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# Subclinical schizotypal vs. autistic traits show overlapping and diametrically opposed facets in a non-clinical population

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| **Abstract:** | Background: The overlap of autism spectrum disorder (ASD) and psychosis or schizophrenia spectrum disorders (SSD) has exposed problems central to conceptualising and understanding co-morbidity in psychiatric disorders. Methods: In the present study, we demonstrate that a deep phenotyping approach aids clarification of both overlapping and diametrically opposed features of ASD and SSD on the level of trait facets. Results: We first show overlap of negative and disorganised (but not positive) features of schizotypy with autistic traits in a sample of n=376 German non-clinical subjects using multiple psychometric measures of schizotypy (MSS multidimensional schizotypy scale, OLIFE Oxford-Liverpool Inventory of Feelings and Experiences, and SPQ-B schizotypal personality questionnaire - brief) and the AQ autism spectrum quotient, with control measures for affective spectrum pathology (BDI). Findings were then replicated in a French-Swiss sample (n=264) using MSS, OLIFE, AQ, and in addition the Community Assessment of Psychic Experiences (CAPE). Additional principal component analysis confirmed our finding of the co-existence of both overlapping (loss of function, social communication deficit, and negative schizotypy) as well as diametrically opposed features (AQ attention to detail, positive schizotypy) across the two spectra. Results were validated with Horn's parallel analyses, affirming two component solutions, and PCA using sample-specific, factor-analysis-derived schizotypy scores. Conclusions: Providing a framework for multi-dimensional transdiagnostic characterisation of ASD vs. SSD phenotypes we point out overlapping vs. discriminating facets. In addition to the use of novel multidimensional schizotypy scales, it also shows transcultural consistency of findings, and highlights a particular role for the attention to detail AQ subscale. |

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## Conflict of interest

The authors confirm that they do not have any conflicts of interest.

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**Author contribution statement**

SG and IN conceived of the study and obtained funding. TM, UE, SS, and JKP recruited subjects (German cohort) and AAA obtained data from the Swiss cohort. AAA and IN co-ordinated and supervised recruitment for the two study cohorts. TM and AAA analysed data. IN, TM, and AAA interpreted data analyses. IN wrote the first draft of the manuscript, revised by AAA, and all authors approved of the finalised version.

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# Subclinical schizotypal vs. autistic traits show overlapping and diametrically opposed facets in a non-clinical population

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**Abstract**

Background: The overlap of autism spectrum disorder (ASD) and psychosis or schizophrenia spectrum disorders (SSD) has exposed problems central to conceptualising and understanding co-morbidity in psychiatric disorders. Methods: In the present study, we demonstrate that a deep phenotyping approach aids clarification of both overlapping and diametrically opposed features of ASD and SSD on the level of trait facets. Results: We first show overlap of negative and disorganised (but not positive) features of schizotypy with autistic traits in a sample of n=376 German non-clinical subjects using multiple psychometric measures of schizotypy (MSS multidimensional schizotypy scale, OLIFE Oxford-Liverpool Inventory of Feelings and Experiences, and SPQ-B schizotypal personality questionnaire – brief) and the AQ autism spectrum quotient, with control measures for affective spectrum pathology (BDI). Findings were then replicated in a French-Swiss sample (n=264) using MSS, OLIFE, AQ, and in addition the Community Assessment of Psychic Experiences (CAPE). Additional principal component analysis confirmed our finding of the co-existence of both overlapping (loss of function, social communication deficit, and negative schizotypy) as well as diametrically opposed features (AQ attention to detail, positive schizotypy) across the two spectra. Results were validated with Horn's parallel analyses, affirming two component solutions, and PCA using sample-specific, factor-analysis-derived schizotypy scores. Conclusions: Providing a framework for multi-dimensional transdiagnostic characterisation of ASD vs. SSD phenotypes we point out overlapping vs. discriminating facets. In addition to the use of novel multidimensional schizotypy scales, it also shows transcultural consistency of findings, and highlights a particular role for the attention to detail AQ subscale.

**Key words:** autism quotient (AQ); autism spectrum disorder (ASD); interpersonal; schizotypy; subclinical

## Introduction

The overlap of autism spectrum disorders (ASD) and psychosis / schizophrenia spectrum disorders (SSD) has generated considerable attention in research over recent years (Chisholm et al., 2015). ASD and schizophrenia spectrum disorder appear to share common features both on the phenotype level (De Crescenzo et al., 2019) as well as social cognition (Fernandes et al., 2018) and neural networks (Lanillos et al., 2020). Within both disease groups, however, a continuum or spectrum has been hypothesised, which includes not only subclinical variants but also minor manifestations of disease as well as single traits that are associated with the disorder (or disease spectrum) without meeting clinical criteria for a disorder (Ford et al., 2018).

Subclinical traits can be conceptualised as phenotype markers commonly distributed across the general population without indicating presence of a psychiatric diagnosis and of adaptive significance (Del Giudice et al., 2014). Screening instruments such as the autism spectrum quotient (AQ) have not only been successfully used in identifying subjects with possible ASD (Woodbury-Smith et al., 2005) and differentiating between clinical vs. non-clinical states (Abu-Akel et al., 2019), but also to identify autistic traits within the general population (Ruzich et al., 2015b). The AQ measures multiple facets of this autism spectrum, grouped into subscales for *communication*, *social skills*, *imagination*, *attention to detail*, and *attention switching* (Baron-Cohen et al., 2001; Ruzich et al., 2015b). Twin studies have provided evidence that this AQ phenotype is indeed heritable (Hoekstra et al., 2007), which lends further support to a biological spectrum hypothesis within ASD,

including autistic traits and subclinical expressions in the absence of a clinical diagnosis (Bralten et al., 2018).

Similarly, schizotypy has been proposed as a phenotype marker of psychosis proneness, often conceptualised as a multi-dimensional personality trait including positive, negative, and disorganised dimensions or facets (Catts et al., 2000; Ettinger et al., 2015; Grant et al., 2018; Kwapil and Barrantes-Vidal, 2015; Lenzenweger, 2010). Schizotypy is prevalent in the general population and associated with biological functions that have been shown to be altered in schizophrenia (Ettinger et al., 2015; Nelson et al., 2013). It has also crucially influenced the definition of disorders in the schizophrenia spectrum like schizotypal personality disorder (Schultze-Lutter et al., 2019), and it might have utility in early detection and intervention for psychosis (Flückiger et al., 2019; Flückiger et al., 2016). In non-clinical cohorts, schizotypy has been associated with the occurrence of psychotic-like, paranoid, and negative symptoms (Barrantes-Vidal et al., 2013).

In contrast to clinical ASD and SSD, the relationship of their subclinical spectra is far less understood, and research in recent years is only starting to unravel their interactions (Del Giudice et al., 2014; Dinsdale et al., 2013; Ford et al., 2018). While many models can be proposed to explain this relationship (Chisholm et al., 2015), two have dominated the debate in recent years: The overlapping model, were both spectra share common phenotypic features and risk factors, and the diametric model (Abu-Akel and Bailey, 2000; Crespi and Badcock, 2008), where they occupy the extremes of a unidimensional continuum, deviating in opposite directions from normality. A recent study using the AQ and the schizotypal personality questionnaire

(SPQ), a self-report instrument for schizotypal features based on the DSM-IIIR criteria of schizotypal personality disorder (Raine, 1991), found rather broad overlaps between multiple subscores / facets of each phenotype (Gong et al., 2017). Subsequent network analyses suggested that autistic social and communication facets are related to negative schizotypy, while positive schizotypy was negatively correlated with subclinical autistic traits (Zhou et al., 2019).

