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Neurocognitive profiles of marginally housed persons with comorbid substance dependence, viral infection, and psychiatric illness

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Introduction: Individuals living in single-room occupancy (SRO) hotels constitute a socially marginalized group with exposure to multiple factors with adverse effects on neurocognition, including substance use, viral infection, psychiatric illness, and brain injury. Consequently, marked heterogeneity in neurocognitive functioning is

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observed. This study aimed to identify and describe distinct neurocognitive profiles within a marginally housed sample. *Method:* Two hundred and forty-nine ($N = 249$) SRO hotel residents (mean age = 43.5 years) were recruited. A battery of tests assessed neurocognition across six domains: premorbid IQ, verbal memory, attention, inhibition, mental flexibility, and decision making. Clinical examinations collected information pertaining to substance use and psychiatric diagnoses, viral infection, psychiatric symptoms, risk behaviors, and everyday functioning. Cluster analysis was used to identify subgroups of individuals with similar neurocognitive profiles and was supplemented with a discriminant function analysis. Analyses of variance and chi-square tests were used to validate the derived clusters on key clinical and functional variables. *Results:* A three-cluster solution was found to be optimal. Cluster 1 ($n = 59$) presented as overall higher functioning, whereas Cluster 3 ($n = 87$) exhibited overall lower functioning with a relative strength in decision-making skills. Cluster 2 ($n = 103$) was characterized by neurocognitive abilities that generally bisected the performance of the other groups, but with a relative weakness in decision-making skills. Discriminant function analysis indicated the six neurocognitive variables comprised two underlying dimensions that accounted for between-group variance. Clusters meaningfully differed on demographics, substance use, viral exposure, psychiatric symptoms, neurological soft signs, and risk behavior. *Conclusion:* Neurocognitive functioning provides the basis for identifying meaningful subgroups of marginally housed individuals, which can be reliably differentiated on key variables. This approach facilitates an understanding of the neurocognitive dysfunction and associated vulnerabilities of marginalized persons and ultimately may elucidate intervention targets.

Keywords: Cluster analysis; Neurocognition; Substance-related disorders; Dual diagnosis; Substandard housing.

Individuals living in single-room occupancy hotels (SROs) constitute one of the most marginalized groups in society and are considered by the United Nations as “at risk for homelessness.” In fact, many marginally housed persons have a history of transient, unstable housing, as well as homelessness (Robertson et al., 2004; Shannon, Ishida, Lai, & Tyndall, 2006). The living conditions of SRO residents are often substandard, yet this continues to be an increasingly common housing solution for socially marginalized people, in both developing and industrialized nations, contributing significantly to social and health inequities (Vlahov et al., 2007). Consequently, marginally housed persons face numerous mental and physical health risks. Dwelling in an SRO was reported to be associated with HIV and hepatitis C virus (HCV) infection, incarceration, physical assault, and severe drug use (Shannon et al., 2006). The prevalence of HIV infection has been noted to be fivefold the regional norm (Robertson et al., 2004), consistent with two to three times greater likelihood of engaging in health risk behaviors, including injection drug use and unprotected sex compared to stably housed peers (Aidala, Cross, Stall, Harre, & Sumartojo, 2005). Marginally housed people are also likely to experience worse clinical consequences from HIV infection, impaired social functioning, and poor perceived health-related quality of life (Weiser et al., 2009). Regarding psychiatric illness, the lifetime prevalence rates for psychosis and major depression are reported to be upwards of 40% in homeless persons (Fazel, Khosla, Doll, & Geddes, 2008). Prevalence

rates for concurrent substance use and mental disorders in the homeless are also notably high (Koegel, Sullivan, Burnam, Morton, & Wenzel, 1999; Strehlau, Torchalla, Li, Schuetz, & Krausz, 2012). When compared to substance users with stable housing, the alcohol, drug, and mental health problems experienced by the homeless and marginally housed are of greater severity (Eyrich-Garg, Cacciola, Carise, Lynch, & McLellan, 2008). Other negative exposures of marginalized individuals include high rates of childhood trauma (Pluck et al., 2011; Torchalla, Strehlau, Li, Schuetz, & Krausz, 2012), frequent use of the hospital emergency room (Kushel, Perry, Bangsberg, Clark, & Moss, 2002), and an increased rate of food insecurity (Weiser et al., 2009). Recently, we characterized the physical and mental health of a large cohort of individuals living in SRO hotels in the Downtown Eastside (DTES) of Vancouver, British Columbia (The Hotel Study; Vila-Rodriguez et al., 2013). This sample presented with a high degree of multimorbidity with markedly elevated rates of psychosis (47.4%), HIV infection (18.4%), neurological illness (45.8%), and substance dependence (95.2%). Ultimately, a fivefold increased mortality rate was observed over a two-year follow-up period. This finding is in keeping with the heightened mortality rate of the Canadian marginally housed population, whereby even after accounting for low income, remaining life expectancy for men is 10 years less than that of the national cohort, and seven years less for women (Hwang, Wilkins, Tjepkema, O’Campo, & Dunn, 2009).

