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Brief report

Oxytocin plasma levels in psychiatric patients with and without recent suicide attempt

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ABSTRACT

Easily available biomarkers for suicidality would be valuable for the identification of individuals at risk. Oxytocin has been shown to be associated with mental illness. We assessed basal oxytocin plasma levels of patients with (SA, $n=41$) and without (NSA, $n=40$) a 1-year history of attempted suicide. SA and NSA groups did not differ with respect to oxytocin levels. Plasma oxytocin may not be a biological suicide marker candidate.

1. Introduction

A history of attempted suicide is a major risk factor for completed suicide. Therefore, patients with a history of suicide attempts are an important target population for suicide prevention measures. Thus, the identification of individuals specifically at risk for suicidal acts remains a crucial task which is, however, so far met unsatisfactorily.

Biological markers may contribute to the capability to identify individuals with an increased risk for future suicidal acts. The most robust association of a biological alteration with suicidal behavior has been found for decreased cerebrospinal fluid (CSF) 5-hydroxyindoleacetic acid levels. With regard to markers assessed in blood, basal cortisol levels, a pathological dexamethasone suppression test and cholesterol levels have been investigated most intensively (Träskman-Bendz and Mann, 2000; Hawton and van Heeringen, 2009). However, the results of these studies remain controversial.

Oxytocin is a nine amino acid peptide hormone which has major effects on a variety of somatic functions including milk ejection, uterine muscle contraction at birth and orgasm. Its association with psychological features has been increasingly investigated in recent years. It has been related to mother–infant and pair bonding, trust, fear reduction and generally a sense of well-being (IsHak et al., 2011). The application of intranasal or intravenous oxytocin has been found to have an impact on a variety of psychological functions including trust (Kosfeld et al., 2005), generosity (Zak et al., 2007), encoding of positive social memories (Guastella et al., 2008), communication skills during a couple conflict (Ditzen et al., 2009) and emotion recognition (Guastella et al., 2010), but also envy and *schadenfreude* (Shamay-Tsoory et al., 2009).

Oxytocin has also, although inconsistently, been reported to be associated with psychiatric disorders bearing a high risk for suicidal behavior including depression (Ozsoy et al., 2009; Parker et al., 2010) and schizophrenia (Goldman et al., 2008). Moreover, the oxytocinergic system may be involved in the mechanisms which underlie adult attachment styles (Costa et al., 2009), some of which in turn have been found to be associated with suicidal behavior (Grunebaum et al., 2010; Lizardi et al., 2011). However, research on the role of oxytocin in suicidality is scarce and has so far been conducted mostly in CSF.

In this study, the potential association of plasma oxytocin levels with a recent history of attempted suicide in psychiatric inpatients was investigated.

2. Methods

2.1. Patients and clinical assessments

Consecutive male and female patients with the diagnosis of an affective disorder or a depressive adjustment disorder who were currently treated as psychiatric inpatients were screened. Those who fulfilled the inclusion criteria were, after giving written informed consent, grouped according to whether they had attempted suicide within the last year or never had attempted suicide in their

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life. Patients who had attempted suicide longer than 1 year ago were excluded from participation. Further exclusion criteria were pregnancy, lactation and severe somatic illness.

Blood was drawn for oxytocin assessment, and a clinical interview was conducted including demographic and clinical variables, data on involvement into social interactions (with partner, family, friends, physicians) and several questionnaires. These were the Adult Attachment Scale (AAS), a scale measuring adult attachment style dimensions including comfort with closeness and intimacy (Close subscale), comfort with depending on others (Depend subscale), and worry about being rejected or unloved (Anxiety subscale) (Collins and Read, 1990), the *Fragebogen zur sozialen Unterstützung* (F-SozU), a widely used self-report questionnaire for the assessment of social support in German (Sommer and Fydrich, 1991) and the Beck Depression Inventory (BDI) (Beck et al., 1961).

The study procedure was approved by the Ethics Committee of the Innsbruck Medical University.

2.2. Oxytocin measurement

Blood samples were drawn in the morning into chilled EDTA tubes and centrifuged at 1600*g* for 15 min at 4 °C. After storage at −70 °C oxytocin concentrations were determined with an enzyme immunoassay kit (Correlate ™ EIA, Oxytocin, assay designs, D), according to the manufacturer's protocol. Briefly, sample extraction was performed with 0.1% trifluoroacetic acid followed by purification with a C18 Sep-Pak column. Samples were run in duplicates and groups were measured simultaneously on a microplate.

2.3. Statistical analysis

For comparison of the two groups (suicide attempt in the last year, no suicide attempt ever) with regard to socio-demographic, clinical and questionnaire data, *t*-test, Mann-Whitney *U*-test, χ^2 test and Fisher's exact test were used, depending on the variable type (normally distributed, non-normally distributed, categorical, binary). Spearman rank-correlation coefficients were employed to evaluate associations between oxytocin levels and both sociodemographic variables and questionnaire data.