In the present study, we test two competing hypotheses that are respectively predicated on the overlapping and diametric models of ASD and SSD. According to the overlapping model, where ASD and SSD are claimed to share common risk factors and aetiology (Craddock and Owen, 2010), autistic traits are expected to be associated with schizotypal traits. In contrast, according to the diametric model, where ASD and SSD are claimed to be associated with reciprocal biological causes (Crespi and Badcock, 2008), autistic and schizotypal traits are expected to be diametrically opposed. These hypotheses are tested using different measures of psychometric schizotypy in two cross-cultural cohorts. Phenotyping for schizotypy included different instruments, covering schizotypy measures based both on clinical and personality psychology conceptualisation. This included both established and novel schizotypy instruments, such as the multi-dimensional schizotypy scales (MSS). The MSS is a novel self-report instrument for assessing schizotypy (Kwapil et al., 2018b), and together with other scales we thus aim to provide a novel reassessment of this hypothesis using a refined phenotype extensively tested for its validity and relation to interview-based measures (Kemp et al., 2020; Kwapil et al., 2018a) .

## Methods

*Subject cohort 1: German cohort*

We included a cohort of n=376 psychiatrically healthy subjects (245 female / 131 male; mean age 24.04 years, SD 4.44) recruited through advertisement in and around Marburg. All subjects gave written informed consent to a protocol approved by the ethics committee of the Medical School of Philipps University Marburg. Subjects were carefully screened using the SCID-I screening tools (First and Gibbon, 2004; Wittchen et al., 1997) to exclude current or previous psychiatric disorders; further exclusion criteria were history of traumatic brain injury, CNS pathology, and uncontrolled general medical conditions (e.g. uncontrolled diabetes or hypertension), as well as any psychotropic medication or concurrent or previous alcohol or substance dependence.

*Subject cohort 2: French-Swiss cohort*

The cohort consisted of n=264 psychiatrically healthy subjects (207 female / 57 male; mean age 20.66 years, SD 2.79) recruited from a French speaking university population in Lausanne. All subjects gave written informed consent and the data collection was conducted in accordance with the ethics guidelines of the University of Lausanne. Subjects self reported that they have no psychiatric disorders or a history of traumatic brain injury.

*Deep phenotyping for autistic and schizotypal traits*

In the German cohort, study participants used the online platform SoSciSurvey (D.J.Leiner, software Version 3.1.06; www.socisurvey.de) to complete

questionnaires characterising their self-report subclinical autistic and schizotypal traits, respectively. We used the 50-item full version of the autism questionnaire AQ (Baron-Cohen et al., 2001) in its German version (Freitag et al., 2007), a widely used instrument measuring autistic traits in clinical and non-clinical populations (Ruzich et al., 2015b), which includes subscales for social skills, attention switch, attention to detail, communication, and imagination. In the current sample, the AQ showed a reliability of Cronbach's alpha = 0.72 (subscales: AQ Social Skills α = 0.463, Attention Switch α = 0.483, Attention to Detail α = 0.610, Communication α = 0.391, Imagination α = 0.505).

For assessment of schizotypal traits in the German sample, we used three instruments, the novel multidimensional schizotypy scale MSS (Kwapil et al., 2018b) and the established Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE) (Mason and Claridge, 2006) and Schizotypal Personality Questionnaire-Brief (SPQ-B).

The MSS, containing 77 items, was developed to assess a multidimensional model of schizotypy, including subscales positive, negative, and disorganised, and is well characterised for its relation to both psychosis spectrum and other dimensional markers, and has shown good to excellent reliability (Kemp et al., 2020; Kemp et al., 2018). In our sample, the MSS total score showed a reliability of Cronbach's α = 0.82, and subscales showed a Cronbach's α of 0.89 for Positive, 0.78 for Negative and 0.92 for Disorganised. The O-LIFE contains 104 items, and assesses schizotypy across the four dimensions Unusual Experiences (UnEx), Introvertive Anhedonia (IntAn), Cognitive Disorganisation (CogDis), Impulsive Nonconformity (ImpNon). All subscales have shown acceptable to good reliability (Grant et al.,

2013). In the current sample, the scales showed a reliability of Cronbach's α = 0.84 (OLIFE total), 0.86 (UnEx), 0.76 (IntAn), 0.87 (CogDis), and 0.61 (ImpNon).

The SPQ has been developed based on DSM-III-criteria for schizotypal personality disorder and provides subscores for the Cognitive-Perceptual, Interpersonal, and Disorganised dimensions. The short form contains 22 items and has recently been validated across multi-national studies (Fonseca-Pedrero et al., 2017), demonstrating adequate internal consistency and validity. In our sample, the SPQ-B scales showed a reliability of Cronbach's α = 0.74 for the SPQ-B total score, and subscale reliabilities of 0.622 (Cognitive-Perceptual), 0.720 (Interpersonal), and 0.715 (Disorganised).

For an assessment of subclinical affective symptoms, we used the German version of Beck's Depression Inventory (BDI) with a Cronbach's alpha of α = 0.80 in the current sample (Hautzinger, 1991).

In the Swiss cohort, study participants used LimeSurvey, an online platform, to complete questionnaires characterising their self-report subclinical autistic and schizotypal traits. Autistic traits were assessed with the French version (Sierro et al., 2016b) of the AQ-50 (Baron-Cohen et al., 2001) (Cronbach's alpha total score α = 0.74, Social Skills α = 0.54, Attention Switch α = 0.55, Attention to Detail α = 0.67, Communication α = 0.42, Imagination α = 0.44). Schizotypal traits were assessed using three different questionnaires: (1) the French version of the MSS (Kemp et al., 2020; Kemp et al., 2018) (Cronbach's α = 0.91). In our sample, the subscales showed a Cronbach's α of 0.84 for Positive, 0.85 for Negative and 0.91 for

Disorganised;, (2) the French version (Sierro et al., 2016a) of the 43-item, short Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; (Mason et al., 1995)) (Cronbach's α = 0.83). In our sample, the subscales showed a reliability of Cronbach's α = 0.76 (UnEx), 0.54 (IntAn), 0.75 (CogDis), and 0.57 (ImpNon); and (3) the French version (Brenner et al., 2007) of the Community Assessment of Psychic Experiences (CAPE-42; (Stefanis et al., 2002)) (Cronbach's α = 0.92). In our sample, the subscales showed a Cronbach's α of 0.84 for Positive and 0.85 for Negative).

For an assessment of subclinical affective symptoms, we used the depressive subscale of the CAPE-42 (Cronbach's alpha = 0.86).

*Statistics*

We used SPSS (IBM Statistical Package for Social Sciences, version 22, Armonk, NY) to calculate bivariate and partial correlations between AQ and schizotypy dimension scores. For sake of completeness, we also correlated total scores. Reliability measures were calculated as Cronbach's alpha coefficients.

