Cohyard Foundation	'	ACTIVE MA N = 1	ACTIVE MAINTENANCE N = 16,729		Ŵ	MANIPULATION OF INFORMATION N = 26,727	OF INFORMATIO 26,727	NO		MAINT. N=1	MAINT. + MANIP. N = 19,153	CONTIN	CONTINUOUS UPDATING N = 11,616	ATING	SECONE	SECONDARY MEASURES N = 24,321	URES	WM N = 100,134
458 Columnat Backward Ordering Number Spanin Althrineter Spanin Spani		Digit Span	Spatial Span	Digit Span	ı	Letter-		TBX List	Spatial Span					CANTAB				
1. 1. 1. 1. 1. 1. 1. 1.	iort	Forward	Forward	Backward		Number Span	Arithmetic	Sorting	Backward	Digit Span	Spatial Span	N-back	PASAT	SWM	CPT	TMT-B	COWAT	Total
458 - 458 - 458 - - 458 - - 458 - - 458 - - 458 - - 458 - - 458 - - - 515 - 515 - - - - 515 - <td></td> <td></td> <td>:</td> <td>:</td> <td>;</td> <td></td> <td></td> <td></td> <td></td> <td>669</td> <td></td> <td>:</td> <td></td> <td></td> <td></td> <td>;</td> <td></td> <td>669</td>			:	:	;					669		:				;		669
1,		458	1	458	1	1	1	1	1	458	;	ı	:	1	:	515	;	1,889
80 66 67 80 33 70 70 80 1272 1272		;	:	;	;	:	:	;	;	;	;	2,104	;	1	1,052	;	:	3,156
1,272 1,272 1,272 648 7.0 645 645 645 645 645 645 645 645 645 645 645 645 645 645 645 645 645 645 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70 645 70		80	99	1	1	79	1	1	99	80	33	ı		1	33	79	80	296
1,272		;	;	;	;	;	;	;	;	;	;	;	:	;	1	1,570	;	1,570
710 645 710		1,272	1	1,272	1,272	628	1	1	1	636	635	ı		1				5,715
455 - 456 - - 455 - 455 - 451 - 451 453 - 451 - 451 - 451 - 451 451 - - 451 -		710	645	710	;	;	;	;	645	710	;	;	:	645	645	708	710	6,128
2,033 - 2,018 - - 2,018 - - 2,018 - - 2,018 - - 2,018 - - 2,018 - - 2,018 - - 2,018 - - 3,917 1,995 1,995 - - 1,445 1,445 1,469 - - 1,212 - - 1,712 - - 1,445 - - - 1,445 1,445 - <td></td> <td>455</td> <td>:</td> <td>455</td> <td>454</td> <td>;</td> <td>1</td> <td>1</td> <td>1</td> <td>455</td> <td>1</td> <td>;</td> <td>313</td> <td>1</td> <td>1</td> <td>451</td> <td>453</td> <td>3,036</td>		455	:	455	454	;	1	1	1	455	1	;	313	1	1	451	453	3,036
1,357 1,362 1,362 1,469 1,469 1,362 1,362 1,212 1,212 1,72 1,445		2,033	1	2,018	ı	:	1	1	1	2,018	;	ı	;	1	:	3,917	1,995	11,981
1		1,357	1	1,362	;	1,148	1,469	1	1	1,362	;	1,212	;	!	177	1,445	1,462	10,994
989 989 <td>_</td> <td>1</td> <td>1</td> <td>1</td> <td>1</td> <td>1</td> <td>1</td> <td>1</td> <td>1</td> <td>782</td> <td>1</td> <td>1</td> <td>;</td> <td>1</td> <td>1</td> <td>;</td> <td>1</td> <td>782</td>	_	1	1	1	1	1	1	1	1	782	1	1	;	1	1	;	1	782
4,497 4,481 4,481	9	686	686	686	;	:	:	:	686	686	686	;	;	1	:	686	1	6,923
1,034 1,034 660 1,034		4,497	1	4,481	1		1	1	1	4,481	;	ı		1		,		13,459
4 -		1,034	:	1,034	099	:	:	;	1	1,034	;	:	;	!	:	;	1	3,762
1,312 1,312 1,312		1	1	1	ı	1	1	1	1	1	1	860		859	847	;	1	2,566
""" """" """" """" """" """" """" """" """" """" """" """" """" """" """" """" """" """"	ı	1	1	1	1	1	1,312	1	1	1,312	337	511	:	1	331	516	525	4,844
<		;	1	;	1	1		1,359	1	1	;	;	;	!	;	;	;	2,718
2,100 2,124 1,504 2,124 836 989 44 44 1,504 52 196 64 170 217 218 15,029 1,700 14,947 2,386 3,554 2,781 4,418 16,963 2,190 9,799 313 1,504 7,482 10,407 6,432		1	1	1	1	1	1	1	1	1	1	4,212	;	1	4,247	;	1	8,459
44 - 44 - 45 -		2,100	:	2,124	;	1,504	:	;	;	2,124	;	836	;	1	1	;	686	2/9'6
15,029 1,700 14,947 2,386 3,554 2,781 4,418 16,963 2,190 9,799 313 1,504 7,482 10,407 6,432		44	:	44	1	195	:	:	1	52	196	64	:	!	150	217	218	1,180
	TEI.	15,029	1,700	14,947	2,386	3,554	2,781		4,418	16,963	2,190	662'6	313	1,504	7,482	10,407	6,432	100,134