The multitude of risk factors that marginally housed persons routinely encounter across the lifespan (such as developmental, substance use, viral infection, psychiatric illness, and brain injury) is apt to impose a substantial neuropsychological burden. Indeed, within the context of the individuals' premorbid neurocognitive capacities, these factors are likely to differentially damage and dysregulate brain circuitry critical to neurocognition—depending upon the extent and type of noxious exposure. Nonetheless, subgroups of individuals with common neurocognitive profiles may be identifiable for at least two reasons. First, individuals who share etiologies that dysregulate common brain circuitry are apt to exhibit a similar neurocognitive profile of dysfunction. Second, equifinite processes may come into play, such that different external factors may insult brain circuitry in a similar fashion, leading to comparable profiles of functioning (Lange, Iverson, & Franzen, 2008).

The aim of the current study was to optimally characterize the neurocognition of a cohort of SRO hotel residents from the DTES (see Vila-Rodriguez et al., 2013). The Hotel Study provided a unique opportunity to examine the neurocognitive functioning of a marginally housed population against a rich backdrop of clinical data collected through extensive medical and psychiatric examinations. Cluster analysis techniques were used to group individuals based on similar patterns of neurocognitive functioning across the domains of premorbid IQ, verbal memory, attention, and executive functions. This approach is ideal for this population, as it preserves inherent heterogeneity and allows inspection of within- and between-group neurocognitive patterns (Lange et al., 2008; Lange, Iverson, Senior, & Chelune, 2002). A second aim was to validate the derived clusters by examining whether meaningful differences exist between the subgroups on putative risk factors of neurocognitive dysfunction and on core clinical and functional characteristics. Elucidating common patterns of neurocognitive functioning and their associated characteristics is valuable because it may assist in optimizing intervention strategies, particularly given that these individuals are challenged to navigate a universally available, yet complex, high threshold system of care.

Given the paucity of literature on the neurocognition of marginalized populations, our approach is exploratory in nature. Nevertheless, on the basis of known associations between common risk factors and neurocognition, conjectures are forwarded regarding *general* profile patterns. First, we anticipated that a low-functioning neurocognitive profile would be associated with more severe psychotic

symptoms (Dominguez, Viechtbauer, Simons, van Os, & Krabbendam, 2009; Lindsberg, Poutiainen, & Kalska, 2009), increased depression (Hammar & Årdal, 2009), and poorer social and role functioning (Morgan & Heaton, 2009). Second, given the vulnerability of frontal brain circuitry to various risk factors in this population (e.g., Murrough, Iacoviello, Neumeister, Charney, & Iosifescu, 2011; Yücel, Lubman, Solowij, & Brewer, 2007), we anticipated that a profile of more prominent weakness in executive functions would emerge. Such a profile may be predominately associated with an increase in health risk behaviors (Bousman et al., 2010).

METHOD

Participants

Two hundred and ninety three ($N = 293$) individuals were recruited from four different SRO hotels, located in the DTES of Vancouver, British Columbia, as part of a 5-year longitudinal study (see Vila-Rodriguez et al., 2013). A total of 288 individuals participated in baseline neurocognitive assessments, with 39 participants excluded because of missing or invalid data on more than one neuropsychological measure; yielding a final sample size of 249. A description of the sample is provided in Table 1. Ethics approvals for the study were obtained from the Clinical Research Ethics Board of the University of British Columbia and the Simon Fraser University Office of Research Ethics. All participants provided written informed consent, which included consent to communicate clinically significant findings to participants' physicians, and received honoraria.

Materials and procedure

Neurocognitive assessment

Neuropsychological tests of memory, attention, and executive abilities were administered to participants by trained research assistants. Premorbid IQ was estimated using the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001). Verbal memory was assessed using the Hopkins Verbal Learning Test Revised (HVLt-R; Brandt & Benedict, 2001) immediate recall score. Sustained attention was measured using the signal detection (A') score from the Rapid Visual Information Processing (RVIP) subtest of the Cambridge Neuropsychological Test Automated

TABLE 1
Sample characteristics

<i>Characteristic</i>	<i>%</i>	<i>M (SD)</i>	<i>Mdn</i>	<i>Range</i>
Age (years)		43.5 (9.3)	44.0	23–68
Education (years)		10.4 (2.3)	10.0	3–16
Premorbid IQ (WTAR)		97.5 (8.9)	97.0	77–122
Symptoms of psychosis (PANSS)				
Positive		15.4 (5.7)	14.0	7–36
Negative		16.3 (6.1)	15.0	7–39
General		35.5 (8.3)	35.0	12–59
Total		67.1 (17.4)	65.0	31–129
Depressive symptoms (BDI)		11.7 (10.5)	9.0	0–46
Social functioning (SOFAS)		39.6 (10.5)	38.0	20–69
Role functioning (RFS)		12.0 (3.3)	12.0	5–24
Ethnicity ^a				
White	60.2			
Aboriginal	28.7			
Black	2.5			
West Asian	2.5			
Latin American	0.8			
Other/unknown	5.3			
Psychiatric diagnosis ^b				
Schizophrenia spectrum	12.7			
Other psychoses	20.4			
Major depression	15.7			
Bipolar disorder I or NOS	5.2			
Bipolar disorder II	1.2			
Substance induced disorders	26.5			
Active psychosis at testing	46.7			
Substance dependence disorder ^b				
Alcohol	16.5			
Cannabis	33.7			
Cocaine	70.7			
Methamphetamine	23.3			
Heroin	35.7			
Viral infection				
HIV ^c	16.7			
Hepatitis C ^c	70.3			
Hepatitis B ^d	41.0			
Herpes simplex ^e	92.0			
Cytomegalovirus ^c	69.0			
Traumatic brain injury				
Any reported head injury ^f	61.0			
With loss of consciousness ^e	31.3			
With memory loss/confusion ^e	19.3			