To compare latent component loadings between instruments, we further conducted separate principal component analyses (PCA) in SPSS, including the five AQ subscales and the subscales of MSS, O-LIFE, SPQ-B, and CAPE. Extraction of components was based on the criterion eigenvalue > 1, without allowing rotation of components, and based on the correlation (rather than covariance) matrix, comparable to methods used by Dinsdale and colleagues (Dinsdale et al., 2013).

Correlation heatmaps were constructed using the R/RStudio (RStudio Team, 2015) version 3.5.0, RStudio Team, 2016, Boston, MA.) package *ggcorrplot* (https://cran.r-project.org/web/packages/ggcorrplot/). Visualisations of factor analysis results were constructed with the R package *factoextra* (https://cran.r-project.org/web/packages/factoextra/).

Where applicable, Bonferroni correction was applied to account for multiple testing.

## Results

*Association between autism spectrum and schizotypy dimensions*

Descriptive statistics and sex differences (including effects sizes) for the two samples are summarised in Table 1. After correcting for multiple testing, significant sex differences were only found in the German sample for MSS Negative, O-LIFE IntAn and ImpNon, SPQ-B Disorganised (all males > females), and BDI sum (females > males).

Insert Table 1 Here

AQ total score was positively correlated with sum scores of all schizotypy instruments in both the German (MSS total $r=0.497$, $p=7.85\times10^{-25}$, O-LIFE total $r=0.505$, $p= 1.04\times10^{-25}$, SPQ-B total $r=0.493$, $p=1.94\times10^{-24}$, see Table 2) and the French-Swiss (MSS total $r=0.511$, $p=5.95\times10^{-19}$, O-LIFE total $r=0.540$, $p=2.33\times10^{-21}$) sample.

Insert Table 2 Here

On subscale level, a positive correlation between AQ and schizotypy dimensions was also found for most subscales. Across instruments and samples, associations were most robust between the negative and disorganised schizotypy dimension scores and the AQ subscales Social Skills and Communication, and the positive

schizotypy dimension scores and the AQ Attention to Detail subscale. Using BDI/CAPE Depressive to remove variance related to concurrent affective symptoms did not substantially change this pattern. The results of correlation analyses, corrected for (1) depressive symptoms (BDI/CAPE) and (2) depressive symptoms and negative schizotypy are reported in the Supplementary Material ST2.

Correlation matrices between the two samples for questionnaires completed in both cohorts (AQ, MSS, O-LIFE) were compared using the *cor.test* function of the R *stats* package revealed a significant ($t(df=223)=31.86$, $p<2.2\times10^{-16}$) correlation of r=0.906 (95% confidence interval 0.879 - 0.927). Post hoc comparisons revealed that only the correlations of MSS Total and AQ Imagination differed significantly (Fisher's $z=3.36$, $p=7.8\times10^{-4}$) between the German (r=0.329) and the French-Swiss (r=0.069) cohort after correcting for multiple comparisons.

Insert Figure 1 Here

*Principal component analyses*

Across schizotypy instruments and samples, all PCA extracted two principal components (see Figure 2), together explaining between 48.71 and 56.20% of variance (mean = 51.21%, SD = 1.83), with the first component explaining 34.72% (SD = 2.10) of the variance, and the second component explaining 16.50% (SD = 1.39) of the variance, on average (see Table 3 for details). Additionally, Horn's parallel analyses, adjusting for sample error-induced inflation of eigenvalues (run with the R package *paran* (Dinno, 2018)) indicated the retention of two components for all analyses, except for CAPE in the French-Swiss sample (see Supplementary Material ST3 for details). Similarly to previous studies (Dinsdale et al., 2013;

Russell-Smith et al., 2013), all subscores loaded positively on the first component while the second component showed a more diametric structure, with opposite loadings from scales measuring positive schizotypy and autistic traits: Here, AQ subscales Social Skills, Communication, and Imagination, and partially negative schizotypy dimensions loaded negatively (in the German sample) or positively (in the French-Swiss sample), while the AQ Attention to Detail subscale as well as the positive and disorganised (except O-LIFE CogDis in the French-Swiss sample) schizotypy dimensions of the different instruments loaded inversely (positively in the German sample and negatively in the French-Swiss sample).

The inverse loadings across the two samples does not affect the fundamental finding of diametric dimensions of autistic and schizotypy traits.

Insert Figure 2 Here

To evaluate the effect of intercorrelation of factors, we computed additional PCA allowing oblique rotation, which largely replicated the non-rotated solution (see Supplementary Table ST4). To examine latent factors underlying the different schizotypy instruments, we conducted exploratory factor analyses across all schizotypy items within each sample, yielding very comparable factor structures. Entering the resulting factor scores into PCA together with the AQ scales resulted in, again, comparable loading patterns across two components in both samples, validating our previous results (see Supplementary Material ST5 and ST6). For the attention to detail subscale of the AQ, an additional correlation analysis on the single item level is given in Supplementary Table ST1.

## Discussion

Our study provides novel findings advancing and refining the understanding of the relationship between the autism and psychosis/schizophrenia spectra. Adding to previous studies of clinical cohorts, a first novel aspect of our study is the extension to focus on the non-clinical range of those two disease dimensions, providing a detailed analysis of both overlapping and diametrically opposed facets of the two spectra, and in addition extending these findings to show convergent and cross-cultural validity across the two studied cohorts. This provides an important ground for interpreting transdiagnostic cognitive and neuroimaging studies in the field, which might address the underlying functional or structural basis of these interrelations.

Specifically, we demonstrate that different facets of the phenotypes show diverging associations, i.e. overlaps (high positive correlations) for part of the autistic traits, but diametrically opposing relations for others. The latter facets are highly consistent with the notion of a diametrical model (Chisholm et al., 2015; Crespi and Go, 2015), which suggest that ASD and psychosis occupy opposite extremes of the same cognitive continuum (Abu-Akel and Bailey, 2000; Crespi and Badcock, 2008). Furthermore, the correlational patterns demonstrate that autistic traits are strongly related to negative and disorganised features, but not positive features of schizotypy. This is consistent with recent findings that aspects of the positive symptom show an inverted, i.e. negatively correlated and thus diametrically opposed relationship with autism (Crespi et al., 2019; Zhou et al., 2019).

Recent transdiagnostic approaches to ASD and SSD have tried to explain the association between the spectra using different models, in particular the diametrical

model, and the models of associated liabilities and multiple overlapping aetiologies (Chisholm et al., 2015; Crespi et al., 2010). The first component of our PCA analysis lends support to the notion that ASD and SSD feature overlapping phenotypes and thus exhibit shared areas of deficits. Indeed, many studies have demonstrated the ASD and SSD can result in similar impairments across several domains including social cognition and functioning (Harvey et al., 2019; Pinkham et al., 2019; Pinkham et al., 2008), as well as neurocognition and emotional processing (Eack et al., 2013). However, it has been contended that the commonalities between ASDs and SSDs are mostly superficial, and generally of opposite underlying causes (Crespi, 2020) (for an in-depth discussion of evolutionary and genetic aspects, see (Crespi and Go, 2015)).