Table 2. Working memory measures currently available in COGENT. See Table 1 for Cohort descriptions. Note that an individual participant can have multiple working memory datapoints (and many do), each of which can be utilized in Genomic SEM as the program fully accounts for sample overlap. Abbreviations: TBX, NIH Toolbox; PASAT, Paced Auditory Serial Addition Test; CANTAB SWM, Cambridge Neuropsychological Test Automated Battery - Spatial Working Memory; CPT, Continuous Performance Test, TMT-B, Trail Making Test - Part B; COWAT, Controlled Oral Word Association Test.

the phenotypes themselves, and the phenotypic covariance matrix is empirically estimated from the raw phenotypic data. The fit function used will be maximum likelihood (ML), and goodness-of-fit of the models will be assessed by the Root Mean Square SEM [60] to compare with the genetic structural models. In the phenotypic SEM, the latent working memory factor represents Phenotypic Factor Models. We will perform phenotypic factor analysis of the working memory data within each sample with Onyx Error of Approximation (RMSEA) in addition to SRMR, AIC, and CFI described above [59,60,65].

For this application, we generated a CFA model in an exemplary COGENT working memory dataset comprised of 315 healthy German adults who completed Arithmetic, Digit Span, Spatial Span, N-back, CPT, Trails B, and COWAT. These are 7 of the most common working memory measures available in COGENT. In **Figure 3**, the common factor *phenotypic* model of working memory is a very good fit to the data [67]. The common factor *Gwm* model will be derived similarly using the genetic covariance structure of working memory in Genomic SEM [59,65].

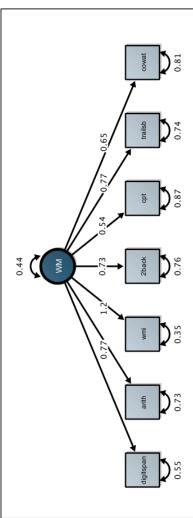


Figure 3. Phenomic SEM of Working Memory ("WM"). A subset of 315 healthy control adults from our Munich, Germany cohort completed a neuropsychological battery comprised of many core measures we propose to study. All 7 subtests loaded on a common working memory factor that accounted for 44% of the variance in performance. This model fit the data well: $\chi = 14.33$, RMSEA = .043, SRMR = .033, CFI = .981, TLI = .968. Genetic factor models of Gwm in Genomic SEM will be derived and tested mirroring as above but based on the genetic covariance structure of the underlying working memory subtests and domains.