Note. WTAR = Wechsler Test of Adult Reading; PANSS = Positive and Negative Syndrome Scale; BDI = Beck Depression Inventory; SOFAS = Social and Occupational Functioning Assessment Scale; RFS = Role Functioning Scale; NOS = not otherwise specified.

^a*n* = 244. ^b*n* = 245. ^c*n* = 239. ^d*n* = 229. ^e*n* = 238. ^f*n* = 241.

Battery (CANTAB; Fray, Robbins, & Sahakian, 1996). Three measures indexed various aspects of executive function. First, the color–word trial of the Stroop Color–Word Test assessed response inhibition. Mental flexibility was evaluated by the total adjusted errors score from the Intra-Dimensional Extra-Dimensional (IDED) subtest of the CANTAB (Fray et al., 1996). Finally, the Iowa Gambling Task (IGT; Bechara, Damasio, Damasio, & Anderson, 1994) total net score was employed to assess decision-making skills and response to reward.

Clinical assessment

Trained research assistants, psychiatrists, and/or neurologists conducted clinical assessments. These sessions were discrete from the neurocognitive testing sessions.

Risk factors. To retrospectively quantify substance use (alcohol, cocaine, methamphetamine, heroin) in 4-week intervals, the Time Line Follow Back method (TLFB; Sobell, Sobell, Klajner, Pavan, & Basian, 1986) was employed, and an

average was computed to index substance consumption around the time of neurocognitive testing (one month preceding, current month, one month following¹). Diagnoses of psychiatric disorders and substance use disorders were made according to the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text revision; *DSM-IV-TR*; American Psychiatric Association, 2000) through consensus with the Best Estimate Clinical Evaluation and Diagnosis (BECED; Endicott, 1988) using all available data. This also included a diagnostic interview with the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) and a mental status examination by a psychiatrist (see Table 1 for prevalence of the primary diagnoses). To index exposure to viral infection, participants provided blood samples for serological studies of antibodies to the following five viruses: HIV, HCV, hepatitis B, herpes simplex, and cytomegalovirus. Of note, seropositivity for HIV indicates current infection, whereas seropositivity for the other viruses represents an index of exposure and is indicative of either a current or a past infection. Traumatic brain injury was assessed using a self-report medical questionnaire that indexes history of a head injury and whether it was accompanied by loss of consciousness and/or associated with memory loss and confusion.

Clinical and functional characteristics. Severity of psychotic symptoms was assessed with the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). For the current study, we examined Positive, Negative, and General subscale scores, with higher values indicative of more severe symptoms. A short version of the PANSS, administered on a monthly basis, was used to capture psychosis status at the month of neurocognitive testing. The Beck Depression Inventory 2nd Edition (BDI-II; Beck, Steer, & Brown, 1996) was used to measure depressive symptoms. The Cambridge Neurological Inventory (CNI; Chen et al., 1995) was administered by a neurologist or a psychiatrist to assess neurological soft signs (NSS) along the dimensions of motor coordination, sensory integration, complex sequencing, and disinhibition. The ratings for each dimension were summed to yield a total NSS score, with higher scores representing a greater number of NSS. The Extrapyramidal Symptom

Rating Scale (ESRS; Chouinard & Margolese, 2005) was administered to assess extrapyramidal symptoms (EPS) along the dimensions of dystonia, dyskinesic movements, and parkinsonism. Again, the ratings for each dimension were summed to yield a total EPS score, with higher scores reflecting a greater number of EPS. Adherence to antiretroviral (ARV) medication was assessed using a TLFB to retrospectively quantify the number of days that medication was taken over a 4-week interval surrounding the time of neurocognitive testing. The Maudsley Addiction Profile (MAP; Marsden et al., 1998) was used to index health risk behaviors. Participants were asked to report the number of days that they engaged in injection drug use and the number of times that they shared a crack pipe within the previous 30 days. For this same time interval, the number of unprotected sexual partners and the number of times that participants engaged in sexual intercourse without using a condom were recorded. These latter two indexes were multiplied to mitigate the potential effect of individuals being involved in monogamous relationships in which a greater number of unprotected sexual encounters with the same partner may be perceived as low risk. To assess everyday functioning, the Social and Occupational Functioning Assessment Scale (SOFAS; Goldman, Skodol, & Lave, 1992) and the Role Functioning Scale (RFS; Goodman, Sewell, Cooley, & Leavitt, 1993) were administered. Total scores from each measure reflect ratings determined by trained research assistants based on all available information regarding participants' social, occupational, and role functioning. Higher scores on the SOFAS and RFS are indicative of better functioning.