Our findings of the diametric relationship between autistic vs. positive schizotypal trait dimensions converge on a number of lines of evidence from both clinical and non-clinical population. In non-clinical populations, studies have shown that both autistic and positive schizotypal trait dimensions are diametrically associated with self-reported social and executive functioning (Shi et al., 2017), suppression of non-target salient stimuli (Abu-Akel et al., 2018a), and the processing of global and local information (Russell-Smith et al., 2010). On a neural level, diametric effects were observed on activations within the socio-cognitive and attentional subdivisions of the temporoparietal junction (Abu-Akel et al., 2017), as well as the glutamate/GABA+ ratio within the superior temporal cortex (Ford et al., 2019). There is also robust evidence for diametric correlations of ASD and SSD genetic risk factors with self-reported empathy (Warrier et al., 2018).

In clinical populations, studies comparing ASD and SSD relative to healthy controls revealed diametric functional brain-related patterns within the social brain during mentalizing (Ciaramidaro et al., 2015), visual perspective-taking (Eack et al., 2017), and social judgment (Stanfield et al., 2017), structurally in gray and white matter volumes across the cortex (Mitelman et al., 2017), and metabolically in anterior cingulate, motor and somatosensory regions (Mitelman et al., 2018). However, it has also been pointed out that different or even opposing neural-level effects might result in shared alterations in ASD and schizophrenia (Crespi, 2020).

Collectively, current state of knowledge would suggest these results support the position that ASD and SSD are best characterized in terms of shared and divergent (and likely diametric) mechanisms (Pinkham and Sasson, 2020). However, since research to date continues to heavily rely on tasks that are limited in their ability to offer a mechanistic account of how ASD and SSD could be related, there is a need to develop paradigms that can distinguish disorder-specific behavior. Such methodological advances would be a critical next step to understanding how ASD and SSD, and their joint action affect behavior and function.

Understanding the autism – psychosis relationship is central to transdiagnostic conceptualisations of co-morbidity in psychiatric disorders. It is a paradigm for understanding the relation of different psychiatric phenotypes and resolving challenges in understanding abnormalities in perceptual, cognitive, and emotional dysfunction. While our data are obtained in non-clinical cohorts and thus do not allow direct inference on clinical samples, we still might consider some important implication such as the need for concurrent assessment of ASD and SSD symptoms

in order to pursue a better understanding of pathways associated with the two conditions, and to identify and evaluate treatments and interventions that may ameliorate associated symptoms in either condition. If so, the true state of affairs of individuals with ASD or SSD might be incomplete due to not assessing the effect the other disorder (SSD or ASD).

However, the question that is yet to be answered is whether these diametric effects reflect a trade-off relationship, or that these trait dimensions can simultaneously co-exist within the same individual. A trade-off point of view would necessarily rule out the possibility of an ASD-SSD co-morbidity (Crespi and Go, 2015). Unless we accept the argument that all ASD-SSD co-morbidities are false positives (Crespi and Crofts, 2012), the trade-off notion would have implications for current diagnostic categories of DSM-5 (APA, 2013), which, at least in principle, no longer considers ASD and SSD as mutually exclusive conditions. It also would stand in stark contrast to many reports of elevated rates of co-morbidity above prevalence of the disorders within the general population (Chisholm et al., 2015; Larson et al., 2017; Marín et al., 2018; Zheng et al., 2018), and with emerging evidence suggesting better functional outcomes in individuals with co-morbid ASD-SSD at both the diagnostic (Abu-Akel et al., 2018b; Stanfield et al., 2017; Sunwoo et al., 2019) and symptom levels (Vaskinn and Abu-Akel, 2019), which is consistent with the protective effect notion of ASD in SSD (Rees et al., 2014). Our correlation matrices show positive associations between autistic and schizotypal traits, which lend support to the notion that these traits can co-occur, which is consistent with findings from the general population (Sampson et al., 2020).

Some aspects of the psychometric overlap merit particular attention on the facet / single item level, as our findings illustrate the problem of transdiagnostic specificity in conceptualising psychopathological features. The association between autistic traits (as measured with the AQ) and schizotypy has been criticized for the non-specificity of certain items of the AQ scale (Kaufman, 2011), and in particular the attention to detail subscale. The loading of the attention to detail subscale with positive schizotypy (Figure 2) might thus be due to specific attention to detail items that tap into positive schizotypy (e.g., hearing small noises (item AQ5) and seeing patterns (item AQ23)). Indeed, our supplementary analysis (see Supplementary Table ST1) showed that these two items were most consistently positively associated with positive schizotypy, which seems to highlight the problematic nature of the attention to detail subscale as an 'indicator' of autism in the AQ overall (Hoekstra et al., 2008). However, it has been argued (Abu-Akel et al., 2020) that attention to detail should be considered a dimension that cuts both ways: a small sound may be interpreted in terms of its physical properties (i.e., in mechanistic, system-like terms – hence autistic) or that it conveys a hidden message (i.e., in mentalistic terms – hence psychotic) (see (Crespi and Badcock, 2008), also (Zhou et al., 2019) for an alternate explanation). Thus, rather than seeing the coupling of attention to detail with positive schizotypy as a psychometric artifact, it instead raises the intriguing possibility that both mentalistic and mechanistic interpretations of these details are equally available in some individuals. That said, future research is needed to formulate questions that better characterize attention to detail abilities, in order to more reliably gauge the association between autistic and schizotypal traits. Equally important, disentangling autistic traits from negative symptoms is paramount to understanding the degree to which ASD and SSD are related, which

currently is unfortunately complicated by lack of specificity in available instruments for the assessment of autism traits and negative symptoms, as well as the fact that many (if not most) psychiatric disorders (or disease spectra) will affect social functioning. This aspect is not merely a psychometric issue, but touches on the basic conceptualization of psychopathological phenomena, which has been discussed, for example, within the schizophrenia spectrum disorders (Schultze-Lutter et al., 2019), but not in a transdiagnostic framework.

Among the limitations of our approach is the use of only one autism trait measure, i.e. the AQ. Despite the use of AQ in numerous studies in the field (Ruzich et al., 2015a, b), other alternative measures might be tested, such as the Strengths and difficulties questionnaire (Goodman, 2001) and the Social responsiveness scale (Constantino and Gruber, 2005), or the recently proposed Adult Autism Subthreshold Spectrum (AdAS) scale (Dell'Osso et al., 2017; Donati et al., 2019). Samples sizes of one recent study in China were considerably higher than ours (Gong et al., 2017; Zhou et al., 2019), yet did not include multiple schizotypy measures or cross-cultural validation. While our samples did not include clinical cases, but rather trait expression in non-clinical subjects, there is robust recent evidence for the (epi)genetic overlap of autism and autistic traits (Massrali et al., 2019). Thus, individuals without a clinical disorder might constitute an appropriate model for pathologic functioning, especially since this approach also eliminates the confounding effects of medication, chronicity, or active symptomatology, and can inform hypotheses about the co-occurrence of ASD and SSD, and the nature of their relationship. We note, however, that, unlike the German cohort, we did not verify the absence of psychiatric disorders in the French-Swiss cohort. Finally, our data are

cross-sectional and cannot fully answer aspects of the temporal emergence of symptoms. Prospective and genetic evidence suggest that autistic and schizotypal traits are of neurodevelopmental origin, predating the onset of abnormal personality traits or aspects of other forms of psychopathology and which share common genetic influences (St Pourcain et al., 2018; Sullivan et al., 2013). It is therefore conceivable that adults' endorsement of these traits likely capture childhood-onset rather than later onset traits. Some caution is warranted in interpreting our results in view of the low reliability of AQ subscales. This may be due to the limited number of items in each of the subscales, which is known to lead to poor reliability compared to (sub)scales with more items. This is particularly the case when items do not correlate well with another (Ruzich et al., 2015b).

