N/A	9.70	259	12	69
PSPRS	CGI6	49.05	9.34	11.22	252	20	77
RBANS	Baseline	71.90	N/A	12.93	241	43	119
RBANS	CGI6	69.86	-2.04	13.49	207	41	105
SEADL	Baseline	53.12	N/A	21.58	260	10	90
SEADL	CGI6	35.83	-17.28	18.82	252	10	90



CONCLUSIONS:

We have explored the effect sizes of change on these three instruments associated with CGI changes reflecting mild worsening and moderate worsening. Both the SEADL and the PSPRS captured worsening effectively, and the amount of change on each of these instruments that corresponds to minimal and moderate worsening on the CGI-C was calculated. The RBANS was less sensitive to change as measured by the CGI-C, possibly because it is a focused neurocognitive assessment and does not consider motor symptoms or activities of daily living.

REFERENCES

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