Statistical analyses

Prior to conducting the cluster analysis, a log transformation was applied to the IDED total adjusted errors score to correct a severe positive skew. These scores were then multiplied by -1 so that negative scores reflect poorer performance, in keeping with the interpretation of other neurocognitive scores. To control for age and education, these variables were regressed on scores for HVLIT, RVIP, Stroop, IDED, and IGT (see Manly et al., 2011 for a similar approach). The resultant standardized residuals (z -scores) were used as the dependent variables in the cluster analyses.

Following the guidelines set forth by Lange and colleagues (2002) a two-step cluster analysis approach was adopted using Statistical Package for the Social Sciences (SPSS) 19.0. This stepwise

¹Due to unavailability for follow-up, 36.1% of participants had TLFB data available for only two months, while 4.8% had TLFB data for one month; 6.8% of participants were missing TLFB for all three months surrounding the date of neurocognitive testing.

process has been demonstrated to promote the best cluster recovery (Milligan, 1980). First, two different hierarchical cluster analyses (Ward's method, average linkage method) were employed to determine the number of clusters present in the sample. The squared Euclidean distance coefficient was selected as the similarity measure because it addressed both profile shape and elevation when assigning cluster membership (Everett, Landau, Leese, & Stahl, 2011). The final number of clusters was determined by visually inspecting the dendrogram for natural breaks in the merging of clusters—a widely accepted method (Clatworthy, Buick, Hankins, Weinman, & Horne, 2005; Lange et al., 2002). A large break in the dendrogram signifies that further merging of the clusters may no longer be meaningful. As a second step, a *k*-means algorithm using random seed points was employed to facilitate optimal assignment of cluster membership (Lange et al., 2002), specifying three clusters as determined by the hierarchical dendrograms. Supplementary to the cluster analysis, a direct discriminant function analysis (DFA) was conducted to determine whether there were any relationships between the six neurocognitive variables that were accounting for separation between the three cluster groups and to evaluate the accuracy of these relationships in classifying the cases. This supplementary approach has been used in similar studies (Delano-Wood et al., 2009; Hermens et al., 2011).

In accordance with best practices, the internal validity of the final cluster solution was examined by constructing a multiprofile multimethod correlation matrix using profile means generated from the hierarchical and *k*-means algorithms. Significant, positive correlations among the corresponding profiles from different algorithms are indicative of good internal cluster validity (Lange et al., 2002). Likewise, nonsignificant or negative correlations between noncorresponding profiles across algorithms also support the internal validity.

The external validity of the derived clusters was evaluated by comparing groups on demographics and external variables. Analysis of variance (ANOVA) was used to compare clusters on continuous variables, which included age, education, monthly substance use, total viral exposure, clinical symptomatology, total NSS, total EPS, monthly ARV medication adherence, health risk behaviors, and everyday functioning. Nonparametric procedures were used when the assumption of normality was violated. Chi-square analyses were employed for categorical data, which included gender, *DSM-IV-TR* diagnoses, psychosis status at testing, HIV infection status, HCV infection status, and history of a traumatic brain injury. Post hoc tests

were used to examine sources of specific differences. The alpha level was set to .05, and a Bonferroni correction was applied when multiple comparisons were made within a given domain and for post hoc comparisons. Trends are reported for significant group differences that did not withstand a Bonferroni correction. Effect sizes (ESs) were calculated for each significant pairwise comparison using *d* (mean difference/pooled standard deviation) for ANOVAs (corresponding to ESs of small = 0.2, medium = 0.5, large = 0.8; Cohen, 1992), *r* for nonparametric analyses (corresponding to ESs of small = 0.1, medium = 0.3, large = 0.5; Cohen, 1992), and the odds ratio for chi-square analyses.

RESULTS

Cluster analysis

No differences were found between included and excluded cases (due to invalid or missing neurocognitive data) on age or education ($ps > .05$). The two-step cluster analysis revealed a three-cluster solution to be optimal: Cluster 1, $n = 59$ (23.7%); Cluster 2, $n = 103$ (41.4%); Cluster 3, $n = 87$ (34.9%). The neurocognitive profile for each cluster is shown in Figure 1, with the group mean plotted for each variable and error bars representing 95% confidence intervals. For illustrative purposes, Figure 2 provides corresponding corrected T-score profiles based upon the established normative test references. Profiles are described in terms of strengths and weaknesses when a given mean differs from the overall mean score (across the six neurocognitive variables) of its respective profile, by at least 0.5 absolute standard deviations (see Dawes et al., 2008). Cluster 1, the smallest group, is characterized

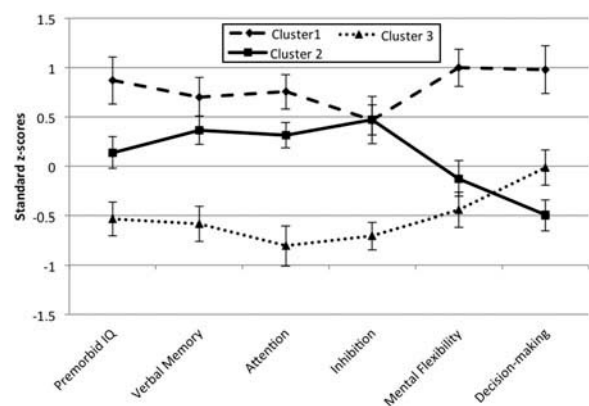


Figure 1. Profiles of means for neurocognitive measures by cluster group using uncorrected z-scores. Errors bars represent 95% confidence intervals.