In conclusion, our study provides evidence from a transdiagnostic deep phenotyping approach in non-clinical individuals, whereby conflicting models of ASD-SSD relationships can be resolved on a trait facet level, considering refined phenotypes. Our main findings are thus the confirmation of a symptom-specific (rather than construct-specific) diametrical vs. overlapping model, which is stable across cultures and multiple schizotypy scales. Our study also points to unresolved aspects of ambiguous definitions of (sub)clinical phenotypes, as shown with the attention to detail aspect. From a general population perspective, the diametric dimensional account can enhance our understanding of inter-individual phenotypic variations within either condition. Future work extending this line of research can contribute to the building of informed multidimensional models of psychopathology, which can aid in revision of current definitions of clinical disorders.

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**Author contribution statement**

SG and IN conceived of the study and obtained funding. TM, UE, SS, and JKP recruited subjects (German cohort) and AAA obtained data from the Swiss cohort. AAA and IN co-ordinated and supervised recruitment for the two study cohorts. TM and AAA analysed data. IN, TM, and AAA interpreted data analyses. IN wrote the first draft of the manuscript, revised by AAA, and all authors approved of the finalised version.

**Table 1**
Mean values (total and separately for female/male participants) of AQ and schizotypy scores for the German (G) and French-Swiss (F-S) cohorts

| | German sample: mean (SD) | | | | French-Swiss sample: mean (SD) | | | |
|---|---|---|---|---|---|---|---|---|
| *AQ* | female | male | d | total | female | male | d | total |
| Social Skills | 2.26 (1.44) | 2.41 (1.56) | -0.16 | 2.31 (1.48) | 3.22 (1.88) | 2.98 (1.64) | 0.11 | 3.17 (1.83) |
| Attention Switch | 3.83 (1.90) | 3.87 (1.82) | -0.08 | 3.84 (1.87) | 4.24 (2.12) | 4.00 (2.13) | 0.09 | 4.19 (2.12) |
| Attention to Det. | 3.75 (2.05) | 3.76 (1.99) | -0.02 | 3.75 (2.03) | 4.74 (2.24) | 4.25 (2.56) | 0.18 | 4.64 (2.32) |
| Communication | 1.62 (1.43) | 1.88 (1.51) | -0.23 | 1.71 (1.46) | 2.16 (1.62) | 2.32 (1.61) | -0.08 | 2.20 (1.61) |
| Imagination | 1.84 (1.57) | 2.34 (1.71) | -0.31 | 2.01 (1.63) | 2.34 (1.68) | 2.79 (1.73) | -0.22 | 2.44 (1.70) |
| Total | 13.30 (5.10) | 14.25 (5.18) | -0.24 | 13.63 (5.14) | 16.71 (6.0) | 16.33 (5.60) | 0.05 | 16.63 (5.88) |
| *MSS* | | | | | | | | |
| Positive | 0.92 (2.45) | 0.92 (2.35) | -0.05 | 0.92 (2.42) | 4.84 (4.30) | 3.58 (4.19) | 0.24 | 4.57 (4.30) |
| Negative | 2.28 (2.52) | 3.33 (3.12) | **-0.52*** | 2.65 (2.78) | 4.33 (4.14) | 5.61 (5.00) | -0.24 | 4.61 (4.36) |
| Disorganised | 1.50 (3.73) | 1.28 (2.68) | -0.05 | 1.42 (3.40) | 4.96 (5.27) | 4.47 (5.99) | 0.07 | 4.86 (5.42) |
| Total | 4.70 (7.11) | 5.52 (6.14) | -0.30 | 4.99 (6.79) | 14.13 (9.89) | 13.67 (12.3) | 0.04 | 14.03 (10.4) |
| *O-LIFE* | | | | | | | | |
| UnEx | 2.36 (3.68) | 2.12 (3.14) | -0.05 | 2.28 (3.50) | 3.76 (2.78) | 2.96 (2.78) | 0.24 | 3.59 (2.79) |
| IntAn | 3.66 (3.24) | 4.88 (3.63) | **-0.39*** | 4.08 (3.42) | 2.29 (1.82) | 2.46 (1.79) | -0.07 | 2.33 (1.81) |
| CogDis | 6.08 (5.06) | 4.73 (4.18) | -0.25 | 5.61 (4.81) | 5.64 (2.83) | 4.75 (2.69) | 0.26 | 5.45 (2.82) |
| ImpNon | 5.56 (2.94) | 7.31 (2.80) | **-0.74*** | 6.17 (3.01) | 3.36 (2.06) | 3.02 (2.00) | 0.14 | 3.29 (2.05) |
| Total | 17.66 (11.1) | 19.04 (9.37) | -0.24 | 18.13 (10.5) | 15.06 (6.76) | 13.19 (6.83) | 0.23 | 14.66 (6.81) |
| *SPQ-B* | | | | | | | | |
| Cog.-Perceptual | 0.89 (1.36) | 0.86 (1.17) | -0.03 | 0.88 (1.30) | n/a | n/a | n/a | n/a |
| Interpersonal | 1.70 (1.93) | 1.68 (1.85) | -0.03 | 1.69 (1.90) | n/a | n/a | n/a | n/a |
| Disorganised | 0.51 (1.05) | 0.99 (1.44) | **-0.58*** | 0.68 (1.22) | n/a | n/a | n/a | n/a |
| Total | 2.71 (3.15) | 3.09 (3.24) | -0.19 | 2.84 (3.18) | n/a | n/a | n/a | n/a |
| *BDI* Sum | 4.58 (5.89) | 3.12 (3.48) | **-0.21*** | 4.07 (5.23) | n/a | n/a | n/a | n/a |
| *CAPE* Positive | n/a | n/a | n/a | n/a | 30.77 (6.44) | 29.02 (6.28) | 0.23 | 30.39 (6.43) |
| Negative | n/a | n/a | n/a | n/a | 28.03 (6.21) | 27.84 (6.46) | 0.03 | 27.99 (6.25) |
| Depressive | n/a | n/a | n/a | n/a | 18.79 (4.49) | 16.75 (4.43) | 0.38 | 18.35 (4.56) |

SD=standard deviation, d= Cohen's d effect size for the comparison of male/female scores, *significant sex difference with $p$ <0.0025 (threshold Bonferroni-corrected for 20 comparisons), n/a : not available.