In addition, the joint effect of oxytocin levels, socio-demographic variables, clinical variables and questionnaires on attempted suicides was tested by means of multiple logistic regression. Both the forward stepwise selection and the backward stepwise elimination method were used to determine statistically significant predictors. As we were primarily interested in a potential effect of the oxytocin level on attempted suicide probability, we compared the final regression model without oxytocin level as a predictor with the same model plus oxytocin as an additional predictor by means of the likelihood ratio test (within the logistic regression framework).

All statistical tests were performed at a 5% level of significance.

3. Results

Of 125 patients screened for participation, complete data were available for 81 individuals fulfilling inclusion/exclusion criteria. Forty-one patients had made a suicide attempt within the last year (SA group) and 40 had no lifetime history of attempted suicide (NSA group). Table 1 shows demographic and clinical data of patients included and the results of oxytocin and psychological scale assessments. Patients with a recent history of attempted suicide were significantly younger, had higher current depression rating scores and were more likely to have a family history of both mental disorders and suicide (Table 2).

SA and NSA groups did not differ significantly with respect to oxytocin levels. Further, there were no significant associations between oxytocin levels and age, gender, AAS, F-SozU or BDI scores. Separate analyses for male and female patients revealed that in men oxytocin levels in the SA group (2.3 ± 0.9 pg/ml, mean ± S.D.) were lower than those in the NSA group (3.6 ± 2.0 pg/ml) attaining trend-level significance ($Z=1.71$, $p=0.095$). No such differences were seen in women.

Multiple logistic regression analysis showed a significant effect on attempted suicide only for age, family history of suicide and BDI. Oxytocin level did not show a significant effect on suicide attempts. The latter finding remained unchanged when removing BDI from the list of predictors.

With regard to social interaction issues the two groups differed significantly in several items including "being able to talk about all problems with my general practitioner", "feeling understood by my psychiatrist", "good cohesion between my parents/siblings and me", "frequency of contacts with my general practitioner", "being a member in a club", "could contact my neighbor any time when I'm not fine" and "feeling understood and accepted by my friends" with suicide attempters scoring lower in each of these items.

4. Discussion

In this study in 81 patients with an affective spectrum disorder, we found no significant differences between those with a suicide attempt within the last year and those without a lifetime history of attempted suicide with regard to oxytocin plasma levels. Further, there was no significant correlation of oxytocin levels with measures of social attachment, social support or depression.

Although oxytocin has been related to mental illness, the potential role of oxytocin in suicidal behavior has rarely been investigated so far. In a study measuring CSF oxytocin levels, although with the primary focus on aggression and personality disorders, a possible inverse relationship between CSF oxytocin and history of suicidal behavior was suggested (Lee et al., 2009). Recently, a longitudinal study found a trend towards lower CSF oxytocin levels in suicide attempters versus healthy volunteers with no predictive potential for subsequent completed suicide. In accordance with our results, plasma oxytocin levels did not differ between patients and controls. However, oxytocin correlated significantly with the planning subscale of the Suicide Intent Scale (Jokinen et al., 2012).

Plasma levels of arginine vasopressin (AVP), a biochemically closely related neuropeptide which, however, has been suggested to be in some way a counterpart of oxytocin in effect, were found to be significantly higher in patients who had recently attempted suicide (Inder et al., 1997). However, these findings have, with regard to AVP neurophysin (its carrier protein), been challenged later (Pitchot et al., 2008). And a study measuring AVP concentrations in both plasma and CSF also did not find differences between suicide attempters and non-attempters (Brunner et al., 2002). In contrast, AVP immunoreactivity levels were elevated in several regions of post-mortem brains in suicide victims (Merali et al., 2006).

The results of our study do not suggest that basal plasma oxytocin concentrations have a role as a biological marker for suicidal behavior. However, most of the intriguing recent findings concerning oxytocin and psychological functioning have been reported in interventional studies in which a high but short peak of oxytocin was produced. Oxytocin has an ultra-short half-life and changes in behavior may be dependent on a rapid alteration with peaks much higher than the basal values we assessed in this study. Moreover, CSF oxytocin levels may generally be of higher validity for studying behavioral features since they reflect brain processes more appropriately than peripheral parameters. However, the collection procedure clearly is not applicable for routine assessment. As a further limitation, it should be noted that our study group consisted of suicide attempters and, thus, the results may not be generalizable for those actually completing suicide.

Thus, although plasma oxytocin may not be a promising candidate as a peripheral biological marker for suicide attempts, its definite role in the context of suicidality remains to be evaluated.