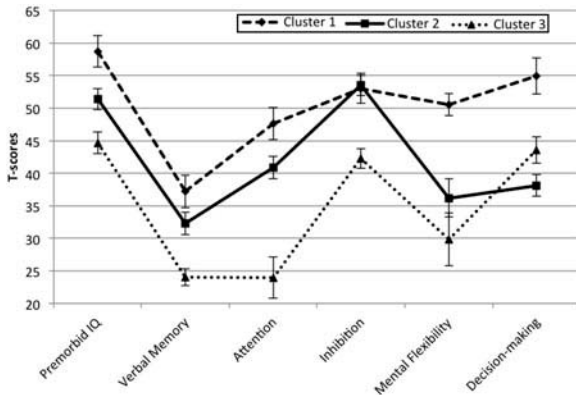


Figure 2. Profiles of means for neurocognitive measures by cluster group using demographically corrected T-scores. Error bars represent 95% confidence intervals.

by a higher level of neurocognitive functioning across domains relative to the other clusters (see Figure 1). Normatively, this cluster exhibits strong estimated premorbid IQ and shows most neurocognitive abilities falling within normal limits, with a prominent impairment (greater than 1 *SD* below the mean) in verbal memory (see Figure 2). Cluster 2, the largest group, is characterized by functioning that generally bisected the other two cluster groups and often tracked closest to the sample mean across most domains, but with a relative weakness in decision-making skills. The corresponding normatively based profile suggests that verbal memory is the most impaired domain of functioning, falling well below average. Nonetheless, mental flexibility and decision-making abilities are also impaired, with average-range premorbid IQ estimate and inhibitory control. Finally, Cluster 3 is marked by the lowest functioning overall compared to the other clusters with a relative strength in decision-making skills, which is within normal limits. Likewise, the

premorbid IQ estimate also falls within normal limits. The normative profile further suggests that verbal memory, attention, and mental flexibility performances are impaired.

Discriminant function analysis

Two discriminant function (DF) variates were generated, and both contributed significantly to separation of the three cluster groups. The first DF accounted for 81.1% of the between-group variance, Wilk's lambda = .166, $p < .001$. The second DF accounted for the remaining 18.9% of the variance, Wilk's lambda = .614, $p < .001$. The most substantial contributors to the first DF variate (in descending order) were tests of sustained attention, premorbid IQ estimate, verbal memory, and mental flexibility. Tests of decision making and inhibition made the greatest contribution to the second DF. The overall DFA model correctly classified 98.7% of cases, with 100% correct classifications for Clusters 1 and 3, and 97% correct classifications for Cluster 2. To eliminate bias in the classification of cases, the leave-one-out (jackknifed) classification procedure was employed as a cross-validation method. The overall correct classification of cases with this approach was marginally lower than the original model at 96.6%, with 96.6% correctly classified for Cluster 1, 94% correct for Cluster 2, and 100% correct for Cluster 3.

Cluster validation

Internal validity

The multiprofile multimethod correlation matrix is displayed in Table 2. Overall, the

TABLE 2
Multiprofile multimethod correlation matrix

Profile	Ward's method			Average linkage method			K-means method		
	wH1	wH2	wH3	aH1	aH2	aH3	K1	K2	K3
wH1	—								
wH2	-.49	—							
wH3	.20	-.83	—						
aH1	.75	-.75	.29	—					
aH2	-.20	.89	-.89	-.46	—				
aH3	-.26	-.55	.75	-.04	-.84	—			
K1	.49	-1.00	.83	.75	-.89	.55	—		
K2	-.26	.94	-.77	-.67	.94	-.70	-.94	—	
K3	-.03	-.77	.94	.20	-.94	.90	.77	-.83	—

Note. Correlations were computed using Spearman's rho; wH = Ward's hierarchical analysis; aH = average linkage hierarchical analysis; K = *k*-means analysis. Italics denote the largest positive correlation between a given profile and one of the three profiles derived from an alternative method.