**Table 2.** Correlation coefficients of AQ and schizotypy scores for the German (G) and French-Swiss (F-S) cohorts

| | | | *AQ* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Social Skills | | Att. Switch | | Att. to Detail | | Communication | | Imagination | | Total | |
| | | | G | F-S | G | F-S | G | F-S | G | F-S | G | F-S | G | F-S |
| *MSS* | Positive | f | 0.097 | 0.100 | 0.193 | 0.217 | 0.186 | **0.286*** | 0.203 | 0.227 | 0.000 | 0.042 | **0.237*** | **0.290*** |
| | | m | -0.011 | 0.300 | 0.119 | 0.398 | **0.326*** | 0.285 | 0.019 | **0.498*** | 0.139 | -0.128 | 0.215 | **0.472*** |
| | | all | 0.053 | 0.142 | 0.164 | **0.258*** | **0.239*** | **0.293*** | 0.129 | 0.276 | 0.061 | -0.008 | **0.229*** | **0.327*** |
| | Negative | f | **0.325*** | **0.465*** | **0.240*** | 0.087 | 0.099 | 0.172 | 0.140 | **0.428*** | **0.292*** | 0.146 | **0.357*** | **0.400*** |
| | | m | **0.573*** | **0.462*** | 0.211 | 0.273 | -0.074 | 0.141 | **0.338*** | **0.505*** | **0.383*** | 0.017 | **0.442*** | **0.454*** |
| | | all | **0.440*** | **0.450*** | **0.227*** | 0.126 | 0.028 | 0.151 | **0.244*** | **0.446*** | **0.351*** | 0.125 | **0.405*** | **0.404*** |
| | Disorganised | f | **0.271*** | **0.328*** | **0.340*** | 0.237 | 0.063 | 0.160 | **0.411*** | **0.448*** | 0.177 | 0.043 | **0.405*** | **0.381*** |
| | | m | 0.258 | 0.301 | 0.047 | **0.455*** | 0.154 | 0.101 | 0.184 | **0.495*** | 0.219 | 0.046 | 0.278 | **0.463*** |
| | | all | **0.267*** | **0.322*** | **0.235*** | **0.289*** | 0.095 | 0.147 | **0.324*** | **0.456*** | **0.194*** | 0.039 | **0.357*** | **0.399*** |
| | Total | f | **0.355*** | **0.413*** | **0.376*** | **0.257*** | 0.149 | **0.281*** | **0.359*** | **0.516*** | **0.256*** | 0.102 | **0.489*** | **0.496*** |
| | | m | **0.488*** | 0.437 | 0.199 | **0.468*** | 0.133 | 0.204 | **0.311*** | **0.616*** | **0.397*** | -0.014 | **0.488*** | **0.571*** |
| | | all | **0.416*** | **0.414*** | 0.308 | **0.309*** | 0.142 | **0.260*** | **0.350*** | **0.538*** | **0.329*** | 0.069 | **0.497*** | **0.511*** |
| *O-LIFE* | UnEx | f | 0.106 | 0.150 | 0.208 | 0.234 | **0.254*** | **0.300*** | 0.169 | **0.281*** | 0.024 | -0.064 | **0.272*** | **0.302*** |
| | | m | -0.082 | 0.226 | 0.085 | 0.262 | **0.472*** | 0.392 | 0.091 | **0.482*** | 0.167 | -0.202 | 0.267 | **0.421*** |
| | | all | 0.035 | 0.170 | 0.166 | **0.244*** | **0.326*** | **0.328*** | 0.137 | **0.317*** | 0.071 | -0.106 | **0.265*** | **0.326*** |
| | IntAn | f | **0.366*** | **0.462*** | **0.334*** | **0.265*** | 0.098 | 0.154 | **0.239*** | **0.505*** | **0.244*** | 0.158 | **0.417*** | **0.479*** |
| | | m | **0.637*** | **0.500*** | 0.288 | 0.318 | -0.016 | -0.017 | **0.490*** | **0.538*** | **0.466*** | 0.175 | **0.581*** | **0.468*** |
| | | all | **0.483*** | **0.465*** | **0.315*** | **0.274*** | 0.055 | 0.109 | **0.355*** | **0.513*** | **0.354*** | 0.165 | **0.493*** | **0.476*** |
| | CogDis | f | **0.255*** | **0.319*** | **0.498*** | **0.352*** | 0.104 | 0.180 | **0.390*** | **0.385*** | 0.150 | 0.080 | **0.463*** | **0.421*** |
| | | m | 0.288 | 0.439 | 0.257 | **0.588*** | 0.058 | 0.315 | 0.276 | **0.662*** | 0.292 | 0.016 | **0.374*** | **0.691*** |
| | | all | **0.253*** | **0.345*** | **0.413*** | **0.403*** | 0.088 | **0.219*** | **0.330*** | **0.432*** | 0.174 | 0.051 | **0.410*** | **0.473*** |
| | ImpNon | f | 0.026 | 0.203 | 0.082 | 0.201 | 0.020 | 0.169 | 0.137 | **0.339*** | -0.048 | 0.011 | 0.071 | 0.294 |
| | | m | -0.032 | 0.092 | -0.140 | 0.138 | 0.140 | 0.184 | 0.068 | 0.204 | 0.011 | -0.040 | 0.018 | 0.209 |
| | | all | 0.026 | 0.185 | 0.015 | 0.190 | 0.061 | 0.177 | 0.139 | **0.307*** | 0.021 | -0.008 | 0.084 | **0.278*** |
| | Total | f | **0.302*** | **0.381*** | **0.463*** | **0.376*** | 0.169 | **0.291*** | **0.379*** | **0.515*** | 0.157 | 0.052 | **0.490*** | **0.518*** |
| | | m | **0.382*** | 0.424 | 0.228 | **0.463*** | 0.204 | 0.334 | **0.395*** | **0.659*** | **0.396*** | -0.042 | **0.517*** | **0.629*** |
| | | all | **0.335*** | **0.392*** | **0.385*** | **0.397*** | **0.181*** | **0.308*** | **0.391*** | **0.538*** | **0.254*** | 0.019 | **0.505*** | **0.540*** |
| *SPQ-B* | Cognitive-Perceptual | f | 0.130 | n/a | **0.250*** | n/a | 0.147 | n/a | 0.159 | n/a | 0.064 | n/a | **0.259*** | n/a |
| | | m | 0.123 | n/a | 0.115 | n/a | 0.238 | n/a | 0.160 | n/a | 0.188 | n/a | 0.276 | n/a |
| | | all | 0.128 | n/a | **0.204*** | n/a | 0.177 | n/a | 0.160 | n/a | 0.110 | n/a | **0.265*** | n/a |
| | Interpersonal | f | **0.370*** | n/a | **0.353*** | n/a | 0.119 | n/a | **0.325*** | n/a | 0.176 | n/a | **0.437*** | n/a |
| | | m | **0.478*** | n/a | 0.299 | n/a | 0.083 | n/a | **0.370*** | n/a | 0.286 | n/a | **0.481*** | n/a |
| | | all | **0.411*** | n/a | **0.334*** | n/a | 0.107 | n/a | **0.341*** | n/a | **0.217*** | n/a | **0.452*** | n/a |
| | Disorganised | f | **0.299*** | n/a | 0.210 | n/a | 0.188 | n/a | **0.309*** | n/a | 0.185 | n/a | **0.390*** | n/a |
| | | m | 0.148 | n/a | 0.132 | n/a | **0.387*** | n/a | 0.176 | n/a | 0.161 | n/a | **0.343*** | n/a |
| | | all | **0.231*** | n/a | 0.172 | n/a | **0.265*** | n/a | **0.257*** | n/a | **0.199*** | n/a | **0.375*** | n/a |
| | Total | f | **0.388*** | n/a | **0.366*** | n/a | 0.199 | n/a | **0.364*** | n/a | 0.198 | n/a | **0.499*** | n/a |
| | | m | **0.345*** | n/a | 0.247 | n/a | 0.277 | n/a | **0.309*** | n/a | 0.262 | n/a | **0.472*** | n/a |
| | | all | **0.374*** | n/a | **0.321*** | n/a | **0.227*** | n/a | **0.348*** | n/a | **0.235*** | n/a | **0.493*** | n/a |
| *CAPE* | Positive | f | n/a | 0.192 | n/a | **0.308*** | n/a | **0.338*** | n/a | **0.363*** | n/a | 0.021 | n/a | **0.401*** |
| | | m | n/a | 0.087 | n/a | 0.335 | n/a | 0.174 | n/a | 0.384 | n/a | -0.090 | n/a | 0.315 |
| | | all | n/a | 0.177 | n/a | **0.316*** | n/a | **0.306*** | n/a | **0.360*** | n/a | -0.015 | n/a | **0.384*** |
| | Negative | f | n/a | 0.445* | n/a | **0.335*** | n/a | 0.172 | n/a | **0.530*** | n/a | 0.123 | n/a | **0.503*** |
| | | m | n/a | 0.409 | n/a | 0.322 | n/a | 0.395 | n/a | **0.518*** | n/a | -0.013 | n/a | **0.567*** |
| | | all | n/a | **0.437*** | n/a | **0.333*** | n/a | **0.226*** | n/a | **0.526*** | n/a | 0.091 | n/a | **0.516*** |

*significant sex difference with $p < 5.95 \times 10^{-4}$ (threshold Bonferroni-corrected for 84 comparisons), n/a : not available.

**Table 3.**
Results of principal component analysis (PCA) in the German (G) and French-Swiss (F-S) cohorts showing component loadings

| | | Component 1 | | Component 2 | |
|---|---|---|---|---|---|
| | | G | FS | G | FS |
| | explained variance | (33.07%) | (35.49%) | (16.55%) | (14.99%) |
| *AQ* | Social Skills | 0.740 | 0.721 | -0.307 | 0.352 |
| | Att. Switch | 0.572 | 0.555 | 0.010 | -0.188 |
| | Att. to Detail | 0.121 | 0.427 | 0.634 | -0.422 |
| | Communication | 0.729 | 0.794 | -0.156 | 0.128 |
| | Imagination | 0.624 | 0.204 | -0.182 | 0.594 |
| *MSS* | Positive | 0.345 | 0.521 | 0.748 | -0.584 |
| | Negative | 0.613 | 0.633 | -0.204 | 0.355 |
| | Disorganised | 0.583 | 0.697 | 0.411 | -0.162 |

| | | Component 1 | | Component 2 | |
|---|---|---|---|---|---|
| | | G | FS | G | FS |
| | explained variance | (31.56%) | (35.56%) | (17.15%) | (14.98%) |
| *AQ* | Social Skills | 0.695 | 0.674 | -0.371 | 0.410 |
| | Att. Switch | 0.618 | 0.589 | -0.034 | 0.037 |
| | Att. to Detail | 0.152 | 0.431 | 0.524 | -0.324 |
| | Communication | 0.724 | 0.772 | -0.183 | 0.204 |
| | Imagination | 0.575 | 0.154 | -0.240 | 0.649 |
| *O-LIFE* | UnEx | 0.392 | 0.593 | 0.760 | -0.551 |
| | IntAn | 0.662 | 0.644 | 0.344 | 0.374 |
| | CogDis | 0.676 | 0.721 | -0.256 | -0.170 |
| | ImpNon | 0.223 | 0.555 | 0.526 | -0.373 |

| | | Component 1 | | Component 2 | |
|---|---|---|---|---|---|
| | | G | FS | G | FS |
| | explained variance | (35.09%) | n/a | (16.64%) | n/a |
| *AQ* | Social Skills | 0.683 | n/a | -0.407 | n/a |
| | Att. Switch | 0.567 | n/a | -0.182 | n/a |
| | Att. to Detail | 0.207 | n/a | 0.634 | n/a |
| | Communication | 0.691 | n/a | -0.391 | n/a |
| | Imagination | 0.546 | n/a | -0.290 | n/a |
| *SPQ-B* | Cog.-Perceptual | 0.538 | n/a | 0.519 | n/a |
| | Interpersonal | 0.741 | n/a | 0.185 | n/a |
| | Disorganised | 0.601 | n/a | 0.436 | n/a |

| | | Component 1 | | Component 2 | |
|---|---|---|---|---|---|
| | | G | FS | G | FS |
| | explained variance | n/a | (37.54%) | n/a | (18.66%) |
| *AQ* | Social Skills | n/a | 0.691 | n/a | 0.387 |
| | Att. Switch | n/a | 0.606 | n/a | -0.025 |
| | Att. to Detail | n/a | 0.463 | n/a | -0.384 |
| | Communication | n/a | 0.781 | n/a | 0.148 |
| | Imagination | n/a | 0.188 | n/a | 0.784 |
| *CAPE* | Positive | n/a | 0.659 | n/a | -0.429 |
| | Negative | n/a | 0.790 | n/a | -0.070 |

**Figure 1.**

Correlation matrix ("heat map") showing the correlation of Autism Questionnaire (AQ) and schizotypal trait questionnaires (SPQ-B, Schizotypal Personality Questionnaire-Brief; MSS, Multidimensional Schizotypy Scales; OLIFE, Oxford-Liverpool Inventory of Feelings and Experiences) in the German (left) and French-Swiss (right) cohort. Square colour and size indicates size of correlation coefficients. Asterisks indicate significant correlation coefficients after correction for multiple comparisons. Figures constructed with the R package *ggcorrplot*.