TABLE 3
Significant between-group differences for external validation variables

Variable	Cluster			Test statistic	Comparisons	Effect size
	1 (<i>n</i> = 59, 23.7%)	2 (<i>n</i> = 103, 41.4%)	3 (<i>n</i> = 87, 34.9%)			
Education years, <i>M</i> (<i>SD</i>)	11.10 (2.23)	10.33 (2.39)	10.00 (2.04)	$F = 4.35^*$	1 > 3	$d = 0.52$
Gender (% male)	86.44	69.90	81.61	$\chi^2 = 7.02^*$	1 > 2 [†]	$OR = 2.74$
Average alcohol days, <i>Mdn</i> (IQR)	0.83 (4.42)	0.33 (1.00)	0.67 (5.58)	$H = 7.21^{*†}$	3 > 2 [†] ; 1 > 2	$r = .18; .17$
Average heroin days, <i>Mdn</i> (IQR)	0.00 (12.00)	0.33 (9.33)	0.00 (1.13)	$H = 9.29^{**}$	1 > 3 [†] ; 2 > 3	$r = .20; .22$
Heroin dependence (%)	40.68	44.66	21.84	$\chi^2 = 11.50^{***}$	1 > 3; 2 > 3	$OR = 2.45; 2.91$
Days injected, <i>Mdn</i> (IQR)	2.00 (30.00)	4.00 (21.00)	0.00 (6.00)	$H = 7.89^{*†}$	2 > 3	$r = .21$
HIV infection (% +)	3.39	16.50	24.14	$\chi^2 = 11.10^{***}$	2 > 1; 3 > 1	$OR = 5.60; 9.01$
Total virus exposure, <i>M</i> (<i>SD</i>)	2.52 (1.08)	2.85 (1.16)	3.21 (1.22)	$F = 5.76^{***}$	3 > 1	$d = 0.59$
PANSS, negative symptoms, <i>M</i> (<i>SD</i>)	13.88 (4.25)	16.20 (6.63)	17.92 (6.11)	$F_{BF} = 7.83^{***}$	3 > 1; 2 > 1 [†]	$d = 0.74; 0.39$
Total NSS, <i>M</i> (<i>SD</i>)	11.86 (10.05)	12.65 (9.03)	17.72 (8.21)	$F = 7.84^{***}$	3 > 1; 3 > 2	$d = 0.64; 0.59$

Note. *OR* = odds ratio; *IQR* = interquartile range; *H* = Kruskal–Wallis nonparametric test statistic; PANSS = Positive and Negative Syndrome Scale; BF = Brown-Forsythe; NSS = neurological soft signs.

* $p < .05$. ** $p < .01$. *** $p < .005$. [†]Not significant following a Bonferroni correction.

profiles derived from the three different algorithms employed positively correlate with their respective profiles generated by each algorithm, while demonstrating nonsignificant or negative correlations with noncorresponding profiles, suggesting adequate internal validity.²

External validity

Table 3 summarizes the significant differences observed between groups, pairwise comparisons, and the corresponding effect sizes. In brief, compared to Cluster 3, Cluster 1 participants were significantly more educated, exhibited less severe negative symptoms, and suffered a lower rate of HIV infection and total virus exposure (sum of 5 viruses). Further, compared to Cluster 3, Cluster 2 participants reported significantly more days per month of heroin use, and a greater proportion of individuals were diagnosed with heroin dependence, with trends noted towards more injection drug use and fewer days per month of alcohol use. Additionally, compared to Cluster 1, Cluster 2 showed trends towards a proportionally higher female composition and more severe negative symptoms. Cluster 3 was characterized by lower education, more severe negative symptoms, and exposure to a greater number of viruses than Cluster 1. Cluster 3 participants also exhibited a

significantly lower rate of heroin dependence and days per month of heroin use, as well as elevated total NSS in comparison to the other clusters. No significant differences were found between clusters on age, diagnoses of psychiatric illnesses or substance dependence disorders (other than heroin dependence), days per month of drug use (other than heroin use), HCV infection, depressive symptoms, total EPS, days per month of ARV medication adherence, risky sexual behaviors, or everyday functioning ($ps > .05$). A summary of the results by cluster group is provided in Table 4.

DISCUSSION

We identified three distinct neurocognitive profiles within a large sample of SRO hotel residents. Our findings generally supported our initial expectations regarding the profiles and their associated features. Participants in Cluster 1 ($n = 59$) emerged with overall higher neurocognitive functioning than the other derived clusters. Compared to standard norms, this group exhibited functioning within normal limits except for impairment in verbal memory. This profile is in keeping with Cluster 1 members having higher years of education, as well as a lower incidence of HIV infection and less severe negative symptoms. These associated features, in conjunction with a strong premorbid IQ estimate, might be considered to be protective factors. For instance, better premorbid intellectual functioning was previously linked to a lower likelihood of engaging in health risk behavior that

²Only one bivariate relationship did not correspond as expected. Profile 1 of the *k*-means algorithm correlated more strongly with Profile 3 of the Ward's algorithm than with Ward's Profile 1 (see Table 2).