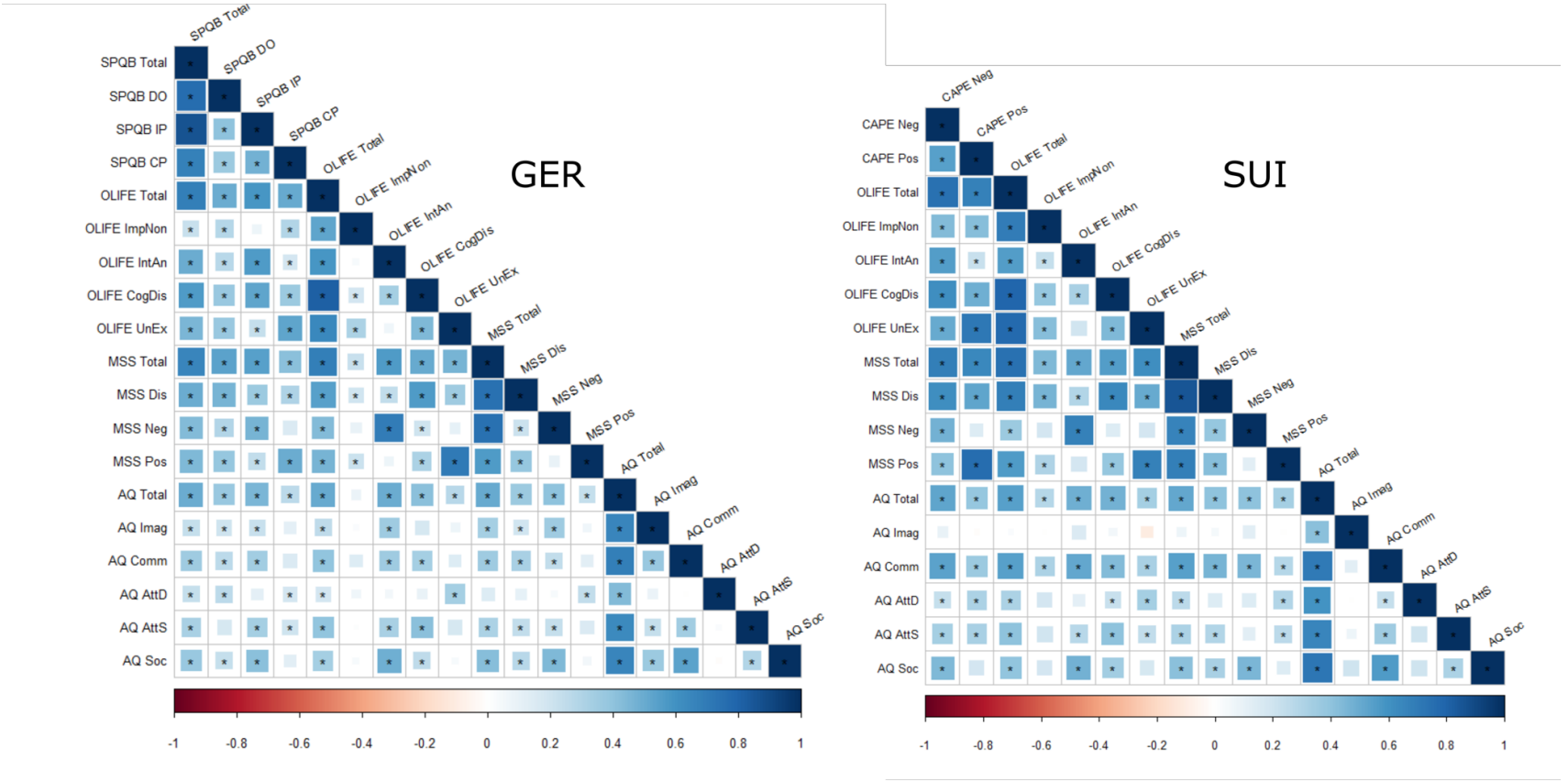
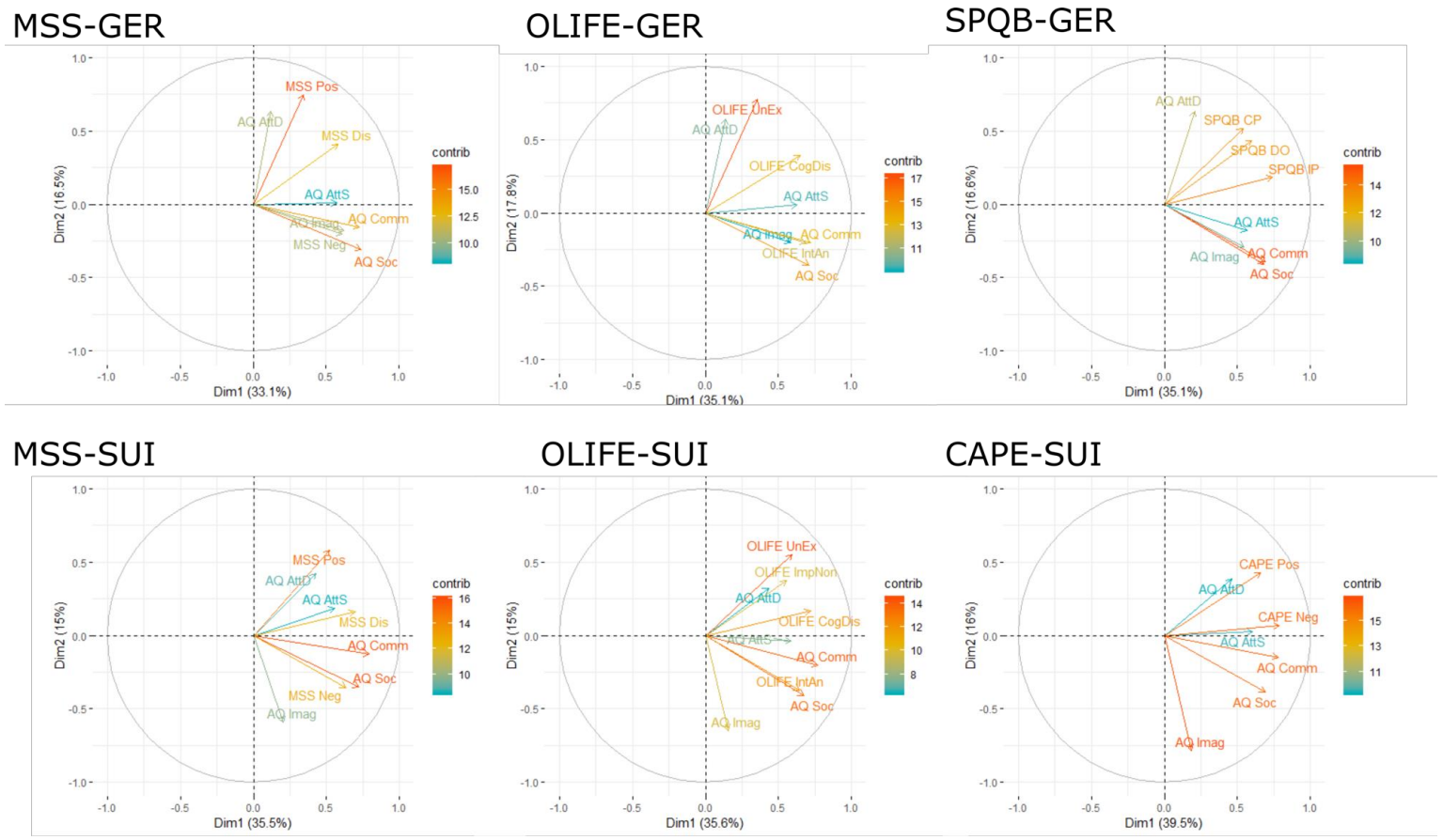


**Figure 2.** Visualisations of PCA results in the German (GER) and French-Swiss (SUI) cohorts. Figures constructed using the R package *factoextra*. For better visual comparability, loading matrices for the German cohort have been multiplied by -1. Note that scales measuring positive schizotypy and autistic traits have opposite (diametric) loadings. Generally, AQ subscales Social Skills, Communication, and Imagination, and partially negative schizotypy loaded orthogonally to the AQ Attention to Detail subscale, positive and disorganised schizotypy.



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