TABLE 4
Summary of results

<i>Descriptor</i>	<i>Cluster 1</i>	<i>Cluster 2</i>	<i>Cluster 3</i>
Neurocognition	Highest functioning group within the sample. Normatively, strong premorbid IQ, and average range attention and executive functions, with impaired memory.	Intermediate functioning group within the sample, with a relative weakness in decision-making skills. Normatively, average-range premorbid IQ, attention, and inhibition, with impairments in memory, mental flexibility, and decision-making skills.	Lowest functioning group within the sample, with a relative strength in decision-making skills. Normatively, average-range premorbid IQ, inhibition, and decision-making skills, with impairments in attention, memory, and mental flexibility.
External variables	More years of education, lower rate of HIV infection, lower total virus exposure, and less severe negative symptoms.	More heroin use, with trends towards more females, more injection drug use, less alcohol use, and more severe negative symptoms.	Fewer years of education, less heroin use, lower rate of heroin dependence, greater total virus exposure, more severe negative symptoms, and greater total neurological soft signs.

leads to HIV infection in opiate users (Mitchell, Severtson, & Latimer, 2007).

In contrast, participants in Cluster 2 ($n = 103$) are best described as functioning intermediate to the other clusters in the sample, with a relative weakness in decision-making skills within the context of rewards and punishments. Compared to standard norms, persons in Cluster 2 are often functioning below normal limits, but nonetheless exhibit average-range premorbid IQ and neurocognitive inhibitory control. The variability in executive functions of this cluster is not surprising given that the measures used represent dissociable dimensions. Affective decision-making processes are generally considered to be mediated, at least in part, by the orbitofrontal region of the ventromedial prefrontal cortex (Bechara, 2003), and this can be dissociated from processes, such as inhibitory control, that are known to be governed by regions situated within the dorsolateral prefrontal cortex division of the brain (Stuss & Levine, 2002). Relatedly, Cluster 2, with its prominent decision-making deficit, was accompanied by elevated rates of heroin use and dependence, with a trend towards more injection drug use. These individuals may engage in immediately rewarding, riskier health behaviors without considering potential long-term adverse consequences (see Bechara, 2003, for review). Such a propensity may be indicative of dysregulated frontal brain circuitry (Ersche et al., 2005). Furthermore, when compared to the higher functioning Cluster 1, individuals in Cluster 2 demonstrated an elevated rate of HIV infection, a feature that has been previously linked to health risk behavior in the marginally housed (Aidala et al., 2005; Robertson et al., 2004). Addressing the decision-making impairments of these members of Cluster 2 may be crucial to

successful interventions that promote safer health behavior and infection prevention. Such targeted interventions have previously demonstrated success in reducing risk behavior in an HIV-positive, crack cocaine using sample (Ross, Timpson, Williams, & Bowen, 2007).

Finally, with the exception of reward-contingent decision-making skills, participants in Cluster 3 ($n = 87$) displayed poorer neurocognitive functioning than the other clusters. Normatively, this group is remarkably impaired in verbal memory, attention, and mental flexibility. Nonetheless, their decision making, inhibitory skills, and estimated premorbid IQ abilities fall within normal limits. This pattern of variability in executive functioning suggests that, despite poor mental flexibility, these individuals still demonstrate adequate decision-making capacity in the context of reward contingencies. Overall, the more pronounced impairment pattern of Cluster 3 is in keeping with reports from other literatures, whereby greater neurocognitive dysfunction is observed within the context of more negative symptoms (Dominguez et al., 2009; Lindsberg et al., 2009), greater incidences of comorbid viral infections (Cherner et al., 2005; Letendre et al., 2005; Martin-Thoymeyer & Paul, 2009; Richardson et al., 2005), and a greater number of NSS (Chan et al., 2009). The elevated number of NSS and neurocognitive impairment of this cluster likely reflects poorer brain integrity (Chan & Gottesman, 2008), and insults from multiple pathologies are likely contributory. For example, observations of middle to older aged HIV-positive adults reveal widespread premature age-related brain atrophy, including frontal and temporal regions (Holt, Kraft-Terry, & Chang, 2012). Furthermore, excessive cortical thinning has been reported in individuals with comorbid alcohol and drug use disorders (Momenan et al., 2012), and

cumulative white matter damage has been reported in persons with comorbid alcohol use disorder and HIV (Pfefferbaum, Rosenbloom, Adalsteinsson, & Sullivan, 2007). Individuals in Cluster 3 may suffer from a more pronounced loss of brain integrity associated with greater viral exposure (vs. Cluster 1) and alcohol use (vs. Cluster 2), although the normal range decision making and inhibitory control may suggest some selective sparing. Inevitably, a group of this nature, characterized by substantial multimorbidity and neurocognitive impairments, necessitates the need for greater outreach, given that mental health and addiction issues are one of the primary barriers to health care utilization in marginalized populations (Krausz et al., 2013). These individuals are apt to benefit from interventions that provide a high degree of structure and routine, given their profound memory and attentional deficits. Nonetheless, the group's relative strengths in inhibitory control and decision-making ability may facilitate treatment compliance, as executive functioning has been shown to play an important role in activities such as medication and financial management (see Gorman, Foley, Ettenhofer, Hinkin, & van Gorp, 2009). Moreover, individuals with better decision-making capacity may be more apt to appreciate the consequences of treatment noncompliance.

Contrary to our expectations, we did not find any meaningful differences in everyday functioning across the clusters even though neurocognition has been demonstrated to be a robust predictor of this dimension in a variety of populations (Fett et al., 2011; Gorman et al., 2009; Kalechstein, Newton, & van Gorp, 2003; Morgan & Heaton, 2009). However, this sample generally appears to be functioning at a very low level, leading to a restricted range of scores and reduced variability on everyday functioning measures (SOFAS and RFS; see Table 1). It is possible that more nuanced measures of everyday functioning that are sensitive to gradations in activities of daily living would better capture differences across the derived neurocognitive profiles. Indeed, complex everyday tasks, such as financial and medication management, might be better assessed with novel measures that demonstrate good ecological validity (Scott et al., 2011). Alternatively, it may be that individual neurocognitive domains (rather than a profile) more strongly predict everyday functioning³ (see Fett et al., 2011).

³Indeed, in the current sample, discrete neurocognitive domains were significantly correlated with scores on SOFAS (sustained attention: $r = .15$, $p = .022$; decision making: $r = .19$, $p = .002$) and RFS (decision making: $r = .17$, $p = .010$).

As with all studies, certain limitations should be considered. First, it is possible that some of the differences observed between clusters were spurious, despite rigorous control of error inflation. Thus, further validation of these profiles is warranted. For instance, linking the profiles to underlying brain pathology using neuroimaging techniques could provide more insight into the nature of the subgroups within this sample. Relatedly, it is also possible that the profiles themselves may not be replicable in other samples, despite demonstrated robustness within the current sample using complementary validation techniques. Cluster analysis is a data-driven technique, and where differences lie in the composition of a given sample (HIV rates, degree of multimorbidity), a different number of clusters and/or patterns of neurocognitive functioning may emerge. One critical barrier to cross-validation attempts may lie in the fact that previous studies have examined HIV and mental health issues using samples composed of both marginally housed and homeless individuals (Robertson et al., 2004; Weiser et al., 2009), whereas others have evaluated the same issues in samples composed of exclusively SRO residents (Shannon et al., 2006). In fact, change in housing status has been shown to be associated with changes in health risk behaviors (Aidala et al., 2005). Additionally, differences between the homeless and marginally housed on age, kind of substance use, income spent on substances, and amount of social support received have been previously reported (Eyrich-Garg et al., 2008). This suggests that these populations do not necessarily overlap in their characteristics, despite a seemingly fluid barrier between them. The generation of neurocognitive profiles in these respective samples is apt to reveal differences. Nonetheless, the profiles in this sample meaningfully differed on clinical characteristics and real-world behaviors, and this provides essential groundwork in understanding the inherent neurocognitive complexity in a marginalized population and could serve as a useful frame of reference for future studies that aim to build upon this nascent base of literature.

A second limitation to consider is that, although the test battery employed was composed of valid standardized measures that capture impairments expected in persons with psychosis and comorbid substance abuse, other neuropsychological measures might characterize groups differently. Moreover, within the battery selected, the IGT total net score entails dimensions of both risk taking and problem solving, and a low score does not discriminate between persons with poor cognition who fail to

learn from rewards and punishments, and individuals who are able to evaluate the reward contingencies yet still made risky decisions (Arentoft, Thames, Panos, Patel, & Hinkin, 2013). Application of theoretical decision-making models to decompose the IGT into its constituent parameters has been previously used to determine the relative contributions of neurocognitive, motivational, and response processes to overall decision-making performance (Busemeyer & Stout, 2002). At a broader level, however, the total net score can still be considered to represent a global index of decision-making ability that is sensitive to impairments commonly observed in various populations of persons with mental illness (substance use, mood disorders, schizophrenia), as compared to healthy controls (Mukherjee & Kable, 2014).

A final limitation is that we did not collect detailed clinical data on specific viruses at the time of neurocognitive testing. It is possible that unmeasured HIV-related factors known to influence neurocognitive functioning, such as viral load (Letendre et al., 2004), CD4 nadir (Ellis et al., 2011), and stage of HIV illness (Reger, Welsh, Razani, Martin, & Boone, 2002), contribute to observed group differences. We also did not examine specific combinations of viruses that may interact to impact functioning. Consequently, the reported effects may differ with more comprehensive clinical data.

In conclusion, this is the first study to identify and describe neurocognitive profiles in a socially marginalized sample. Three complementary clustering algorithms revealed consistent neurocognitive profiles that were reliably differentiated on several external factors, including real-world behaviors. Nonetheless, the ecological validity of these profiles is contingent upon the extent to which future findings demonstrate that the clusters replicate and generalize to other samples. Importantly, this study revealed that specific neurocognitive vulnerabilities and differential resource needs emerged from the cluster profiles. Individuals with the broadest neurocognitive impairments are apt to require additional resources and greater outreach to cope with the burden of multiple comorbidities that challenge their engagement in a complex healthcare system. Likewise, individuals with selective impairments may require more targeted interventions that address the specific consequences of their neurocognitive weaknesses and the putative risk factors that contribute to those impairments. As a better understanding of this population emerges through ongoing empirical investigations, use of theoretically driven models, such as structural equation modelling, will likely provide a fruitful approach to examine the complex

relationships between neurocognition and various clinical and functional outcomes.

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